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ABSTRACT

ASSESSING THE VIABILITY OF THE SHIFTING BALANCE PROCESS

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For over sixty-five years evolutionary biologists have debated the relative importance of drift, selection and genetic constraints. One view contends that with population sub-structure drift and selection interact such that genetic constraints are more easily overcome than in panmictic populations. In that view the shifting balance of selective and genetic factors within a subdivided population can overcome many genetic constraints. An alternate view holds that drift is an unimportant factor in evolution. The two views continue to fuel major debates within evolutionary biology. This dissertation attempts to assess the relevance of the shifting balance view.

Progress in shifting balance theory is reviewed in chapter one. That review concludes that the shifting balance process is viable under many scenarios, but that the efficacy of the process is highly model dependent. Especially important are the types of gene interaction that produce genetic constraints. Chapter two reviews evidence for epistatic effects on fitness. It concludes that there is overwhelming evidence that gene interactions between loci create genetic constraints, but that few specific examples are thoroughly understood.

Chapters three through five use spatially, genetically and individually specific Monte Carlo simulations to assess the shifting balance process. The shifting balance process requires small effective deme size in order for drift to occur and new gene

combinations to be found. Migration between demes increases effective population size and allows export of new gene combinations. Migration's influences on these two aspects of the shifting balance process are therefore in conflict. Chapter 3 investigates the effect of migration rate on the shifting balance process. It concludes that there is a small window of migration rates over which the process can operate effectively. Chapter four analyzes several alternate gene interaction models and concludes that the efficacy of the shifting balance process is highly dependent on specifics of gene interaction. Chapter five investigates the efficacy of the shifting balance process under variable migration rates. It concludes that alternating periods of high and low migration can radically increase the efficacy of the shifting balance process.

To the Winnebago Trickster and the Crooked Life Road.

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INTRODUCTION

Sixty five years after its introduction, Sewall Wright's shifting balance process (Wright 1931) remains a controversial centerpiece of evolutionary theory. The theory predicts that drift and selection may interact in a structured population so that adaptation can proceed in ways not available to populations in panmixia. This dissertation reviews the literature on the shifting balance process as well as evidence for multiple peak epistasis. It also presents several novel theoretical results based on Monte Carlo simulations which test the viability of the shifting balance theory under a variety of scenarios.

The purpose of the simulation tests of the shifting balance process is first to determine whether there are any circumstances under which the shifting balance process might work. Secondly, a diversity of models are compared to see if the process is equally viable under all models. Finally, a model which relaxes one of the ecological simplifications in previous models is used to determine if increased complexity in the shifting balance process is likely to increase or decrease the efficacy of the process.

Chapter 1

THE SHIFTING BALANCE PROCESS: A REVIEW OF THE THEORY

Introduction

Sewall Wright's Shifting Balance Process (SBP) (Wright 1932; Wright 1982b) incorporates the major microevolutionary forces of drift, mass selection, and group selection. For this reason it is a central paradigm of evolutionary biology (Wade and Goodnight 1991). In the SBP drift, mass selection and group selection are tied together in the context of genetic and developmental constraints. Such constraints are increasingly viewed as major evolutionary factors (Gould and Lewontin 1979; Stearns 1980; Vrba and Eldredge 1984). SBP is the most synthetic theory of microevolutionary dynamics. The result of this synthesis is a combined body of theory which implies that historical contingency is an important factor in the adaptation and diversification of organisms. This microevolutionary view, in which constraints and historical contingency are integral, anticipates recent trends in the interpretation of macroevolutionary data (Eldredge and Gould 1972; Gould and Eldredge 1977; Derrickson and Ricklefs 1988; McLennan *et al.* 1988). Despite these implications of the SBP the complexity of interacting genetic, selective and population dynamic factors involved has prevented rigorous investigation or universal acceptance of the shifting balance view. Assessment of the roles of the SBP and its components are still in their infancy. This chapter reviews the current state of

knowledge about shifting balance theory.

Adaptive Peaks- What They Are

The concept of the adaptive peak was first used by Wright (1932) as an area of higher fitness on an adaptive landscape. There are, however, three fundamentally different types of adaptive landscapes. Provine (1986) has pointed out that some confusion has arisen from Wright's original ambiguity between two of these fundamental types. Wright's (1932) original diagrams (figure 1.1a) represented individual fitness surfaces in a nonquantitative way (Provine 1986; Wright 1988). These diagrams represent the possible genotypes plotted against the fitness of an individual of that genotype. The actual diagrams that Wright used to discuss adaptive landscapes in 1932 and in many subsequent papers, are not fully interpretable because multiple genetic dimensions are compressed into two graphical dimensions (Provine 1986; Wright 1988).

It is possible to accurately describe an adaptive surface for a two locus, two allele system (figure 1.1b). If multiple peaks are present on such a surface, offspring of crosses between those two optimal genotypes will be of lower fitness than either parent. This type of adaptive surface can be called a genotypic fitness surface because the expected fitness of an individual with a given genotype is what is plotted.

A second type of adaptive landscape is produced by plotting allele frequencies of a population at multiple loci against the mean fitness of a population of individuals. Figure 1.1c is this type of surface. This surface can be called an allele frequency surface because the allele frequency is being used to predict the expected mean fitness with in a population. The population mean fitness surface is the surface of mean fitnesses associated with a

Figure 1.1 - Fitness surfaces of four different types.

Figure 1.1a is the type of fitness surface originally used by Wright (1932). The axes are unmarked and represent some undefined scaling of genotype so that each point on the surface represents one genotype. Contour lines represent changes in fitness. Fitness peaks and pits are marked by + and - respectively. 1.1b is a genotypic fitness surface with the expected fitness of an individual (W) plotted against the number of doses of a mutant allele at two loci. 1.1c is a population fitness surface. The surface is created by plotting the expected mean fitness of a population against the frequency of mutant alleles at two loci. 1.1d is a phenotypic fitness surface which plots the expected fitness of an individual (W) against the phenotype of that individual.

Figure 1.1

a)
b)
W
1.000
0.989
0.977
0.966
0.955
0.943
0.932
0.920
0.909
0.898
0.886
Copies of A
Copies of B
c)
FREQUENCY OF B
FREQUENCY OF A
d)
W
Z

multi-peaked genotypic fitness surface. This type of graph has several advantages over Wright's original drawings. The SBP requires consideration of selective effects within a subpopulation as well as metapopulation dynamics. The integrated fitness across a population with the allele frequency fitness surface gives a comparison of the expectedfitness of populations at different frequencies. The shape of this allele frequency by mean fitness graph gives not only the expected fitness of a sub-population with a given set of allele frequencies, but also gives the direction in which selection is expected to push the population at any set of allele frequencies. In this type of diagram the slope of the fitness surface indicates the strength of selection on a population at those frequencies. Genotypic fitness diagrams do not provide this insight. Population fitness surfaces give expected mean fitnesses (actual values for a population's mean fitness will often deviate from expectations when population size is small).

The third type of adaptive landscape is a phenotypic fitness surface (figure 1.1d). In this surface, fitness is plotted against the phenotypic value of some trait (Simpson 1953). As long as variance around the mean is small this could represent either the mean phenotype in a population or an individual's fitness. Unlike the previous types of adaptive surfaces, the existence of gene interactions (epistasis) is not explicit. However this type of surface does imply epistasis for fitness (Lande 1976). The phenotypic surface has the advantage of dealing with phenotype rather than genotype, and it is the phenotype not the genotype on which selection acts.

The problem of graphically representing more than two genetic dimensions is inherent with the allele frequency and genotypic fitness surfaces. The phenotypic fitness surface avoids some of the problems of graphing more than two loci at a time. The

phenotypic fitness surface has the disadvantage of not allowing a direct examination of the gene interactions involved in fitness. This is problematic since a phenotype may have more than one possible genetic architecture, each architecture associated with a different point on an allele frequency surface (see figure 1.1a). In the phenotypic fitness surface, multiple population fitness peaks may be indistinguishable by phenotype. All three types of adaptive landscapes described here can represent the existence of multiple stable genetic states. Each is useful and necessary for understanding different facets of the SBP.

Adaptive landscapes - Why they matter

Adaptive peaks are evolutionary constraints. Despite the common genetic machinery of all organisms, constraints on evolution vary between lineages. The reason that constraints vary between lineages is that lineages can exist on different adaptive peaks due to historic differences. If constraints were genetic alone then any two populations exposed to the same selective environment would converge on the same result. The interaction between genetics and selection is what varies between lineages. Selection optimizes within a peak's domain, but prevents movements between peaks. This is because selection limits the variation within a population and creates local constraints to adaptation within a lineage that are contingent on history.

This emphasis on genetic constraints and their interaction with the natural selective environment also implies that historical contingencies are important. Natural selection acts on populations whose genetic architecture is contingent on past environmental selection and past introductions of genetic variation through migration and mutation. This means that while adaptation towards a local adaptive peak (e.g. suboptimum) may occur it will rarely optimize the population fitness in a more global sense. Instead, one of many

stable genetic sub-optima that allows the population to persist in an environment may be reached. The SBP is therefore a process by which populations can occasionally move to a higher stable point. This process is contingent on variation in allele frequencies which is stochastic in origin. The adaptive peak concept and the SBP are important because they define the mechanisms whereby contingencies become an important factor in adaptation.

If adaptive peaks exist, their presence will affect the tempo and mode of evolution (Wright 1982a, 1982b). At the microevolutionary scale population structure and drift are more important when adaptive peaks exist (Wright 1982b). At the macroevolutionary scale allopatric speciation might not be just the gradual accumulation of differences through drift and selection. Instead allopatric speciation within the context of movement between adaptive peaks will usually be a threshold event. On occasion sufficient variation will exist so that a population will enter the domain of a new optimum. Once this happens selection can quickly re-optimize that population. This re-optimization results in post mating barriers to migration between populations which are at different optima. The predicted pattern of change in the SBP is one of periods of relative stasis, punctuated with periods of rapid divergence (Wright 1982b).

The ability of lineages to move between the peaks is the most important aspect of the existence of multiple peaks. Peak shifts can create phenotypic differences and breeding barriers between populations, species and higher taxonomic groups. Adaptive valleys are boundaries within which the immediate evolutionary potential of a lineage is constrained. Without boundaries to the immediate evolutionary potential of a lineage the phylogenetic distinctions between groups are unimportant for future dynamics. Yet if those immediate bounds are considered static then it is difficult to explain the radiation of lineages that has

occurred in the past. The question to be answered is, "how does a lineage constrained to one selective domain reach a new selective domain?". The SBP provides a mechanism for such movement.

The Balance in Shifting Balance

Wright viewed drift as an important evolutionary factor largely because of its effect on the adaptive dynamics of populations (Provine 1986). When gene interactions affect fitness, drift alters the balance between intrademic and interdemic selection. If drift is pervasive in a system then the opportunity for interdemic selection may arise. With drift and gene interaction even demes under the same selective forces can differentiate. The genetic differentiation between demes due to drift can create selective differences between demes. This selection then forces further divergence. If drift is insufficient to change which alleles are favored then its effects will be quickly ameliorated by migration between demes in combination with selection within demes.

Because of the role of drift, population structure can influence the course of evolutionary change. This incorporation of spatial genetic structure is unique to the SBP. Wright viewed the optimal adaptive scenario as including a balance of drift, intrademic selection, and interdemic selection (Wright 1931; Wright 1932). Population structure through its influence on drift can shift the balance of these factors (Wright 1931).

The SBP allows the exploration of multiple adaptive peaks through the combined processes of drift, mass selection, and interdemic selection. Wright (1932; 1978a) saw these processes acting in three phases in a structured population. In phase one, genetic drift within subpopulations allows some demes to enter the domain of new adaptive peaks.

Next, mass selection within those demes would push them towards the new adaptive peak (phase two). Finally if the new adaptive peak is of higher fitness than the other demes in the population that deme may export more individuals than its neighbors. This differential export of individuals under certain circumstances should allow those demes on the higher peak to convert the demes on the lower peaks to the higher fitness peak (phase three).

Progress in Shifting Balance Theory

Since it was first proposed the SBP has provided a qualitative model for researchers studying evolution in structured populations. Wright's quantitative analysis of evolution previous to 1935 was restricted to single locus models (Wright 1931). The SBP, however, was founded firmly in the belief that inter-locus interactions were important in evolution. Wright therefore made a bridging of his qualitative theory and quantitative analysis a lifelong goal (Provine 1986). He made several fundamental advances in this area.

First, Wright determined a method for studying the probability distributions of alleles at multiple interacting loci (Wright 1935). He accomplished this by analyzing traits under the purely additive control of multiple loci. These additive traits were mathematically tractable using his earlier integral approach (Wright 1931). By applying non-linear fitness surfaces to the additive traits Wright modeled systems with multiple adaptive peaks involving multiple loci. This permitted Wright to generate equilibrium expressions for the distribution of allele frequencies across two loci.

Wright (1935) further improved his analysis of the SBP by applying differential equations derived from Kolmogorov's (1931) equations for continuous diffusion effects to

the problem. Wright's forward Kolmogorov equation had independently been arrived at several years earlier by physicists and is therefore referred to as the Fokker-Planck equation. Application of this equation by Wright allowed investigations of non-equilibrium processes. These techniques have formed the basis for most of the subsequent analysis of the SBP. In models of this type, drift is modeled as a diffusion process which, combined with deterministic factors, provides the probability of a given outcome. While diffusion models require assumptions that often restrict their generality (Gillespie 1989) they have proved the most powerful approach yet in understanding the dynamics of peak shifts.

In general the use of diffusion equations in population genetics flourished in the 1940's and 1950's. The application to the SBP however was generally restricted to defining the probability distributions of allele frequencies for single locus (heterozygote disadvantage) or polygenic adaptive landscapes (See Kimura 1964 for review). Lande (Lande 1976; Lande 1985; Lande 1986), however, changed the focus of this approach by applying diffusion equations to a more macroevolutionary question. He used diffusion equations to demonstrate that the time between peak shifts may be large even on a geologic time scale. Lande concluded that when peak shifts do occur they should appear very suddenly. Punctuated equilibrium is, therefore, the expected pattern of morphological change when multiple adaptive peaks exist (Lande 1985; Lande 1986).

Wright clearly recognized the implications of the shifting balance model for macroevolutionary dynamics and was quick to respond (Wright 1982a; Wright 1982b) when the ability of microevolutionary theory to explain punctuated evolution was questioned (Gould and Eldredge 1977). Wright's general prediction that evolution on a rugged adaptive landscape will lead to a macroevolutionary pattern of stasis punctuated by

rapid change was later quantified for a number of specific cases. In the case of polygenic traits in a population large enough to guarantee a constant source of variance and heritability Lande (Lande 1976; Lande 1985; Lande 1986) found that peak shifts would be highly punctuated. Under moderate selection and with moderate variance and heritability and an effective population size (N_e) of 200, peak shifts are expected approximately every 10^{10} or 10^{11} generations. When N_e is between 10^2 and 10^6, the residence time within the adaptive trough would be between 10^2 and 10^3 generations. The expected time to a peak shift increases exponentially with increasing N_e while the residence time of the intermediate form increases logrithmically in theses models (Lande 1985). Numerical simulations (Newman *et al.* 1985) agree with Lande's general conclusions, as do analytical results based on changes in phenotypic variance and environment (i.e. selection) as the cause of peak shifts (Kirkpatrick 1982) .

Wright (1982b) points out that the main difference between neodarwinian models and Eldridge and Gould's (1972) model of macroevolution is not one of tempo but of mode. Rapid character change followed by long periods of stasis may be adequately explained by traditional microevolutionary forces within a species, or as a process which is tied to speciation. Wright noted that peak shifts could occur under both scenarios (Wright 1982a). One mechanism whereby speciation and adaptive peak shifts might be tied together is through founder effect speciation (see Barton and Charlesworth 1984 for a review).

Considerable analytical work has concentrated on the special case of peak shifts in founder populations (Barton and Charlesworth 1984; Charlesworth and Rouhani 1988; Rouhani and Barton 1987a). These models investigate a process which has been

conceptually linked to speciation (Barton and Charlesworth 1984; Carson 1982; Mayr 1963; Templeton 1980), but which is not necessarily contingent on speciation. The models investigate the probability of peak shifts in founder populations which are drawn from large parent populations. Those diffusion approximations indicate that when heritabilities are moderately high, founder event peak shifts will occur very rarely if the phenotypic distance to be shifted is greater than several times the square root of the additive genetic variance. When the phenotypic change required for a peak shift is relatively small, however, the probability of peak shifts is greatly increased by founder events (Rouhani and Barton 1987a). Growth rate and size of the founding population are in this case important factors in determining the probability of those peak shifts.

Using simulations to test the assumptions of the Rouhani and Barton (1987a) model Charlesworth and Rouhani (1988) found that the approximation methods were accurate only when the size of the two adaptive peaks was approximately equal. Up to ten percent of the founded populations shifted under some of these models. The size of the selection coefficient was relatively unimportant in diffusion approximations (Rouhani and Barton 1987a), but was important in the simulations (Charlesworth and Rouhani 1988). The degree to which the population is released from selection during rapid growth after colonization is critical in determining the degree to which the selection coefficient influences the probability of peak shifts (Charlesworth and Rouhani 1988).

The probability of peak shifts in isolated demes or founder populations discussed above constitute only a portion of the SBP. The process was originally envisioned in large spatially structured populations. With near total isolation between demes the overall probability of at least one peak shift occurring should increase (Lande 1985). What is not

clear is what should happen in populations where isolation between demes is not so complete. The effect of migration in reducing or increasing the probability of peak shifts therefore demands attention.

Migration is critical to the third phase of the SBP. Phase three (interdemic selection) has received increased attention recently (Barton and Rouhani 1993; Crow *et al.* 1990; Moore 1996 chapter 3; Moore and Tonsor 1994). The general result of these studies is that phase three proceeds fairly readily when the number of loci involved is low but is slowed significantly by increased numbers of loci (Moore 1996 chapter 3, Crow et al. 1990) . However it is also clear that without a reasonable amount of gene flow phase three will not occur (Barton and Rouhani 1993; Moore and Tonsor 1994; Rouhani and Barton 1987b).

Studies have just begun to look at the combined SBP including all three phases. This melding of the process is critical since there are conflicting factors causing phases one and three. Specifically migration rates need to be low enough to allow demes to drift into the domain of attraction of new peaks. Migration rates must also be high enough to allow the conversion of demes at the lower peak through interdemic selection. Recent studies have demonstrated that there are certain migration rates which allow all three phases of the process to proceed in several different genetic models (Moore 1996 chapter 3, Moore and Tonsor 1994, Barton and Rouhani 1993, Rouhani and Barton 1987b). Previous to those studies it had not been clear that there would be any particular migration rate which would readily allow both phase one and phase three for any genetic system.

Rouhani and Barton (1987b) have compared the probability of peak shifts occurring in a single panmictic population, a one dimensional continuously distributed

population and a two dimensional continuously distributed population. The comparisons were based on a double gaussian fitness surface applied to a continuous character. Expanding on analytical methods previously used in studying peak shift probabilities and statistical mechanics they demonstrated that peak shifts can occur in a population even when there are no discrete barriers to gene flow in the one dimensional case. As in the panmictic case peak shift probability in the one dimensional model was exponentially related to the strength of selection (Rouhani and Barton 1987b). Provided that the neighborhood size is less than about 30, the probability of peak shifts becomes moderately likely in the two dimensional case. In a two dimensional continuous population the size of the neighborhood becomes the overriding factor influencing the probability of peak shifts, and the strength of selection is no longer the dominant factor. It is not clear exactly why these one and two dimensional models behave differently but spatial segregation in genetic variation may be quite different in two dimensional systems. Increased parapatric differentiation may allow more gradual transitions into the domains of new peaks when multiple dimensions exist (Rouhani and Barton 1987b).

Barton and Rouhani (1993) have also studied shifting balance analytically in structured demes. They modeled migration between demes using an island model in which the effect of migration may be treated as a diffusion process. They compared the typical polygenic trait under a double gaussian fitness surface with a chromosomal rearrangement model in which heterozygotes have a disadvantage. They found that, " below a certain critical number of migrants, the demes scatter towards different adaptive peaks, and the allele frequency amongst migrants evolves towards a single intermediate value" (Barton and Rouhani 1993). When, however, the number of migrants (Nm) is large the whole

population evolves together and is likely to be trapped on the lower peak. Barton and Rouhani detected a sharp transition between the two extremes at a N*m* of approximately 1. Just below that critical point adaptation was most efficient because peak shifts were most frequently spread throughout the population. The above conclusions held for the single locus and polygenic models both with and without dominance. This prompted Barton and Rouhani to conclude that the similarity of behavior across models indicated that their conclusions may be robust across many genetic systems. Despite this conclusion it was recognized that adaptation via the shifting balance is more effective with disruptive selection on discrete alleles than in polygenic traits.

Moore and Tonsor (1994) explored the dynamics of a two locus two allele system using Monte Carlo simulations. In those simulations migration was a two dimensional stepping stone model. They found that the probability of peak shifts was again strongly dependent on population structure. Even with deme sizes less than 30 individuals, demes did not shift to new peaks when the per capita migration rates exceeded 0.05. Migration rates below 0.001 were not effective in spreading peak shifts throughout the population. In that study, however, within 12,000 generations over 25% of simulations resulted in a population wide peak shift at the optimum migration rate. Both Moore and Tonsor (1994), and Barton and Rouhani (1993) found that adaptation was most effective when N*m* was between 0.1 and 1. This indicates that this result is fairly general not just across single locus and polygenic systems with an island model migration scheme but also in an oligogenic system with stepping stone migration.

Diffusion approximations which have traditionally used to study peak shifts within an isolated population have recently been applied to the investigation of the SBP as a

whole. Barton and Rouhani (1987) contrast two distinct applications of these techniques. They recognize that diffusion models either have dealt with the single locus underdominant allele or the case where the number of alleles (or loci) is nearly infinite so that an assumption of a nearly gaussian distribution of frequencies may be made. These two type of models represent extremes with respect to the rate of introduction of mutant alleles (Barton and Rouhani 1987). Barton and Rouhani therefore compared a single underdominant allele model with a model which assumes the distribution of probabilities about a peak will be approximately gaussian. They demonstrated analytically that for a one locus two allele model when the number of mutations is low ($N\mu >> 1/4$) the frequency of peak shifts is a product of the probability of fixation of a single mutation and the mutation rate. When the number of mutations is high the results converged with those for the gaussian models generally used for quantitative traits.

While the conclusions of Moore and Tonsor (1994) and Barton and Rouhani (1993) on the optimum level of structure for the SBP agree, there is no expected rate of population wide peak shifts which seems to apply across models. Moore (1996 chapter 3) compared the efficacy of the shifting balance process across several oligogenic models in an attempt to determine whether any generalizations are apparent. In studying 2 through 16 locus models Moore concluded that the rate of population wide peak shifts was inconsistent across models. He did find that increasing the number of allelic substitutions necessary for a specific amount of trait change (i.e. the number of loci involved) decreased the efficacy of the SBP in a given phenotypic fitness surface. Despite this, the effect of changes in the fitness surface was substantial enough that certain 8 locus models were more effective than some 2 locus models.

The shape of the fitness surface in Moore's (1996 chapter 3) models strongly influenced the rate of population wide peak shifts. The amount of genotypic variation within and between demes is one factor which should change with changes in fitness surface. This difference in the amount of genetic variation between demes seems to account for the overriding effect of the fitness surface's shape (Moore 1996 chapter 3). Moore varied the initial conditions of a subset of his simulations to produce differences in initial variance. As variance was increased the rate of population wide peak shifts also increased. The amount of variation about the lower peak relative to the phenotypic distance to a new domain of attraction seemed to be important as predicted by Rouhani and Barton (1987a).

Whitlock (1995) has demonstrated that in general, high levels of variance within a population can induce peak shifts between alternate phenotypic states with little or no drift. He has shown that variance can induce higher rates of peak shifts in founder or bottlenecked populations than drift alone. Whitlock recognizes that other mechanisms which are capable of increasing phenotypic variance are also likely to increase the rate of peak shifts. The additive genetic variance in a metapopulation overall will not determine the amount of additive variance in the individual subpopulations or vice versa (Whitlock *et al.* 1993). Population structure is one factor that can alter the amount of additive genetic variance in a population. Previous studies of the SBP have generally not included increased variance due to population sub-structuring (Whitlock 1995). The few studies that have included these effects (Moore and Tonsor 1994, Moore 1996 chapters 3 and 4) have had relatively high overall peak shift rates.

The models of the SBP to date have found that the SBP can occur. The probability

of peak shifts, under certain models, is low enough that the importance of the process continues to be questioned (Whitlock 1995). Additionally the range of migration rates which allow the entire process is quite narrow in the models of Barton and Rouhani (1993) and Moore and Tonsor (1994).

The small range of migration rates which allow peak shifts in the models discussed above may partly be a product of the simplicity of the models used. Variability of certain ecological parameters such as migration rate, carrying capacity and environmentally induced variation may increase the rate of peak shifts in many cases. Moore (1996 chapter 4) has investigated the effects of variation in migration rate over time in a two dimensional stepping stone model. Fluctuations in migration rate dramatically increased the efficacy of the SBP. Moderate fluctuations in migration rate are likely to be common on a short scale. The geological time scale provides many possibilities for large scale changes in the migration rates of many species (Cronin and Schneider 1990; Van der Spoel 1994). The effects of variation in ecological factors including the strength of selection, population sizes, and migration rates are all potentially important to the SBP on a geological scale.

The SBP provides a mechanism whereby adaptive changes and subsequent reproductive isolation through hybrid breakdown are likely to occur (Rouhani and Barton 1987b). Although in many circumstances the probability of peak shifts within a deme is low, the process seems likely to occur frequently on a geologic time scale. For this reason, patterns of speciation may be strongly influenced by the SBP.

The three phase SBP is quickly becoming a well explored model which incorporates major processes which are likely to influence macroevolutionary patterns of radiation, change and stasis. It includes internal genetic constraints (i.e. phylogenetic

inertia), isolation and drift as well as the possibility of reinforcement of isolation through hybrid breakdown. Ecological realism also demands the recognition of variation in many of the SBP's parameters because the time between peak shifts is expected to be relatively large.

Chapter 2

EMPIRICAL APPROACHES TO INVESTIGATING MULTIPEAKED SURFACES: A REVEIW

Introduction

Adaptive topographies with multiple peaks are the backbone of Sewall Wright's shifting balance process (SBP). When mean population fitness is dependent on allele frequencies at multiple loci the pressure of individual selection to maintain historical gene combinations may prevent increases in population wide fitness. The existence of multiple adaptive peaks implies that internal genetic constraints to adaptation exist (Moore 1996, chapter 1). The SBP, within the framework of adaptive peaks, is likely to influence macroevolutionary patterns of radiation, change and stasis (Wright 1985a, 1985b). Considerable effort has been focused on the exploration of shifting balance theory (Moore 1996, chapter 1). This review responds to a fundamental question that the theoretical work on shifting balance theory cannot answer. That question is "how ubiquitous is the evidence for multiple adaptive peaks?" The relevance of the shifting balance theory is contingent on evidence for adaptive peaks. This review also assesses possible supporting lines of evidence for the SBP which emerge from the studies which may involve multiple adaptive peaks.

Methods of Detecting Gene Interactions

Because gene interactions are so critical to the SBP, the evidence for gene interactions must be discussed. Evidence for gene interactions is elusive. This does not however, imply that gene interactions are rare. In the broadest sense anytime two genes act to produce a common trait there is a gene interaction. It is however only the nonadditive effects that are of interest in the SBP. Adaptive surfaces can be viewed as multiple fitness maxima and minima resulting from nonadditive gene action in the production of a trait relevant to fitness. This is probably a reasonable view of adaptive landscapes with one exception. The exception is that the atomization of organisms into discrete traits eliminates many important possible nonadditive gene interactions (Gould and Lewontin 1979; Wright 1969). The ubiquity of pleiotropy would cause even additive traits to have certain gene combinations which were more favorable than others due to the summed effects on other traits (Wright 1969). The division of whole organisms into subsidiary traits is therefore problematic because gene interactions rely on the definition of a trait. Many gene interactions may be missed if traits are not properly defined.

Evidence of gene interaction from classical genetics

Despite the expectation that many types of gene interaction will be missed if individual traits are the focus of study, strong evidence for epistatic interactions on phenotype is almost as long standing as the study of genetics itself. Bateson and Punnett (Punnett 1923) observed strong gene interaction in a two-locus two allele system controlling comb shape in chickens. In this case true breeding pea and rose comb chickens when crossed will produce only walnut comb F1s. F2s consist of a 9:3:3:1 phenotypic ratio of walnut:pea:rose:single comb individuals. This is an example of discontinuous

variation where four specific phenotypic states can be identified (see figure 2.1). It is easy to envision how selection on such discrete states could create a multi-peaked adaptive landscape.

Introductory genetics texts provide many examples of gene interactions which provide 9:3:3:1 ratios or modified two locus two allele systems. Some examples yield discrete classes as in the case of chicken comb while others seem more continuous because they are additive. It is important, however, to avoid viewing discrete classes which produce an additive gradient of variation as being continuous. This error is easy to slip into since the analogy between continuity and gradation is so strong. How a trait is viewed determines whether multiple peak epistasis is found.

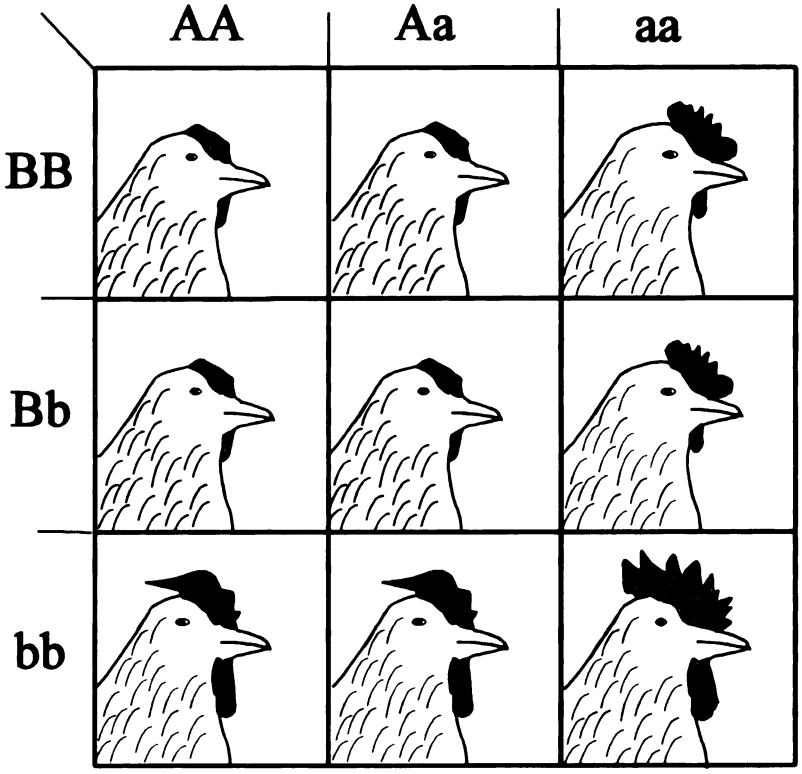
If discrete multilocus combinations produce discrete phenotypic classes then arbitrary scalings can be deceptive. All such traits could produce a multiple peaked surface given the right scaling. It can also be argued that all epistatic interactions may be removed by adjusting the scaling. In the case of natural systems selection determines the scaling. There is no reason to expect that scaling to be additive. The important point is that if there are discrete interactions then the potential for epistatic interactions for fitness exist.

Even when the number of gene interactions increases beyond two loci with two alleles, discrete variation is still found. Wheat grain color is determined by a three-locus two allele system (East 1910; Nilsson-Ehle 1909). Trihybrid crosses for these loci produce seven discrete phenotypic classes. Total pigment content acts additively and superficially appears quantitative. There is, however, epistatic gene action if the trait of interest is the absolute value of the deviation from medium red. In that case those allele combinations which produce very high or very low pigment levels have the highest trait value, and

Figure 2.1 - Chicken combs produced by the combined action of two alleles at each of two loci.

Four different chicken comb are produced by the interaction of alleles at two loci. If at least one copy of the B allele and one copy of the A allele is present the pea Phenotype will result (upper left corner). Double homozygote aabb individuals develop with a single comb (lower right corner). If at least one copy of the A allele is present and the individual is homozygous for the bb allele the individual will have the rose phenotype (lower left). If at least one copy of the B allele is present and the individual is homozygous for the aa allele the individual will have the walnut phenotype (upper right). Mating of two double heterozygote (pea) individuals will produce all four phenotypes.

Figure 2.1



intermediate levels of pigment have lower trait values.

Classical genetics provides us with many examples of traits which are controlled by multiple loci, and which do not easily fit a quantitative model. A few good examples include coat and eye variation in guinea pigs (Wright 1963; Wright 1968), mice (Russell 1949), dogs (Little 1957; Winge 1950), and other mammals (Castle 1940; Wright 1968) as well as color patterns in *Heliconius* (Clark and Sheppard 1971; Mallet 1989; Sheppard *et al.* 1985; Turner 1971). Examples in plants include flower color polymorphisms (Bateson 1909; Lawrence and Scott-Moncrieff 1935; Onslow 1916), tristyly (De Nettancourt 1977) and leaf morphology (Yu 1989). However, even when genes interact to produce a conspicuously additive trait (as in wheat grain pigments) this may not be the 'natural' scale for selection. In fact, all traits with a relatively few interacting loci have the potential to produce a multi peak fitness surface. Genes that seem conspicuously non additive may not produce a multi-peaked adaptive surface although they have that potential.

Evidence of gene interaction from Quantitative Genetics

Quantitative traits may have both additive and nonadditive components contributing to their variance. Heritabilities are determined by the additive variation extant in a population. The residual genetic variance within a population may in part be due to interactions between loci. Non-additive variance components indicate that non-additive gene action is present. Small non-additive components, however, do not indicate the lack of non-additive gene action. If many non-additive interactions exist but there is little polymorphism at the contributing loci the non-additive variance component will be small even though the number of potential interactions is large. If non-additive variance is significant this is a strong indication that non-additive gene action exists.

Optimal breeding regimes in domesticated organisms are often determined by the relative importance of these components of population variance. A number of techniques have therefore been developed to determine the proportion of variance explained by the various sources of genetic variance. These techniques include, ANOVA techniques (Hayman and Mather 1955; Kempthorne 1966), generation means, and testcross designs (Anderson and Kempthorn 1954; Hayman 1958; Jinks 1956; Mather 1949).

Of the techniques mentioned above ANOVA techniques are the most problematic. In the ANOVA method, the epistatic variance component estimates are based on a small fraction of the actual epistatic variance that can actually be separated from other nonadditive effects. This causes a reduction in the power of ANOVA techniques to detect epistatic variance. Epistatic variance components are generally small in comparison with their error estimates using ANOVA (Whitlock *et al.* 1995) although this is not always true (e.g. seed weight in rice, Ram *et al.* 1989). Generation means tests and test cross studies have a greater ability to detect epistatic interactions. Many such tests have detected some level of epistasis. In reanalyzing cases of overdominance in 5 different species Jinks found that in all cases interlocus effects caused an appreciable amount of the effects previously attributed to overdominance (Jinks 1955).

The proportion of the variance in a population attributed to epistasis is affected by the number of potential epistatically interacting loci relative to the number of additive loci and the allele frequencies at each epistatic locus. The expectation in a large population is that selection on a given trait will reduce polymorphism at epistatically interacting loci which produce that trait. The direction of selection on the epistatic alleles will be determined by the frequency of the alleles at other loci. As the level of polymorphism is

reduced at one locus, all loci that could epistatically interact with it will act increasingly additively. The possible epistatic interactions are what is important in the creation of multiple adaptive peaks not the frequency of certain alleles in certain populations at any given time.

Environmental dependence of epistatic variation can allow polymorphisms to persist in a population despite selection. Selection on a trait within a single environment will reduce the polymorphism at loci that have strong interactions in that environment. If the environment is then changed there may be a change in which interactions are important. This will create interactions which have not been acted on by selection previously. In this case exposure to extreme environments can release epistatic variance (Dykheusen and Hartl 1980). Environmental dependence of epistatic variance measures has been demonstrated in *Nicotiana* (Jinks *et al.* 1973). The potential number of gene interactions which are readily detectable in an undisturbed population may therefore be small when compared with the total number of possible interactions which exist.

Overall, quantitative genetics provides a large amount of evidence for epistatic interactions. While many of these interactions are weak when compared to the overall genetic variance this may often be due to the loss of high levels of polymorphism at relevant loci through the action of selection. This is to be expected in a large population when looking at alleles involved in an adaptive peak. Many important fitness peaks may be obscured when quantitative traits are studied independently from each other. Despite these problems there is still evidence that epistatic interactions exist with at least moderate strength and frequency in quantitative traits.

Evidence of gene interaction from molecular genetic studies

One potential source of information about epistatic gene action is through Quantitative Trait Locus (QTL) studies. In this type of study polymorphic markers allow the mapping of a quantitative trait onto specific chromosomal regions (see Cheverud *et al.* 1993; Tanksley 1993) for reviews of these techniques). Multiple factor interactions between map regions may also be identified. While some QTL studies have found little or no evidence for epistatic interactions others have found multiple factor interactions (Whitlock *et al.* 1995). One of the best examples of interlocus interaction identified by QTL work is in sternopleural bristle number in *Drosophila melanogaster* (Long *et al.* 1995). It is important to note that this study was based on a population produced from the hybridization of lines that had previously been selected for either high or low bristle number. Hybridization between lines can expose epistatic interactions which are not found in either parental lineage.

In addition to the 'survey' approach to QTL work discussed above specific candidate loci are frequently identified for study a priori based on possible metabolic importance. This type of approach has identified epistatic interactions in a number of traits (reviewed in Whitlock *et al.* 1995). Combined with the survey techniques in QTL analysis, this method shows great promise in identifying epistatic interactions. While these techniques thus far have only produced weak evidence of epistatic interactions there are several ways in which the number of these interactions identified may increase. The ability to detect epistasis between tightly linked loci requires very high resolution maps which have previously been very difficult to obtain (Cheverud *et al.* 1993; Tanksley 1993). Tight linkage between coadapted gene complexes is, however, exactly what is expected in the

case of coadaptation of genes (Prakash and Lewontin 1968). Therefore, as QTL maps gain resolution the identification of epistatic loci may be accelerated. Additional examples of epistasis may also arise as more studies use populations produced by crossing divergent populations.

Classical genetics, quantitative genetics, and QTL work all indicate there is a potential for gene interactions to be important. While the interactions actually elucidated by these techniques may be less than overwhelming, they seem sufficient to indicate that many adaptive peaks potentially exist. In fact, it is expected that the number of detectable interactions will be low when selection is involved and crosses are within local populations. As expected those QTL studies which demonstrate epistasis are those with the most divergent crosses. It is surprising how many cases of gene interaction exist. What remains unclear is whether any of these examples of gene interaction actually produces adaptive peaks.

Natural Selection As a Non-Arbitrary Ruler

The presence or absence of epistasis as stressed above is dependent on the scaling of traits. None of the examples given so far has referred to epistasis for fitness, the only trait which is truly relevant to adaptive landscapes. The only appropriate and non-arbitrary scaling is provided by natural selection. Not only are rugged adaptive landscapes produced by epistatically controlled traits that have strong directional selection acting on them, but also they are produced by nonlinear fitness functions acting on traits that have predominantly additive genetic compositions. The use of natural selection as the ruler upon which a non-arbitrary scale for adaptive landscapes is scribed is necessary but also

provides some problems.

New sources of gene interactions

Non-linear fitness functions applied to additive traits create epistasis for fitness. Even optimizing selection in which there is a single phenotypic optima is a potential source of epistasis for fitness. A trait that is determined by purely additive gene action will exhibit only nonadditive variation for fitness if it has reached a selective optima (Falconer 1981), p. 394). The absence of response to selection by a population at an optimal equilibrium (i.e. a heritability of 0) means that all genetic variation is nonadditive.

Even when optimizing selection has not yet reached equilibrium conditions there will be multiple sets of alleles across all loci which will result in an optimum phenotype. This means that adaptive peaks exist. One way of envisioning this is to recognize how selection acts on an allele which has a fixed additive effect on trait value. Selection is against an allele which increases trait value if the population mean is higher that the optimum. Selection favors the same substitution if the mean is lower than the optimum (See figure 2.2a).

In the case of wheat grain color two possible scalings were mentioned. The first was based on total pigment content of the grain. This scale would be applied if the trait were under directional selection. This scale does not result in any epistasis. If however stabilizing selection favored the intermediate phenotype, the scaling is based on the deviation from that medium red color. In this second case an adaptive landscape with five peaks would be created. Wheat color is not a true quantitative trait but it demonstrates the potential for conversion of additive trait variance into epistatic variance for fitness. Optimizing selection on a purely additive quantitative trait will also result in nonadditive

Figure 2.2 - Epistasis for fitness produced by optimizing selection (a) and disruptive selection (b) acting on an additive trait.

Alleles which increase the numeric value of the trait are indicated by a + while alleles that reduce the numeric value of the trait are indicated by a -. The + alleles are favored only when there is no more than one other + allele in that genotype. The curves represent fitness plotted against phenotype. Note that there are many different combinations which can provide the same phenotype.

Figure 2.2

FITNESS
GENOTYPE

+--
-+-
--+
++-
+-+
-++
+++
FITNESS
GENOTYPE

+--
-+-
--+
++-
+-+
-++
+++
PHENOTYPE 0 1 2 3 4
EFFECT of a+ SUBSTITUTION DECREASE FITNESS INCREASE FITNESS
PHENOTYPE 0 1 2 3 4
EFFECT of a+ SUBSTITUTION DECREASE FITNESS INCREASE FITNESS

variance components of fitness (Tachida and Cockerham 1988).

Optimizing selection acting on an additive trait produces a qualitatively special type of epistasis. Because the optimal trait may be built up from multiple possible genotypic combinations the epistatic interactions are diffuse throughout the loci involved in the trait. This 'diffuse epistasis' may have special characteristics. For instance, in the case of optimizing selection on a quantitative trait, if the number of loci is large and the phenotypic effect is relatively uniform across loci, $n!/[(n/2)!]^2$ adaptive peaks may exist with n pairs of alleles (Wright 1939). However, the valleys between any two peaks are vanishingly small, and the peaks are expected to have roughly the same mean fitness. Despite these generalizations diffuse epistasis may be very important in producing interesting adaptive topographies under certain circumstances. These circumstances will be discussed when the topic of integration across traits is discussed.

Disruptive selection exists in two forms. Either both phenotypic extremes are locally optimal, or some of the optima are not at the phenotypic extremes . In both cases the selection on an allele is dependent on the frequency of the other alleles effecting that trait. This is due solely to the relative positions of the two phenotypic optima compared to the mean phenotype in a population. Depending on the position of the mean phenotype relative to the phenotypic optima selection may force the population toward one or the other optimum (see figure 2.2b). Selection therefore alters allele frequencies at one locus in a way which is dependent on the frequency of alleles at other loci. In addition if one or both phenotypic optima are not at the phenotypic extremes then multiple genotypic solutions will also produce the same phenotypic optimum allowing genotypic variation between populations on the same phenotypic peak to exist.

Integration across traits by selection can cause epistasis for fitness. Selection acting on one trait may affect the trait mean of other traits due to the pleiotropic effects of genes that effect both traits. The result of this correlated response between traits is that many traits may be constrained by the opposing forces of selection acting on multiple traits simultaneously. Wright recognized that when stabilizing selection acted on a trait, fitness differences could exist between the multiple genotypic optima. These differences would be due to pleiotropic effects of the particular allelic combinations at each particular optima (Wright 1939). Even though different genotypic peaks may not differ in their fitness effects through a particular trait, the pleiotropic effects may cause fitness differences. Selection may often work on pairs of traits. The selection on one trait can be dependent on the state of a second trait. This correlational selection integrates across traits. Unlike integration via metabolic or developmental pleiotropy this integration is imposed by the environment. Even if two traits are completely genetically independent multiple adaptive peaks will exist if the fitness of a given allele at one locus is dependent on the alleles present at another locus. In the case of correlational selection certain alleles at loci controlling a trait are only favored if appropriate alleles are present in loci affecting a second trait.

Gene Interactions Revisited

The previous sections provided evidence of gene interaction in arbitrary traits. These arbitrary traits indicate that there are many possible interactions that could provide multiple peaks. Certain types of interaction have not, however, been addressed. Natural selection works on populations of whole organisms and gives us a nonarbitrary scale for measuring gene interaction. Gene interactions between traits are integrated by natural

selection. Therefore we must at least consider that evolutionary constraints on any given trait of an organism exist due to selection on other traits. In the SBP these constraints are not necessarily insurmountable. They should however be difficult to detect since they are expected to produce near fixation of particular genetic combinations across geological time scales, thus disguising the very interactions which drive the SBP.

Where to look for multiple peak epistasis

Multiple adaptive peaks can exist even when genetic polymorphisms for multiple peaks do not exist. Variation within a population will rarely span the domain of multiple adaptive peaks because selection will tend to maintain most population within the domain of a single peak. Because variation within a population will usually not include multiple adaptive peaks, evidence must come from those special situations where variation spanning multiple peaks is expected. Multiple peaks are most likely to exist when the third phase of the SBP is incomplete due to isolation of demes, or when selection has had insufficient time to remove variation (i.e. in novel environments).

Most previously mentioned examples of epistasis in the formation of traits exist in domesticated species. Many traits in domesticated organisms are released from natural selective forces and exposed to novel selective forces. For this reason variation which would not be found in natural populations may be present. In addition, examples of epistatic polymorphism may exist because the traits are not under strong selection even in natural systems. Examples of adaptive peaks in a natural system will be much more difficult to detect. Rarity of epistatic polymorphisms for fitness in natural populations is an expected result of the SBP. The situation where multiple adaptive peaks will most easily be detected is when either the external environment or the internal genetic

environment of an organism is variable.

Within a population, the genetic variation should remain within the domain of one adaptive peak for long periods. Therefore, epistasis for fitness will be nearly nonexistent within any given population. If, however, the external environment is changed, the pleiotropic interactions and the correlated selection between traits may change. The change in interactions is expected whenever environmental effects are not uniform across all traits that a locus influences. In that case, when the environment is changed the correlation between traits which is due to the pleiotropic effects of a locus will change. The mapping of genotype onto phenotype has now changed. Until a selective equilibrium has been reached the probability of detecting variation which spans multiple peaks is increased. Within a population, periods during and shortly after large scale environmental changes are the most conducive to the detection of epistasis for fitness.

Differences in coadapted gene complexes between populations are likely to provide evidence of adaptive peaks. These differences can accumulate only when the SBP is ineffective. Specifically, the third phase cannot have occurred if such variation is to be preserved between populations. Multiple peak polymorphism across demes is most likely in situations where multiple demes of at least periodically small size are highly isolated. The isolation needed to prevent the third phase of the SBP requires immigration of less than approximately one individual every 100 generations (Barton and Rouhani 1993, Moore and Tonsor 1994). Crosses between such demes are most likely to expose variation spanning multiple adaptive peaks.

Differences in internal genetic architecture should be most pronounced between subspecies and species. Here the possibility of the third phase occurring is largely

eliminated. In cases where species can produce hybrid offspring, multiple adaptive peaks might be found in the variation between those species. In the case of between species (or subspecies) hybrids the expectation is that each parent is the product of a somewhat different selective environment. Lowering of fitness therefore must be relative to either parent in either environment. This is true for both interpopulational and interspecific crosses.

Evidence from classical and population genetics

Classical genetics has provided examples of epistatic interactions that are clearly linked to fitness. Adaptive peaks have been clearly defined in few if any cases (e.g. Clark and Sheppard 1971; Clark *et al.* 1968; Nagel *et al.* 1989). Several genes are known to ameliorate the effects of sickle cell anemia (Nagel *et al.* 1989). There are also apparently fitness costs associated with some of these modifying genes (Nagel *et al.* 1989). The exact shape of the fitness surface for these genes is unknown and would be expected to change in a spatially concordant way with malaria risk. If multiple peaks exist in this system population structure alone is unlikely to be capable of protecting the polymorphism. Presumably spatial and temporal variability in selection provide adequate explanation for the polymorphism.

Targeting particular proteins for study when they are suspected of being of particular importance has also had some success in identifying epistatic genes which seem to effect fitness components (e.g. Cavener and Clegg 1981; Dykhuizen and Hartl 1980; Goolish and Burton 1989; McKechnie and Geer 1988). The presence of the polymorphisms necessary for the identification of these interactions may be the result of different factors in each case. Epistasis for fitness may be created by the introduction to a

new environment (Dykhuizen and Hartl 1980). It may be preserved by population structure (Goolish and Burton 1989) , or be the product of many factors including spatial and temporal variation in the environment (Cavener and Clegg 1981; McKechnie and Geer 1988) .

One of the weakest pieces of evidence for adaptive peaks also is one of the more ubiquitous. Selection for coadapted gene complexes will create aggregations of alleles that are favorable only as a group. It is to be expected that these aggregations of alleles will show up as linkage disequilibria between coadapted loci. While recombination may break up such aggregations, population structure and physical linkage of genes may allow favorable combinations to segregate. Therefore, many loci that interact epistatically are tightly linked physically (see Hedrick *et al.* 1978 for review).

Alternative explanations for the presence of linkage disequilibrium weaken this type of evidence for multiple peak landscapes. Physical linkage within a chromosome surely must be eliminated as a cause of the disequilibrium. Because the opportunity for coadaptation of genes is increased by physical linkage the two factors may often be difficult to separate. Despite these caveats some examples of disequilibrium between loci (Barker 1979; Clegg *et al.* 1972; Hedrick *et al.* 1978; Klitz and Thomson 1987; Lewontin and White 1960) seem to support the existence of multiple adaptive peaks.

One exceptional case of disequilibrium in a natural system is in shell banding and color patterns in snails of the genus *Cepaea*. In *C. nemoralis* and *C. hortensis* multiple shell pattern and color loci are in disequilibrium (Jones *et al.* 1977). The loci are tightly physically linked but also have been shown to strongly interact in the determination of fitness. The most fit peak appears to vary between location. Local selection therefore acts

to preserve the polymorphisms between populations in this system.

Chromosomal inversion can allow the independent evolution of groups of genes within multiple lines of *Drosophila pseudobscura*. Population structure in this case results in populations with different inversion types (Prakash and Lewontin 1968). The existence of heterosis between karyotypes from within the same population without such heterosis in inter-populational crosses has caused some to conclude that the inversion types carry coadapted gene complexes (Dobzhansky 1951). Prakash and Lewontin (1968) detected a pattern of allelic variation within the inversions that indicated coadaptation of at least two loci. This implies multiple adaptive peaks although again little can be said about the shape of the surface. In this example variation spanning multiple adaptive peaks probably is maintained because the coadapted gene combinations are protected from recombinational decay by linkage and the inversion types.

Frequency dependent selection on chromosomal inversion types also generates a multiple peaked adaptive surface even without coadaptations developing within the inversions. This type of multiple peaked surface may be common (see Whitlock *et al.* 1995 for discussion). This is due to underdominance for fitness among the karyotypes. Frequency dependent selection on a trait that is under control of multiple genes can also create hybrid breakdown for fitness within a species. In some *Heliconius* butterflies local selection favors phenotypes that resemble parental types in wing pattern (Mallet 1989; Mallet *et al.* 1990). Hybrids that do not resemble either parental population are selected against. Similar circumstances exist in other butterflies where mimicry is important (Turner 1977). Whether frequency dependent selection causes reduced fitness in the F1 or the F2 depends on the dominance relationships in the two crossed populations.

Underdominance for fitness at a single locus produces the most simple type of multi-peaked adaptive surface. As mentioned above chromosomal inversion types seem to be common sources of underdominance although not all examples are clear cut. In some cases of pericentric inversions, underdominance may not be present (Coyne *et al.* 1993). Underdominance for fitness exists in the snail *Partula.* Variation in the direction of shell coiling within populations of *Partula* exists (Johnson 1982; Lipton and Murray 1979) and is due to the action of a single gene (Neiman *et al.* 1990). Difficulties in mating between different coiling types have been shown (Gittenberger 1988; Lipton and Murray 1979).

Optimizing, disruptive, and correlational selection

Despite the difficulties in detecting optimizing selection (Endler 1986; Travis 1989) many examples of optimizing selection exist (see Travis 1989, Endler 1986 for reviews). Many documented instances of optimizing selection are less than concrete. The vast number of demonstrations, however, adds credence to the alleged ubiquity of optimizing selection.

Two types of optimizing selection can exist (Endler 1986; Gavrilets and De Jong 1993; Travis 1989). In one type of optimizing selection, selection acts directly on the focal trait to create an optimal phenotype. Selection on gall size in the *Solidago-Eurosta* system (Weiss and Abrahamson 1986) is one example where this type of optimizing selection may be going on. This type of optimizing selection directly creates diffuse epistasis between all the alleles acting on the trait.

Indirect selection via pleiotropic genes that act on multiple traits that are directly related to fitness creates the second type of optimizing selection (Gavrilets and De Jong 1993). This type of optimizing selection seems to be the predominant type in studies to

date. Selection on sternopleural bristle number in *D. melanogaster* is an example of this mode of selection (Kearsey and Barnes 1970; McGill and Mather 1971).

Indirect optimizing selection is expected to only exhibit diffuse epistasis temporarily (Whitlock *et al.* 1995). Selection will remove alleles that have negative effects through multiple traits simultaneously. Similarly, it will fix alleles which increase fitness through their effect on multiple traits. This leaves only alleles that have tradeoffs in their effects on fitness through multiple traits (Wade 1992). Indirect optimizing selection implies that adaptive peaks exist because the directional selection on individual components of fitness is limited by the pleiotropic effect on other components of fitness. Changing the trait value for such a trait requires changing the balance of tradeoffs across traits. Genetic variance is maintained but the population is unable to respond to selection because all the residual variation is non-additive. Here multiple peaks would be evidenced by the existence of different optima between populations.

Most examples of optimizing selection are not clearly identifiable as either of the above two types. What is clear is that there is a great deal of evidence that optimizing selection is common (Travis 1990, Endler 1986). With indirect selection absolute proof of multiple peak epistasis requires examples where the optimum is altered between populations due to the genetic architecture within populations. Given this state of affairs optimizing selection can be viewed as providing a common if not ubiquitous opportunity for multiple adaptive peaks to exist.

The number of examples of disruptive selection on polygenic traits in natural systems is limited. While some good examples exist, few populations have variation that extends over multiple phenotypic peaks. This does not mean that such adaptive peaks are

not available, just that they must be found by crossing individuals of divergent populations or closely allied species. In the African *Pyrenestes* finches there is disruptive selection on beak shape. Beak shapes determine the types of seeds most easily processed with certain intermediate beak types being inferior on both seed types. These intermediate types have lower fitness over certain periods (Smith 1993). Perhaps the most well known example of disruptive selection is in Galapagos finches. Here selection on beak morphology determines the food type upon which individuals feed (Schluter and Grant 1984). In this case reproductive isolation allows the coexistence of multiple peaks. Instances where rapid adaptive radiations have occurred in the relatively recent past should be some of the best places to look for the coexistence of multiple adaptive peaks on separate islands.

Correlational selection, where the state of one trait determines the fitness of the phenotype at another trait is conceptually alluring. Brodie (1992) has provided an interesting example of this in the garter snake *Thamnophis ordinoides*. These snakes have a polymorphism for color/pattern and also for anti predator behavior. Striped snakes are more susceptible to detection than spotted snakes when they are stationary. When striped snakes are moving however it is more difficult to judge their ground speed than it is for a spotted snake. Stripedness is negatively correlated with the propensity to reverse direction and survivorship through the early juvenile stages is enhanced by the appropriate match of behavior and pattern (Brodie 1992). Similar patterns have been shown between resting site choice behavior and coloration in *Biston betularia* (Kettlewell 1955). Correlational selection between host preference and host specialization may be responsible for reduced fitness in hybrids between two sibling species of *Rhagoletis* (Bierbaum and Bush 1992).

Evidence from structured populations and Hybrid breakdown

One striking result of a review of multi-peak epistasis is that without some peculiar circumstances variation within a population will not include multiple peaks (Whitlock *et al.* 1995). Population structure is a critical part of the SBP for this very reason. There are two types of studies that specifically look at the effects of structure on genetic architecture. The first type is through studies of outbreeding depression and hybrid breakdown. This breakdown can occur either between populations or species. The second type is from studies of the efficacy of evolution in populations with different levels of structure.

A reduction in fitness between parents and offspring when the parents come from different populations may be the product of the breakup of coadapted genes. If hybrid offspring (F1) have lower average fitness then either parent the results are consistent with the expectations for the decay of epistatic interactions but may also be produced by underdominance. This is termed outbreeding depression. If the effect increases with subsequent generations (F2, F3, . . .) there is unequivocal evidence for epistasis and this will be called hybrid breakdown.

Evidence for hybrid breakdown is common when lines or populations are provided ample time to diverge (Burton 1990a; Burton 1990b; Hard *et al.* 1992; King 1955; Vetukiv 1956, and see reviews in Gieger 1988; Wright 1977). Interspecific crosses are inherently prone to hybrid breakdown. Interspecific hybrid breakdown is especially interesting because it may often represent the effects of breaking up suites of traits that have coadapted to different selective peaks. (Grant 1975; Stebbins 1955).

The final evidence for the existence of adaptive peaks is that when several

researchers have attempted to test for the effects of population structure on evolutionary dynamics they have found that population structure can affect the ability of a population to adapt to an environment. While some such studies have failed to detect increased or divergent adaptation with population subdivision (Katz and Enfield 1977; Madalena and Robertson 1975; Rathie and Nicholas 1980) others have seen just such results (Cohan *et al.* 1989; Enfield 1977; King 1955; Wade and Goodnight 1991). The critical factor is the mixing rate between subpopulations. Those experiments that demonstrated increased adaptation or divergent modes of adaptation had low or nonexistent mixing rates.

Adaptive peaks combine selection and genetic constraints into a single evolutionary viewpoint. In this view selection acts within the limits of the genetic architecture caused by interactions of genes in determining fitness. The ultimate scale upon which gene interactions are measured is therefore selection. Adaptive peaks may be produced by most models incorporating selection on natural populations, and there is a great deal of empirical evidence for their existence. Because adaptive peaks constrain evolution by natural selection, the ability of populations to shift between adaptive peaks via the SBP may decide the tempo of adaptation in many natural populations.

Summary

This review has emphasized adaptive peaks as a critical feature of the SBP. The reason for this emphasis is two fold. First adaptive peaks are the essential basis of the SBP. Without them drift is just noise in a purely deterministic system. Secondly there is a multiplicity of types of adaptive peaks which may exist and not all of these types will necessarily act identically in the SBP. The evidence that multiple adaptive peaks exist is

persuasive. The evidence for their existence, however, is persuasive mostly by sheer volume however. Examples that suggest the existence of adaptive peaks abound but the clearly delineated fitness effects are rarely available . More concrete examples of multi-peaked fitness effects are needed. This is especially true because the influence of the SBP may be somewhat reliant on the ubiquity of different types of epistasis for fitness.

The search for adaptive peaks should emphasize those areas where peaks are most likely to appear. Population structure is one factor that may preserve multiple adaptive peaks. In order to preserve variation that spans multiple peaks, migration rates between demes must be consistently low enough to prevent interdemic selection. This will prevent the most favorable gene combinations from spreading through a population quickly once a shift has occurred. Other factors which may allow multiple peak polymorphisms to persist include variable selection and introduction to novel environments. If anything less than the most favorable situations for the existence of multiple adaptive peaks are studied then failure to find such epistasis can be claimed as a failure to look in the right place.

Examination of multiple types of genetic models in the SBP leads to the conclusion that population structure is generally critical to the ability of populations to reach new optima. Migration rate between demes, is critical to both the probability of shifts to occur and the ability of shifts to spread throughout a population. Population size is critical to the probability of peak shifts. Variation in migration is likely to increase the efficacy of the process. Even though there are these general conclusions about what conditions are most adaptive, the probability of peak shifts is highly dependent on the genetic models. Some adaptive landscapes will be much more prone to peak shifts than others.

There are additional factors whose effect on the SBP needs to be studied. Variance in phenotype which can temporarily allow the traversing of adaptive valleys could greatly increase the efficacy of the SBP. Variance in phenotype and its effect on fitness surfaces needs empirical study. Finally, the possibility of bridging many of the gaps between micro and macroevolutionary theory should be a logical goal of researchers throughout evolutionary biology. The SBP provides a framework within which those bridges might be built. The empirical evidence for the existence of adaptive peaks as well as the theoretical viability the SBP is strong enough that process is probably of major evolutionary significance.

Chapter 3

A SIMULATION OF WRIGHT'S SHIFTING BALANCE PROCESS: MIGRATION AND THE THREE PHASES

Introduction

Sewall Wright's shifting balance process (SBP) is a mechanism by which complex genetic traits can evolve despite the pressure of individual selection to maintain a historical genetic arrangement (Wright 1982a). A critical concept in the SBP is that of the adaptive topography. In such a topography mean population fitness is dependent on allele frequencies at multiple loci. Wright was interested in topographies with multiple mean fitness optima (peaks) with intervening mean fitness minima (troughs). For this reason gene-gene interactions are of central importance to the SBP (Wright 1977, 1978b, 1982a). Although multiple peaks may arise due to underdominance or multiallelic overdominance at a single locus, Wright saw adaptive topographies as arising primarily from interlocus interactions.

Wright viewed epistasis as pervasive. Kacser and Burns (1981) explicate a mechanism by which epistasis would be as pervasive as dominance for genes whose products function in metabolic chains or networks. Jinks (1983) suggests that epistasis may explain all or most cases of overdominance reported from combining ability experiments. Even for genes with purely additive effects on the phenotype , when the

fitness function is non-linear, phenotypically additive genes will exhibit epistasis for fitness. For example, with optimizing selection, an allele with a positive phenotypic value can have positive or negative fitness effects, depending on the sum of genotypic values for all loci affecting the trait. Because of Wright's interest in epistasis, and because there is mounting evidence for its importance as a mode of gene action, we focus on epistasis as a component of the SBP.

When epistatic interactions exist, the can constrain the ability of a large population to evolve in the direction of the most-fit genotypes. These constraints are the fabled fitness valleys of the multilocus, multipeaked adaptive topography of the type Wright envisioned.

Underlying a multi-peaked adaptive topography is a multi-locus genotypic fitness surface in which the relative fitness of any allele depends on the genotype in which it is manifested (see Provine, 1986, pp. 307-317 for a discussion of the confusion surrounding Wright's original fitness surfaces). The allele frequencies within a (random-mating) deme determine the predominate genotypes within which an allele is manifested. The direction and magnitude of selection acting on epistatically interacting loci is thus determined by the deme's allele frequencies. Likewise, the mean fitness of a deme depends on the frequency of interacting alleles, and this can result in multiple fitness optima in a Wrightian adaptive topography.

In an infinitely large population, evolution by natural selection will bring the population to the local fitness optimum, leaving the remaining fitness surface unexplored. In spatially structured populations with small deme sizes, random genetic drift can result in an exploration of the entire surface. Migration among demes limits the extent of stochastic divergence in allele frequency among demes, and limits the ability of the population as a

whole to move among peaks. To understand the evolutionary process in structured populations, Wright therefore believed that one needed to understand the interactions of random genetic drift, epistatic fitness effects at drifting loci, and the homogenizing effects of migration among demes.

Wright (1977, pg. 455) partitioned the shifting balance process (SBP) into three phases (Wade and Goodnight, 1991). Phase I is the stochastic drift of allele frequencies within demes, which can shift a deme into the attractive domain of an alternative peak. Phase II is the shift of allele frequencies towards the optimum of the 'new' peak through individual selection within the shifted deme. Phase III is the conversion of surrounding demes to a higher peak through immigration from a previously peak-shifted deme (i.e. interdemic selection).

Phase I is most effective with low migration among demes and small effective population size. Phase III occurs most readily with high rates of migration among demes. Only with some intermediate level of migration can both phases I and III occur (Wade and Goodnight, 1991). However, the range of migration rates between 0.0 and 1.0 that allow the SBP remains almost entirely unknown. Wade and Goodnight (1991) found that mean fitness increased at levels of migration below 0.05. However, the genetic causes of changes in mean fitness have not been established. It has been by no means clear that for any given epistatic system there is any constant migration rate which will allow all three phases of the SBP to occur (Hartl and Clark, 1989, pp. 323-324). The purpose of this study was to explore the interaction of migration and the three phases in determining the domain of migration rates for which the SBP is likely. We focus here on the role of migration as a factor governing the time to and frequency of population-wide peak shifts.

When Wright first proposed the SBP (1931), very little was understood about drift, interdemic selection, effective population sizes, or epistatic variation in natural populations. Since then, considerable progress has been made in understanding the potential role of drift in natural populations (Kerr and Wright, 1954, Buri, 1956, Epling, Lewis and Ball, 1960, Bowden, 1982), epistasis in determining fitness differences (Burton 1990, Wade 1985, and for a review see Barker, 1979), and interdemic selection (McCauley and Wade, 1980, Wade, 1977, Wade and McCauley, 1980, 1984, Goodnight, 1985). However, the only empirical test of the SBP as a whole was made by Wade and Goodnight (1991), which indicates that fitness changes in complex traits can be influenced by the population structure in a way that broadly corresponds to the expectations of shifting balance theory.

The necessarily large scale of investigations like that of Wade and Goodnight (1991) slows progress towards an understanding of the role of the SBP in nature. Until more experimental results are available, and as a theoretical underpinning providing increasingly explicit expectations for future empirical studies, a more mechanistic understanding of the interaction of relevant factors is needed.

In order to gauge the relative importance of the shifting balance process we need to know what conditions (if any) are conducive to the SBP, and the ubiquity of those conditions. Because of the complexity of the SBP and the role of stochastic processes, a comprehensive mathematical description has been elusive. Barton and Rouhani (1993) provide the most comprehensive view to date, but because of their need for mathematical tractability their work is limited to purely additive genes or to intralocus allelic interactions. In lieu of a mathematical model we have used a computer simulation to

explore the process. We use a simulation which specifies an individual's genotype, fitness and dispersal behavior. By keeping track of individuals in this way, we have avoided simplifications which prevent insight into the role of migration in the SBP. Our overall goal was to describe the relationship between migration rate and the probability of a population-wide peak shift. We looked for the domain of migration rates in which peak shifts occur with any frequency. We asked if one can expect an optimum migration rate for the SBP under the conditions of any particular population. We also examined the effect of migration rate on the propensity for peak shifts through a combination of phases I and II, and migration rate's effect on phase III. Finally, we examined the relationship between migration rate and the extent of deme extinction/recolonization, and its effect on the propensity for peak shifts.

Methods

The Components of the Simulation

We modeled a diploid, obligately sexual, semelparous species. Density independent mortality (hard selection) took place in the juvenile phase prior to migration and mating. Selection was based on genotype-dependent survival probabilities. Migration was followed by random mating of adults.

A critical aspect of the SBP is the variation of deme (sub-population) size. The variation in deme size (N) allows variation in the absolute number of individuals emigrating from demes (Nm), without requiring differential per-capita migration rates (m) between demes. This can drive the third phase of the SBP (Crow et al., 1990). In addition, variation in deme size will also create variation in the rate of random genetic drift. This

affects phase I as well as altering the relative contribution of immigrant genotypes to the genotype and allele frequencies in the mating pool.

In real populations it is not unreasonable to assume that some type of resource limitation often sets an upper bound (K) on the number of individuals which can survive within a population, and excess reproductive capabilities will tend to force populations towards that K (Verhulst, 1838). Because, in this case, all populations are expected to remain near their carrying capacity, variation in size amongst demes near K must be regenerated each generation by hard selection within demes. In these simulations hard selection associated with the genotypic composition of the demes results in variation in mean fitness among demes.

A finite maximum deme size was imposed by incorporating a carrying capacity (K = 30), and intrinsic growth capabilities into a logistic function ($N_{(t+1)} = N_{(t)} + rN_{(t)}(K-N_{(t)})/K$, r = 1.1). This function determined the maximum number of individuals that could be born into that deme during the next generation ($N_{(t+1)}$). For each offspring, random male and female parents were chosen from within the deme and a randomly drawn copy of the gene at each locus was pulled from each of the chosen parents to produce an offspring (i.e. assortment was fully independent). This procedure was repeated until the necessary ($N_{(t+1)}$) number of offspring were produced. Because all demes have the same r and K, during each generation all demes tend towards the same carrying capacity. This demographic model tends to reduce divergence in deme size based on genotype frequencies and therefore reduce the opportunity for interdemic selection to take place. This is a relatively unfavorable scenario for the SBP.

In the event that at least one individual of each sex was not present that deme was

allowed to go extinct. Recolonization of extinct populations occurred only when individuals of both sexes chanced to migrate into the extinct deme in the same generation.

We simulated a population which contained three different fitness-phenotypes. This allowed variably-sized demes whose average deme size was related to phenotype. Each phenotype had a predefined absolute juvenile survivorship. There was no mortality outside of the juvenile phase. Using two loci, each with two alleles, provided us with nine genotypes. The nine genotypes provided three phenotypes based on the model of epistatic interaction employed by Crow et al. (1990). The average absolute fitnesses were as follows; double homozygote wild type = 0.636, individuals which were heterozygous at one locus but homozygous wild type at the other locus = 0.620, and individuals which had at least one copy of the mutant genotype at each locus = 0.700.

In Crow et al.'s formula the three phenotypes have fitnesses that would be described by the equations:

$$W_1 = 1, \quad W_2 = (1 - s), \quad \text{and } W_3 = (1 + ks)$$

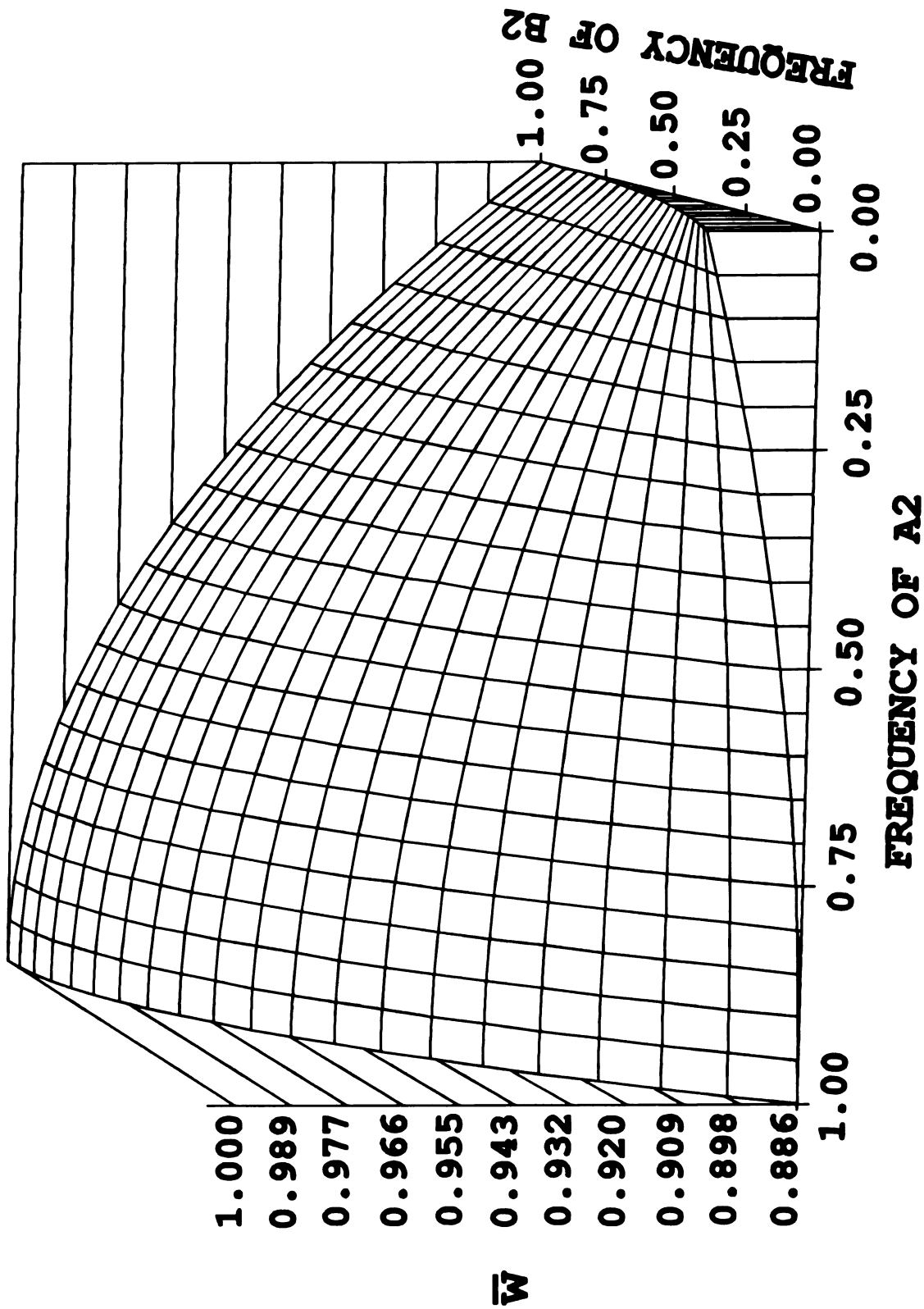
In these simulations s determines the strength of selection and k determines the relative heights of the multiple peaks. For these simulations s was set to .025 and k was set at 4 yielding relative fitnesses of 0.909, 0.886, and 1.000 for the three phenotypes respectively. When random mating and infinite population sizes are assumed this system produces the Wrightian adaptive topography shown in figure 3.1.

These simulations followed single meta-populations (hereafter referred to as populations) which were composed of multiple subpopulations (hereafter termed demes). The migration rates (m) between demes were the per capita probabilities of leaving the parent deme during the dispersal phase. The probability of a given individual migrating to

Figure 3.1 - **Population fitness surface.**

This surface is created by plotting the expected mean population fitness against the frequency of the mutant alleles at 2 loci.

Figure 3.1


FREQUENCY OF A2
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0.50
0.75
1.00
FREQUENCY OF B2
0.00
0.25
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0.75
1.00
M
1.000
0.989
0.977
0.966
0.955
0.943
0.932
0.920
0.909
0.898
0.886

a new deme a given distance away was described by the gamma function:

$\text{Prob}(X) = (m)^X (1-m)$

Where X is the number of demes away the migrant would be traveling. Individuals were allowed to migrate up to 5 demes away from their parent deme. Any individual migrating X demes away was placed in a randomly chosen deme at that distance.

Genetic variation was introduced via mutation. A fixed mutation rate of 5×10^{-6} mutations per copy, per generation, per capita introduced mutants at each locus. This mutation rate was held constant throughout all simulations. For the original simulations only forward mutations were allowed. Subsequent simulations with both forward and back mutations were then run over the range of migration rates in which population wide peak shifts were likely to occur (m = .001, .0025, ..., 0.1).

The initial conditions of the simulated population are as follows: A 10 by 10 matrix of demes was arranged in a torus in order to reduce edge effects. Each deme originally consisted of 15 individuals each of whose gender was randomly chosen. Every individual in the initial population was genotypically identical. Hence all demes were fixed at the local optimum corresponding to the lower peak in figure 3.1. The intent of these simulations was to determine the effect of migration on the movement of demes and eventually populations to the higher peak.

Separate runs were conducted for thirteen migration rates from m = 0.0 to m = 0.5. Thirty trials were run at each migration rate. In addition to the 13 different migration rates, 40 trials were run in a large (K = 3000) panmictic population. This allowed the comparison of different levels of population structure to a totally unstructured population of equivalent size. Each simulation was run for 12000 generations. Data from the 6000th

and 12000th generation were used in the analysis of these simulations.

Analysis of Simulations

The SBP is primarily concerned with events which can alter a population's genotypic composition and therefore its mean fitness. Because the population as a whole is the focal point of investigation our results consist largely of frequencies taken across a population, or of the percentage of trials for which the population falls into a given class. The propensity of a given deme to shift to a higher mean fitness peak is a measure of the combined efficacy of phases I and II of the SBP. We were interested in the propensity for phases I and II to lead to peak shifts. We therefore determined the percentage of trials at given migration rate in which the population had at least one deme shift.

The recruitment scheme used in these simulations tended to produce recruits near carrying capacity. Yet when the per capita migration rate is fixed for all genotypes differences in deme size are a necessary driving force behind the third phase. In order to determine the size difference between demes with different genotypic compositions we placed demes into three different categories based on mean fitness. 'High-peak' demes were defined as demes which were fixed for the highest fitness genotype. 'Low-peak' demes were defined as demes which have an expected mean juvenile fitness above 0.900 but below 1.000. 'Trough' demes were defined as all demes with expected juvenile fitness below 0.900. An ANOVA was performed to test for differences in mean deme size between these deme types.

We were interested in exactly what range of migration rates allowed interdemic selection to convert the entire population to the domain of the higher peak. We therefore calculated, for those trials which had at least one deme shift, the percentage that ended in

the fixation of the higher fitness genotype throughout the population (i.e. the tendency for phase 3 to occur once phases 1 and 2 have occurred) for each migration rate.

One expected characteristic of the shifting balance process is that the global frequency of the highest fitness genotype will depend on the rate of migration between demes. Therefore, the frequency of the highest fitness genotype was determined for each run, from this the mean frequency of the highest fitness genotype was calculated for each migration rate.

The percentage of all trials which led to the fixation of the highest fitness genotype throughout the population is a direct measure of the efficacy of the SBP as a whole. Here the emphasis is on a complete transition from fixation of one genotype to the fixation of another genotype. We therefore calculated the percentage of all 30 populations (i.e. trials) at each migration rate which shifted entirely to the higher adaptive peak.

These simulations allowed the extinction and recolonization of demes. Differential extinction of demes based on genotype, and the differential export of individuals based on deme size are two potentially important sources of interdemic selection which can drive the third phase of the SBP. The mean percent of the original demes remaining at the end of a simulation was compared for simulations which had at least one deme shift versus simulations in which no deme shifts took place. The comparison was made for each migration rate. This provided a comparison of the predominance of extinction over recolonization between populations in which the SBP had been initiated and those in which it had not.

Confidence limits for the data.

For each migration rate (treatment) we performed 30 trials, each of which consisted of 1 population of 100 demes. Because computational constraints restricted the number of trials to 30 per treatment, bootstrapped 95% confidence intervals were estimated by multiple resampling of the available trials. These confidence intervals were computed by bootstrapping 2000 random samples from the 30 trials and excluding the highest and lowest 2.5 percent of the bootstraps. This provides an unbiased estimate of the mean at the cost of biasing the error estimates (Weir 1990). The confidence intervals were universally larger than 95% confidence intervals arrived at using parametric assumptions.

Results

The results of the 6000th generation are qualitatively similar to those from the 12,000th generation. The results of simulations which include back mutation are indistinguishable from those with only forward mutations. Therefore, only results from the 12,000 generation of trials which did not include back mutation are presented.

Results of the Panmixia model

In 40 trials no individuals with the highest fitness genotype were recorded from runs based on a large population with random mating.

Peak shift propensity

Figure 3.2 is a plot of the propensity of demes to shift as a function of migration rate. Demic peak shift propensity is herein defined by the percentage of trails in which at least one deme shifts to the higher fitness peak. In the simulations we ran, migration rates above $m = 0.05$ showed no peak shifts. For all treatments below $m = 0.0075$, zero peak

shift propensity lies outside the 95% confidence intervals.

Prerequisites for phase III

In these simulations the size of a deme depended significantly ($p < 0.0001$) on the expected mean juvenile survivorship of the population (table 3.1). Fitness dependent mean deme size differences occurred despite a recruitment scheme which tended to produce recruits at carrying capacity.

Table 3.1 - The mean number of individuals in demes of different mean fitness.

High peak demes are fixed for the highest fitness genotype, low peak demes Have mean fitness that is less than the high peak demes but equal or greater than the original population mean fitness. trough demes have lower fitness than the original population mean.

Mean Deme Size			
Deme Type	Mean	N	SD
High Peak	26.9528	2973	1.4730
Low Peak	24.3537	17,737	2.6201
Trough	23.4408	152	2.6085

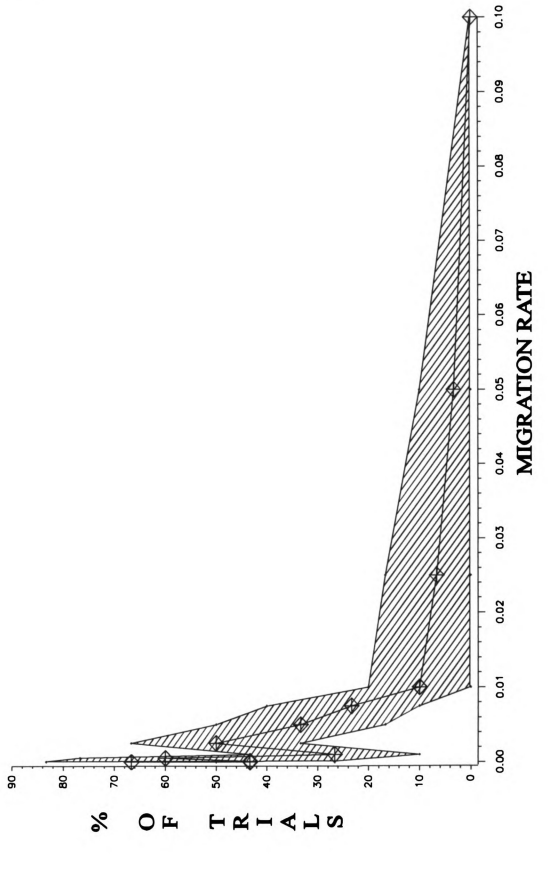
Phase III propensity

Figure 3.3 depicts the percent of trials with a deme shift present that led to the fixation of the higher fitness genotype throughout the population (i.e. the tendency for phase 3 to occur once phases 1 and 2 have occurred). When m is less than or equal to 0.001 phase three never occurred. The tendency for fixation to occur climbs rapidly from 0.0% to 100% between $m = 0.001$ and 0.0075. Above this point, population-wide fixation of genotypes once the first deme has shifted is 100% until the migration rates increase to

Figure 3.2 - The percentage of trials in which at least one deme shifted versus the migration rate.

Shaded areas are 95% confidence intervals.

Figure 3.2


% OF TRIALS
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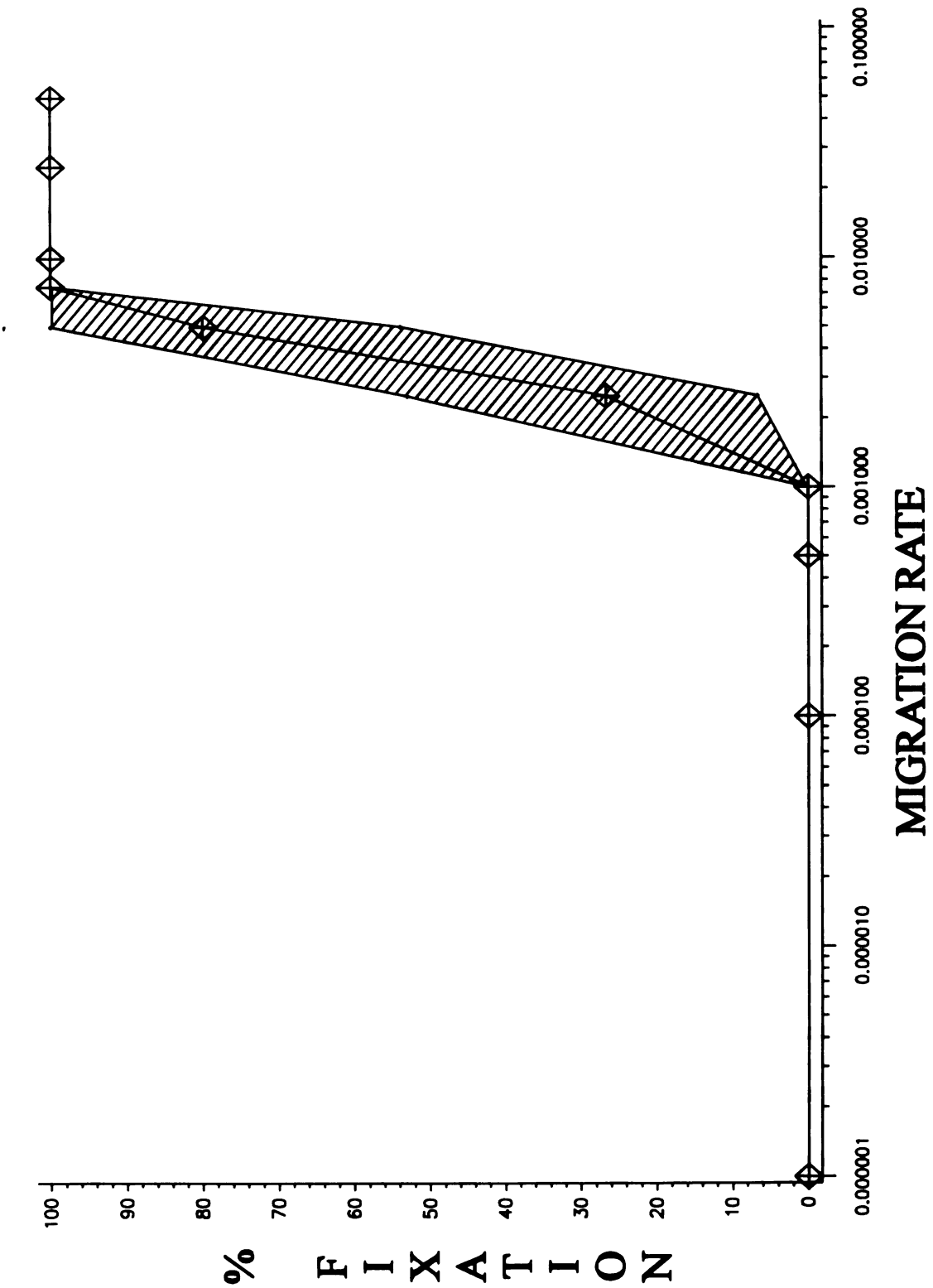
70
60
50
40
30
20
10
0
0.00
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.10
MIGRATION RATE

Figure 3.3 - The percentage of those populations with a deme shift, that experienced a fixation of the highest fitness genotype throughout the entire population versus migration rate.

Shaded areas are 95% confidence intervals.

Figure 3.3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20
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0
0.000001
0.000010
0.000100
0.001000
0.010000
0.100000
MIGRATION RATE

the point where no deme shifts occur (m = 0.05).

SBP as a whole

The frequency of the highest fitness genotype in these simulations was dependent on the migration rate (figure 3.4). The maximum frequency of the highest fitness genotype was 0.35 when m was equal to 0.0025. When m exceeded 0.10 there was a 0.00 frequency of the highest fitness genotype. The frequency of the highest fitness genotype also dropped below 0.10 when the migration rate dropped below 0.0005.

The percentage of trials which lead to the fixation of the highest fitness genotype (figure 3.5) throughout the population is maximized at 30.0 percent fixation of the higher fitness genotype when m = 0.005. No whole-population peak shifts were seen below m = 0.001 or above m = 0.1.

Population size

Figure 3.6 demonstrates that deme extinctions are related to migration rate. Deme extinction rates for trials which have had at least one deme peak shift and trials which have had no peak shifts are similar. However, populations in which demes have shifted have fewer extinctions throughout the range of migration rates.

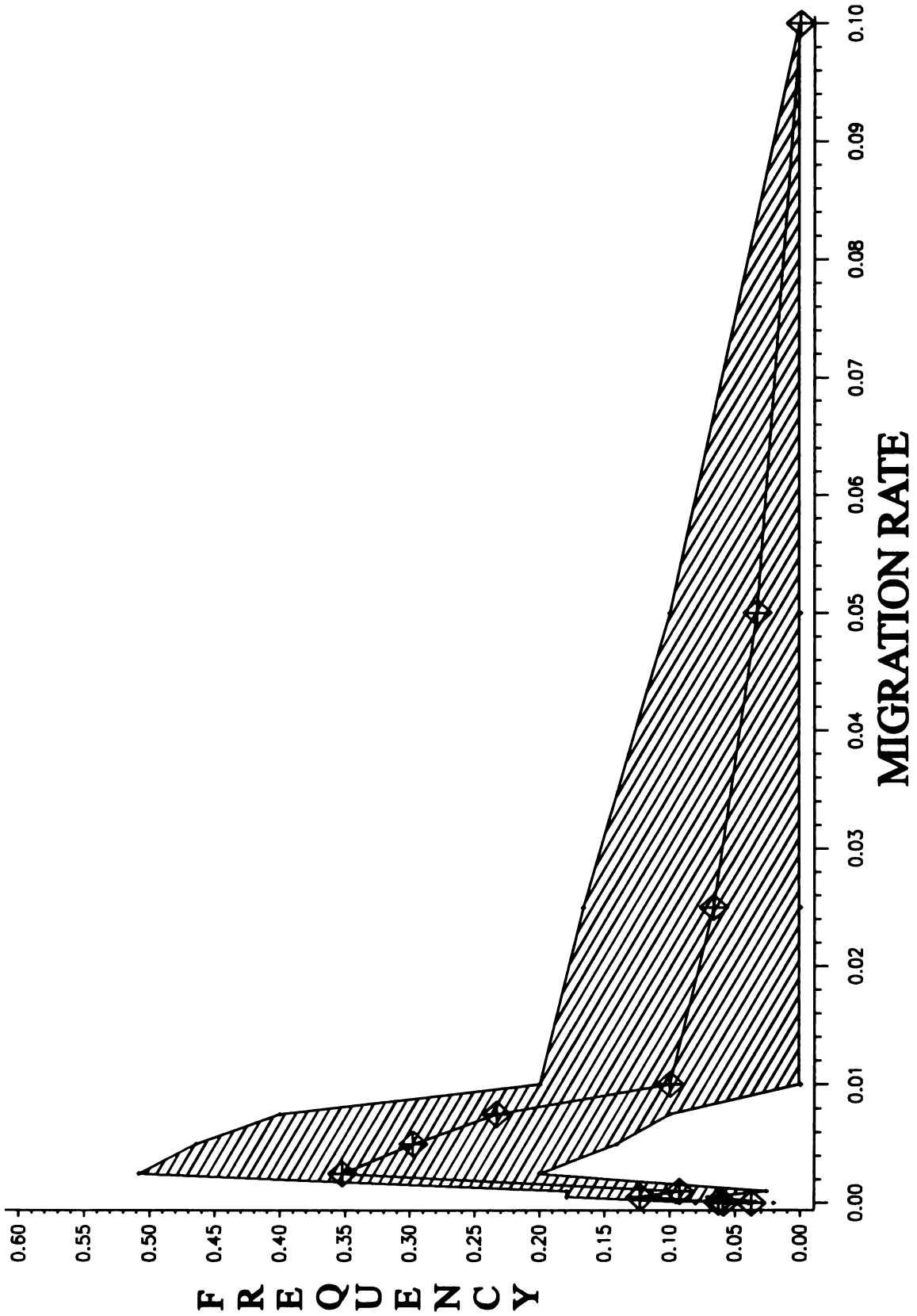
Discussion

A fundamental outcome of the shifting balance process is that when gene interactions affect fitness, population substructuring can increase the mean absolute fitness of a population. This occurs through the interaction of drift, selection, and migration. This study indicates that the migration rates between demes are important in determining genotype frequencies at fitness-related loci when epistasis is involved. These simulations

Figure 3.4 - Frequency of the highest fitness genotype versus migration rate.

Shaded areas are 95% confidence intervals.

Figure 3.4


FREQUENCY
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MIGRATION RATE
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0.07
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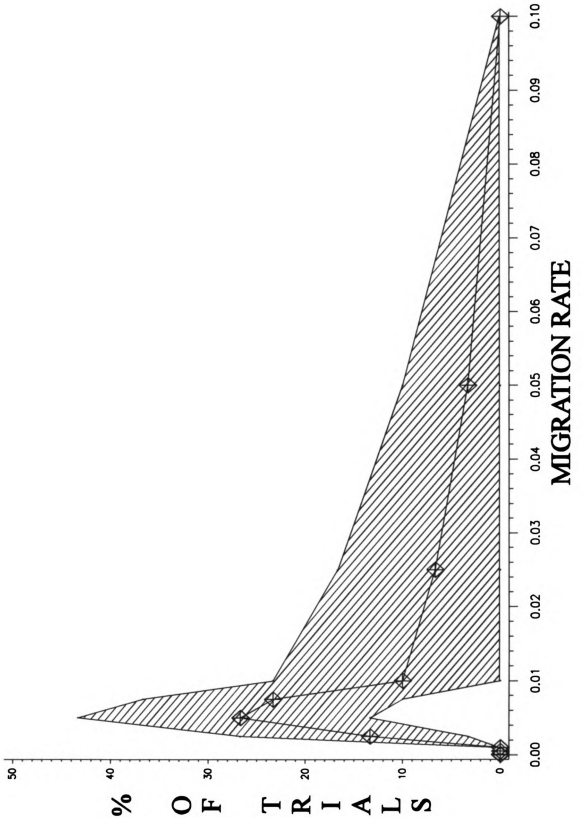
0.10

Figure 3.5 - The percentage of trials in which the highest fitness genotype was fixed throughout the population versus migration rate.

Shaded areas are 95% confidence intervals.

Figure 3.5


% OF TRIALS
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0.04
0.05
0.06
0.07
0.08
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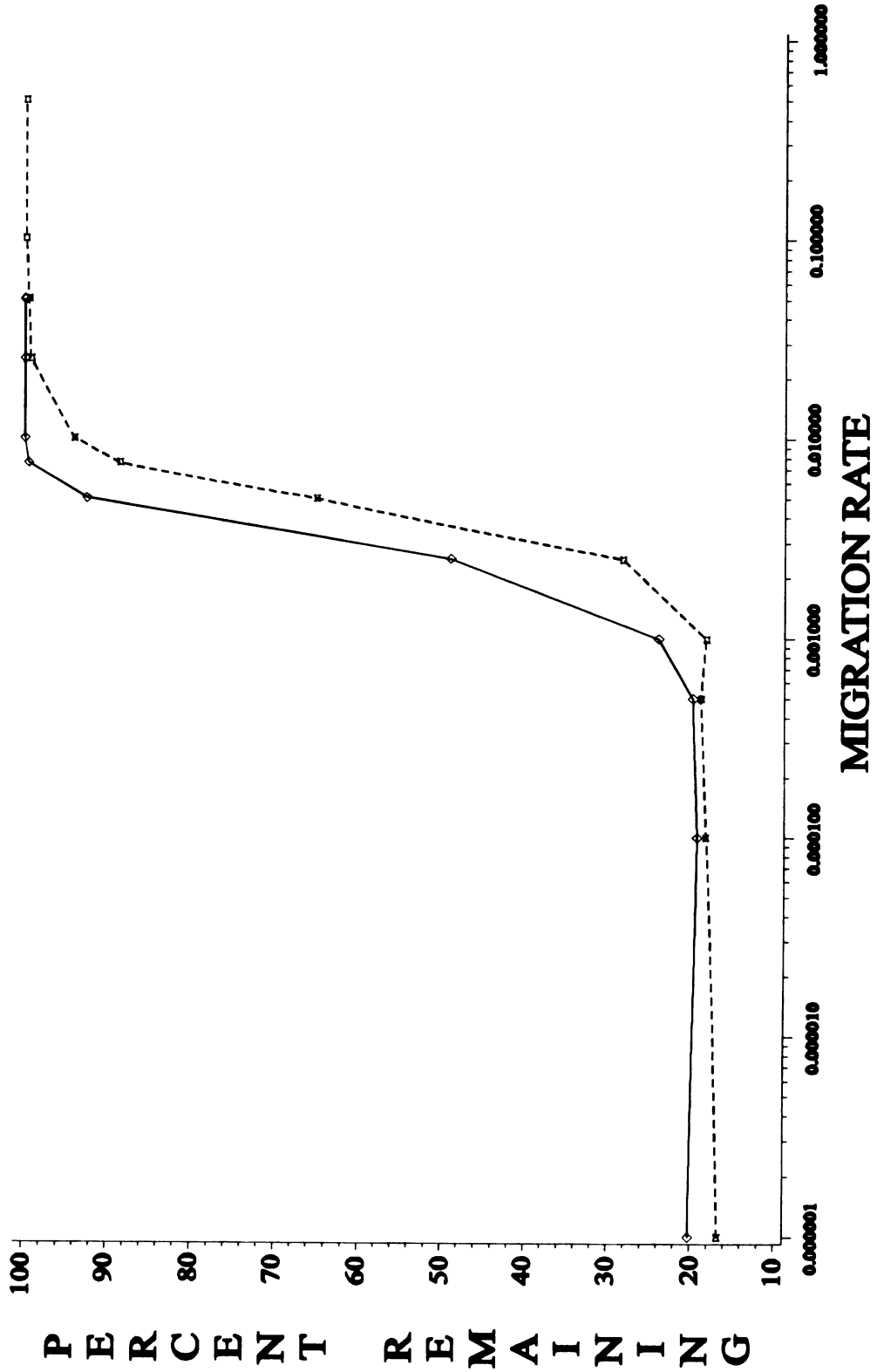
0.10
MIGRATION RATE

Figure 3.6 - Percentage of demes remaining after 12000 generations.

Percentage of demes remaining after 12000 generations versus migration rate for populations which have (diamonds), and have not (squares) had at least one deme which shifted peaks.

Figure 3.6


PERCENT REMAINING
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0.010000
0.100000
1.000000
MIGRATION RATE

demonstrate that there is a non-zero optimum migration rate for the SBP. While the optimum migration rate for the fixation of the highest fitness genotype is low (m = 0.005), extremely low rates of migration actually decrease the frequency of the highest fitness genotype. Below m = 0.0001 population wide fixation of the highest fitness genotype declines to zero. There is actually a range of migration rates in which the shifting balance process is relatively likely to change the genotype frequencies in the direction of increased absolute fitness. In the case of the system examined in these simulations, this range of migration rates does not extend to zero.

The shifting balance process as envisioned by Wright is the result of three phases occurring simultaneously within a deme-structured population. Migration rate influences all three of these phases. Because migration rate has opposing effects on drift and selective diffusion, there is a lower limit on the 'benefit' of lowered migration rate on population fitness.

A number of analytical investigations of the first two phases of shifting balance theory (Lande, 1985, Barton and Rouhani, 1987, Rouhani and Barton, 1987a, 1987b, Charlesworth and Rouhani, 1988) have been made. Recently Barton and Rouhani (1993) have also investigated the three phases combined. All of these studies have centered around a quantitative (i.e. continuously distributed) polygenic trait with optimizing selection. Our simulation did not use a large number of loci each having equal (and additive) effects on the trait of interest.

In the case of a polygenic trait under stabilizing selection we have a fitness difference between two phenotypic peaks of size k with all variation in the phenotype produced by the additive affects of many loci. As mentioned in the introduction, this sets

up epistatic interactions among 'additive loci when the population is near the optimum phenotype. The magnitude of the interaction between two loci is extremely small and all such interactions are equal. This provides quite weak epistasis for fitness between loci, and an astronomical number of approximately optimal combinations of allele frequencies for each of the phenotypic peaks. In a second system the same difference in fitness (H) between two optima is created by a two locus two allele interaction. In this case epistasis for fitness is quite strong and there may only be one set of allelic frequencies which can produce the optimum mean fitness.

Despite these differences, the general conclusions are that peak shifts can occur and that the probability of these peak shifts is dependent on the level of structuring in the population. This agrees with work on quantitative polygenic traits in continuous (Barton and Rouhani, 1993, Rouhani and Barton, 1987b), and discreet populations (Lande, 1985, Barton and Rouhani, 1987, Charlesworth and Rouhani, 1988, Rouhani and Barton 1987a, 1987b). Barton and Rouhani (1993) analyze of all three phases of the SBP for both optimizing selection on an additive polygenic trait and selection against heterozygotes within a locus. They conclude from this that the SBP is likely to produce similar results without regard the type of genetic system which produces an adaptive landscape. Our results support this conclusion by demonstrating that interlocus interactions between a discrete number of loci act in a manner similar to their two models.

Phase III of the shifting balance process has been far less analyzed than the processes underlying phases I and II. Crow et al. (1990) have demonstrated that under a relatively wide set of circumstances phase III would be expected to proceed readily despite the barriers presented by hybrid breakdown. Their model starts with 2 demes at

two different peaks, and examines the effect of migration between the demes on the propensity of the low-peak deme to shift. They conclude that very little migration is necessary to affect the phase III shift. They state that "whatever weaknesses it [SBP] may have are not in the third phase." It should be noted that the strong influence of migration should prevent a deme from shifting to a higher peak when surrounding demes are all on the lower peak. The same sensitivity to migration which makes phase III pervasive over a wide range of migration rates restricts phase I to very low migration rates.

Although our model was restricted to the two locus case, the genetic system used in our simulation was modeled after Crow et al. (1990). As in Crow et al. (1990) our study showed a wide range of migration values over which phase III was effective. All migration rates above 0.001 allowed phase III to occur. This means that in our simulations phase III was frequently successful when m was two orders of magnitude less than s. This occurred despite the following ways in which our simulations differed from Crow et al.'s; 1) the number of demes involved, 2) the initial genotype frequencies, 3) the nature of differences in migrant numbers between demes, 4) the inclusion of phases I, and II.

Barton (1992) has recently presented an alternative interpretation of Crow et al.'s (1990) simulations. Barton points out that differential migration rates between two demes alone can allow the higher migration rate deme to overwhelm the lower migration rate deme's genotype. Given sufficient differences in per capita migration rate, migration and not selective advantage will allow one deme to dominate. However, for two reasons our simulations favor the interpretation of Crow et al. that selection is an important factor. First, we generated all of our variation in genotype frequency and deme size while in the presence of migration. This implies that migration is not successfully swamping out all the

effects of selection and drift. Secondly, because our model included no difference in per capita migration rate between demes, any deme with a novel genotype must have been exporting many fewer individuals than the combined total of all surrounding demes. In this case only the relatively greater resistance of the higher fitness demes to invasion can explain the success of the third phase.

The Crow et al. (1990) model of selective diffusion between demes relies only on difference in migration rates between demes. Our model allows differential extinction and recolonization of demes as well. The ability of remaining demes to re-colonize extinct demes should be more sensitive to migration rate than is the extinction rate of extant demes. This results from the probability of colonization's dependence on two colonists (i.e. a function of m^2) of opposite sex arriving simultaneously. This will lead to the increasing loss of demes to extinction, and a disproportionate decrease in the replacement of these demes by re-colonization as m decreases. This pattern was born out in these simulations (see figure 3.6). A decrease in the number of extant demes at low m will decrease the probability of a peak shift occurring at low migration rates. In addition, as demes go extinct they create holes which are barriers to the exchange of individuals between the remaining demes under isolation by distance or stepping stone migration. For this reason extremely low migration rates probably cause an escalating decrease in the efficacy of the shifting balance as a population persists for long periods without a peak shift.

The mean deme size for low peak demes was less than the mean size for high-peak demes. The extinction rate within populations which had high-peak demes was therefore less than the extinction rate for populations which had no high-peak demes. This allows differential extinction and colonization to become a potential force in the shifting balance

process. The biggest differences in the extinction rate for shifted versus non-shifted demes seem to occur when *m* is less than .025 (see figure 3.6). If different assumptions were made about recolonization, for example, if sets of migrants from a single deme colonized vacant sites, the role of differential recolonization as a cause of interdemic selection could be greatly enhanced. It must be emphasized that the effect of colonization and extinction on the differentiation or homogenization of demes may be quite specific to a given model of propagule movement and composition (Wade and McCauley, 1988).

Periodic fluctuations in migration rate may increase the propensity for fixation of peak shifts throughout a population by decoupling phase III from phase I and II (e.g. Wright 1977, pg. 473). Figure 3.6 demonstrates that there is a threshold below which little or no effective export of high fitness genotypes might be expected. However, it is below this level of migration that one expects to have the highest frequency of demes which will shift. Occasional increases in migration rate could therefore rapidly spread peak shifts which are most likely to have occurred during periods of low migration rate.

Biased migration, fluctuating migration rate, and an increase in the number of demes can all increase the likelihood of the SBP occurring. The model of migration which we have used has been based on equal per capita rates of migration for all demes. The range of migration rates conducive to the shifting balance process should be expanded if migration rate fluctuates, is genotype-sensitive (e.g. *m* increases as deme productivity increases), triggered by extinction, or targeted towards demes with low population density.

The period of stasis between population wide peak shifts may be affected by the number of demes available. Wright envisioned the SBP as being most likely to occur over

tens of thousands of demes (M. J. Wade, pers. comm. 1991). We have included only 100 demes in our simulations. Increasing the number of demes increases the probability of having at least one peak shift occur. This will increase the frequency of population-wide peak shifts at relatively high migration rates.

The generality of any model is limited by assumptions made in the name of tractability. Most of the assumptions made in this analysis were unfavorable for the SBP. Our results can therefore be expanded in that the efficacy of the SBP should be greater under less restrictive assumptions. We discussed above how some more favorable assumptions than those we made would improve the efficacy of the SBP relative to these results. It is more difficult to generalize across different adaptive landscapes (i.e. different genetic models). At present it is impossible to investigate the entire range of possible types of gene interactions. This problem will not be overcome until we have a detailed understanding of what types of epistasis are common in the empirical world. Until such information is available the generality of all models of the SBP will be restricted.

Despite these restrictions we have demonstrated that phases one, two, and three can occur together under one genetic model with very unfavorable population dynamic models. Because we used a genetic model similar to Crow et al. we can also predict that increasing the number of loci involved or decreasing the relative difference in peak heights (k) will increase the critical migration rate necessary for phase three (Crow et al. 1990). Although we can't predict the effect of these factors on phases one and two.

Dominance and the strength of selection should also affect the critical migration rate (Phillips 1993, Crow et al. 1990). In general our model (dominant genotype favored) allows phase three to occur at lower critical migration rates than the reverse model

(recessive genotype favored) (Phillips 1993). The effect of changes in dominance on phase one, however, may be to allow a greater effect of drift due to the ability of the recessive alleles to persist in low peak demes while being protected from selection in heterozygotes. This should increase the range of migration rates which allow peak shifts to occur, so that there may be an offsetting effect of dominance on phases one and three. The effect of changing selection strength on critical migration rates is dependent on the model of dominance used and the recombination rate (Crow et al. 1990).

In conclusion, a simulation relying on a strictly mechanistic model of two epistatic loci in a structured population of finite size demonstrates the efficacy of the shifting balance process. These simulations demonstrate that there is a fundamental conflict between the demands on population structure for success of the first verses the third phase of Wright's theory. The conflicting requirements of these two phases leave a window of migration rates which allow peak shifts to occur and subsequently spread in these simulations. Efficacy of the shifting balance process can therefore be bounded by maximum and minimum migration rates.

Chapter 4

SIMULATION OF THE SHIFTING-BALANCE PROCESS IN OLIGOGENIC TRAITS

Introduction

Sewall Wright's shifting balance process (SBP) is a centerpiece of evolutionary theory in the twentieth century. Its components have been the focus of many recent theoretical studies (Barton 1992; Barton and Rouhani 1993; Barton and Rouhani 1987; Charlesworth and Rouhani 1988; Crow *et al.* 1990; Kirkpatrick 1982; Lande 1985; Moore and Tonsor 1994; Phillips 1993; Rouhani and Barton 1987a; Rouhani and Barton 1987b; Rouhani and Barton 1993; Whitlock 1995). Understanding the SBP may be critical to understanding evolution in a metapopulation context and therefore may have implications for conservation biology (McCauley 1993). The SBP may also allow microevolutionary forces to explain macroevolutionary patterns (Kirkpatrick 1982; Lande 1985; Lande 1986; Wright 1982a; Wright 1982b). Many factors related to the SBP have been investigated theoretically. These include migration rates, population size and founder effect speciation.

Genic interactions and the multi-peaked adaptive landscapes that result from them are fundamental to the SBP. The evidence for the existence of multi-peaked adaptive landscapes is substantial, and there are many ways in which multi-peaked surfaces can manifest themselves (Whitlock *et al.* 1995). Much of the previous theoretical work on SBP has concentrated on additive polygenic traits with multiple phenotypic optima

(Charlesworth and Rouhani 1988; Lande 1985; Phillips 1993; Rouhani and Barton 1987a; Rouhani and Barton 1987b; Rouhani and Barton 1993; Whitlock 1995). Other studies of the SBP have looked at single locus systems or systems of several (oligogenic) loci (Crow, Engles and Denniston 1990; Moore and Tonsor 1994; Phillips 1993; Wright 1941) which produce a multi-peaked surface. A primary goal of this study is to compare the efficacy of the SBP under several oligogenic models in an attempt to determine whether generalizations about the rate of peak shifts across systems are reasonable.

Barton and Rouhani (1993) studied the complete SBP including interdemic selection, and found that both a chromosomal inversion model with homozygote advantage, and polygenic models showed optimal adaptation when the number of migrants (Nm) is slightly less than one. They viewed their results as suggesting "that adaptation via the 'shifting balance' is more effective with disruptive selection on discrete alleles than with disruptive selection on a quantitative trait" (Barton and Rouhani 1993). They also concluded that the pattern of effectiveness of the SBP which they found may be extended to any form of multi-peaked adaptive surface. This conclusion agrees with the simulation results of (Moore and Tonsor 1994) which studied the efficacy of the entire SBP across a wide range of migration rates for a two locus case. They concluded that the entire process occurred readily when Nm ranged between 0.05 and 1.

Barton and Rouhani (1987) had previously compared a single locus models of underdominance to an additive polygenic models of peak shift probabilities in a single deme. They concluded that the probability of adaptive shifts depended mainly on the depth of the adaptive valley. They found that the two models behaved similarly when the deme wide mutation rate ($N\mu$) in the single locus model was high ($N\mu >> 1/4$) but not when it

was low ($N\mu << 1/4$).

Two different types of genetic models have been used in studying the SBP. Nonpolygenic models use relatively few loci with discrete effects on fitness. In this case each locus may have unique interactions with other loci in the production of fitness. In the other major model epistasis is generated by the stabilizing selection acting on a trait with a purely additive polygenic basis. This results in a large number of possible genotypic optima for any given phenotypic optimum. All loci experience weak epistatic interactions when the number of loci is large and the effect of each locus on overall trait value is uniform. This weak and uniform epistasis will be referred to as 'diffuse epistasis' throughout this paper. In the intermediate cases where the number of loci is larger than two and less then a very large number the complete SBP is largely unexplored. Two studies of the third phase of the process have looked at the effects of the number of loci using analytical models (Phillips 1993, and Crow et al. 1990). They have demonstrated that the third phase is more rapid when the number of loci is small (Crow et al. 1990) and when dominant genes are favored (Phillips 1993). In the case of the two locus model of Moore and Tonsor (1994), where the entire SBP was modeled, only one genetic model was explored. Previous studies have left the effectiveness of the complete SBP across oligogenic systems largely unexplored. In this study I attempt to determine how consistent the rates of peak shifts and adaptation are across oligogenic systems. This study investigates the efficacy of the SBP in systems when the expectation for deviations from an additive polygenic model are most likely to occur (i.e. when $N\mu << 1/4$).

Phenotypic and genetic variance are of critical importance to the SBP. Increases in

phenotypic variance alone are capable of inducing peak shifts (Whitlock 1995, Kirkpatrick 1982). In addition, epistatic genes may alter the additive genetic variance when populations are subdivided (Goodnight 1995; Whitlock *et al.* 1993). If the number of loci interacting is large it may be reasonable to approximate drift, and its resulting effect on variance, as a diffusion process. When the number of interacting loci is relatively low or if a relatively few loci affect a trait disproportionately, stochastic changes in variance which are not easily modeled by a diffusion process may be critical.

In the two locus model of Moore and Tonsor (1994) no variation in genotype existed at the onset of the simulations. Variation was generated by mutation during the course of the simulations. Because the genotypic distance between peaks required allelic substitutions at only two loci this did not provide too severe an impediment to the SBP. When substitutions must occur at a greater number of loci, however, mutation may not create new allelic combinations quickly enough to create a detectable rate of peak shifts. If mutation within demes does not create a sufficient number of polymorphic loci then there is still a possibility that migration will create favorable gene combinations by mixing. This however may require migration rates which would overwhelm the local differentiation to the extent that only one peak may be explored. Therefore, the particular shape of the fitness function for a trait may be critical in determining the effectiveness of the SBP.

It is likely that in many cases trait distributions that seem continuous may actually result from the action of relatively few loci (East 1910; Tanksley 1993). Even in traits that have continuous distributions resulting from a large number of interacting loci the majority of genes may be of small effect while a small number of genes have large effects on trait value. Because drift induced variance is critical in the SBP it is not clear how the process

will work in these intermediate cases. This study compares efficacy of the SBP in several genetic systems of two to sixteen loci. Epistasis for fitness is produced by combining nonlinear phenotypic fitness functions for a trait with additive gene action on the same trait. In this regard these models mirror the predominant additive polygenic models of disruptive selection used in most previous studies. They are not, however, systems of large number of loci. They model intermediate numbers of interacting genes. A comparison with the non-additive two locus model of Moore and Tonsor (1994) is also included.

Methods

Computer simulations were used to explore the SBP and extend the models of Moore and Tonsor (1994). Both studies model a diploid, obligate sexual, semelparous species with density independent mortality prior to migration, and mating based on genotype-dependent survival probabilities. Variation in deme size (N) allowed variation in the absolute number of individuals emigrating from demes (Nm), without requiring differential per-capita migration rates (m) between demes. The simulations specified an individual's genotype, fitness and dispersal behavior. Keeping track of individuals in this way avoids simplifications which prevent insight into the SBP.

As in Moore and Tonsor (1994) the simulations followed single meta-populations (hereafter referred to as populations) for 1200 generations. Each population was composed of a 10 by 10 matrix of subpopulations (hereafter referred to as demes) which was arranged in a torus in order to reduce edge effects. The migration rate (m) between demes was the per capita probability of leaving the parent deme during a generation. The probability of a given individual migrating to a new deme a given distance away was

described by the gamma function:

$Prob(X) = (m)^{X(1-m)}$

where X is the number of demes away the migrant would be traveling. Individuals were allowed to migrate up to 5 demes away from their parent deme. Any individual migrating X demes away was placed in a randomly chosen deme at that distance. All simulations were run with $m = .005$. This is near the optimum migration rate in the simulations of Moore and Tonsor (1994).

A finite maximum deme size was imposed by incorporating a carrying capacity (K = 30), and intrinsic growth capabilities into a logistic function ($N_{(t+1)} = N_{(t)} + rN_{(t)}(K-N_{(t)})/K$, r = 1.1). This function determined the maximum number of individuals that could be born into that deme during the next generation ($N_{(t+1)}$). Because all demes had the same r and K, during each generation all demes tended towards the same carrying capacity. Stochastic extinction of demes was allowed and recolonization occurred only when individuals of both sexes migrated into an extinct deme in the same generation.

Sexes were separate and mating was random within demes. Genetic variation was introduced via mutation. A fixed mutation rate of 5×10^{-6} mutations per copy, per generation, per capita introduced mutants at each locus. This mutation rate was held constant throughout all simulations. Forward and back mutation rates were identical throughout these simulations.

Each phenotype in these simulations had a predefined absolute juvenile survivorship. There was no mortality outside of the juvenile phase. Multiple peaks in the genetic adaptive landscape in all of the simulations were generated by the additive effect of multiple loci on a two-peaked phenotypic fitness surface. Each locus had two alleles, one

of which increased trait value, the other of which decreased trait value. All loci had equivalent and additive effects on trait value within a given simulation and there was no dominance of alleles. Epistasis for fitness was generated by applying a nonlinear fitness function to a genotypes phenotype. In all simulations there were two different phenotypic optima separated by an intervening fitness trough.

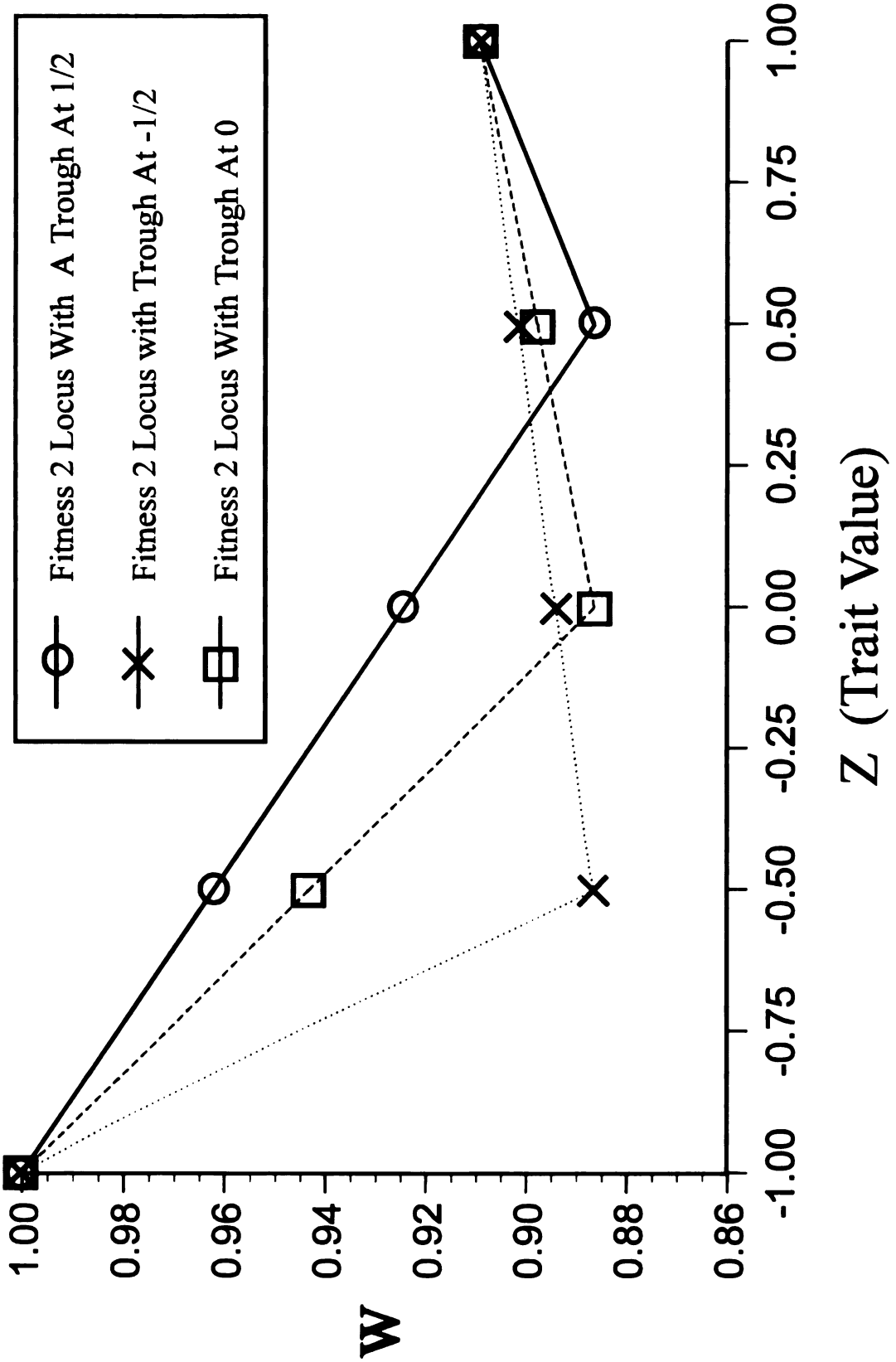
Possible trait values for all simulations were centered on the arbitrary trait value (Z) of 0. The lower of the two phenotypic optima was always at Z = 1, and the higher peak was at Z = -1. The fitness of phenotypes at Z = -1 was constant throughout all the simulations at 0.700. Those individuals with phenotypes at Z = 1 had the same fitness (0.636) throughout all the simulations. The fitness of individuals corresponding to the phenotypic fitness trough was 0.620 throughout the simulations. These values are identical to those in Moore and Tonsor (1994). The decrease in fitness from the optima to the trough was linear in all these simulations.

The focus of this study was a comparison of the effectiveness of the SBP under different genotypic adaptive landscapes. A total of ten different landscapes were compared. Three two locus models were run for comparison with Moore and Tonsor's (1994) model which included dominance of the higher fitness alleles. Dominance of the alleles associated with the higher fitness peak has been shown to greatly increase the propensity for phase three (Phillips 1993). The phenotypic fitness surface for the two locus models is found in figure 4.1. In the two locus model each allele added either -1/2 or 1/2 to the phenotypic value of an individual. The Trough locations for the three models were Z = 1/2, Z = 0 and Z = -1/2. The high and low peaks were located at the extremes of Z = -1 and Z = 1 respectively.

Figure 4.1 - **Phenotypic fitness surface for the 2 locus models.**

Individual fitness is plotted against trait value for 2 locus simulations with trough locations at Z = 1/2, 0 and -1/2.

Figure 4.1


Fitness 2 Locus With A Trough At 1/2
Fitness 2 Locus with Trough At -1/2
Fitness 2 Locus With Trough At 0
W
1.00
0.98
0.96
0.94
0.92
0.90
0.88
0.86
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
Z (Trait Value)

Three different four locus models were run. In all four locus models each allele contributed exactly 1/4 or -1/4 to the phenotype. The optima were again located at the extremes of the phenotypic distribution. The three different four locus models correspond to three different trough locations. The troughs were again located at Z = 1/2, Z = 0 and Z = -1/2 (see figure 4.2). Because the effect of an allelic substitution in the four locus model is half that of a substitution in the two locus model it requires twice as many allelic substitutions to reach an equivalent trough location as it did in the two locus models. As in the two locus models the starting condition was with all individuals on the lower phenotypic optimum, so that all variation between demes in allele frequency had to be generated by mutation and drift within the 12000 generation simulation. The four locus models differs from the two locus model only in the number of allelic substitutions required to change the trait value one unit. This number changed from two to four.

In the eight locus models each allele contributed either 1/4 or -1/4 to the trait value exactly as in the four locus models. Since the optima still remained at Z = 1 and Z = -1 the same number of allelic changes were needed to move between peaks as in four locus model. This allowed an investigation of the effects of changing the number of loci from four to eight loci without increasing the number of allelic substitutions needed to move between peaks. In this model the locations of the optima were not at the extremes of the trait distribution. In the eight locus model the trait distribution extends from -2 to 2. In these models the fitness of individuals dropped off slowly as the optima was surpassed in either the positive or negative direction. This decrease in fitness is linear and symmetrical with the deviation in Z from either $Z_{optimum}$. The maximum reduction in fitness was set at 0.1 (see figure 4.3). As in the four locus models, simulations were followed for 12000

Figure 4.2 - **Phenotypic fitness surface for the 4 locus models.**

Individual fitness is plotted against trait value for 4 locus simulations with trough locations at Z = 1/2, 0 and -1/2.

Figure 4.2

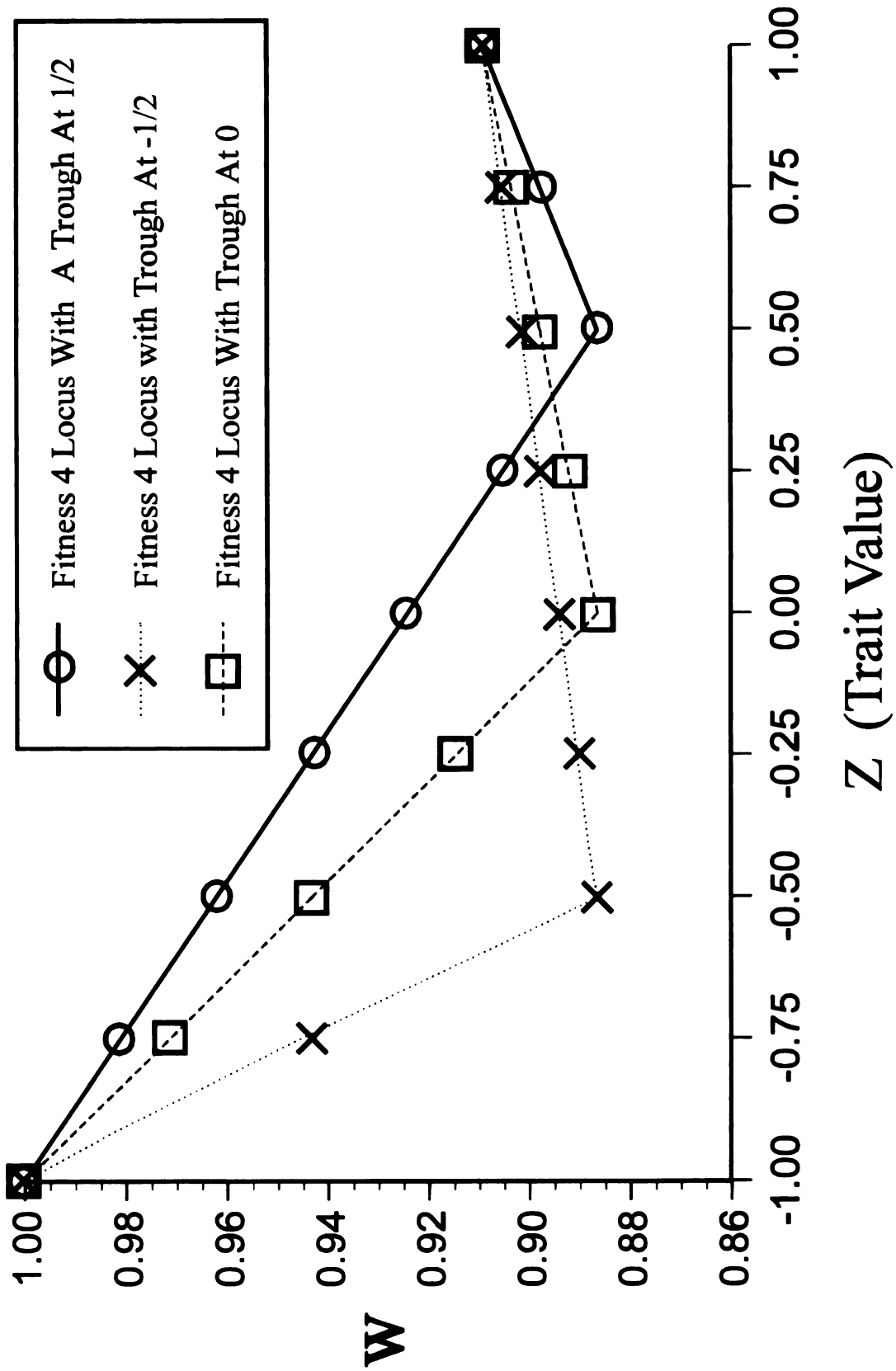
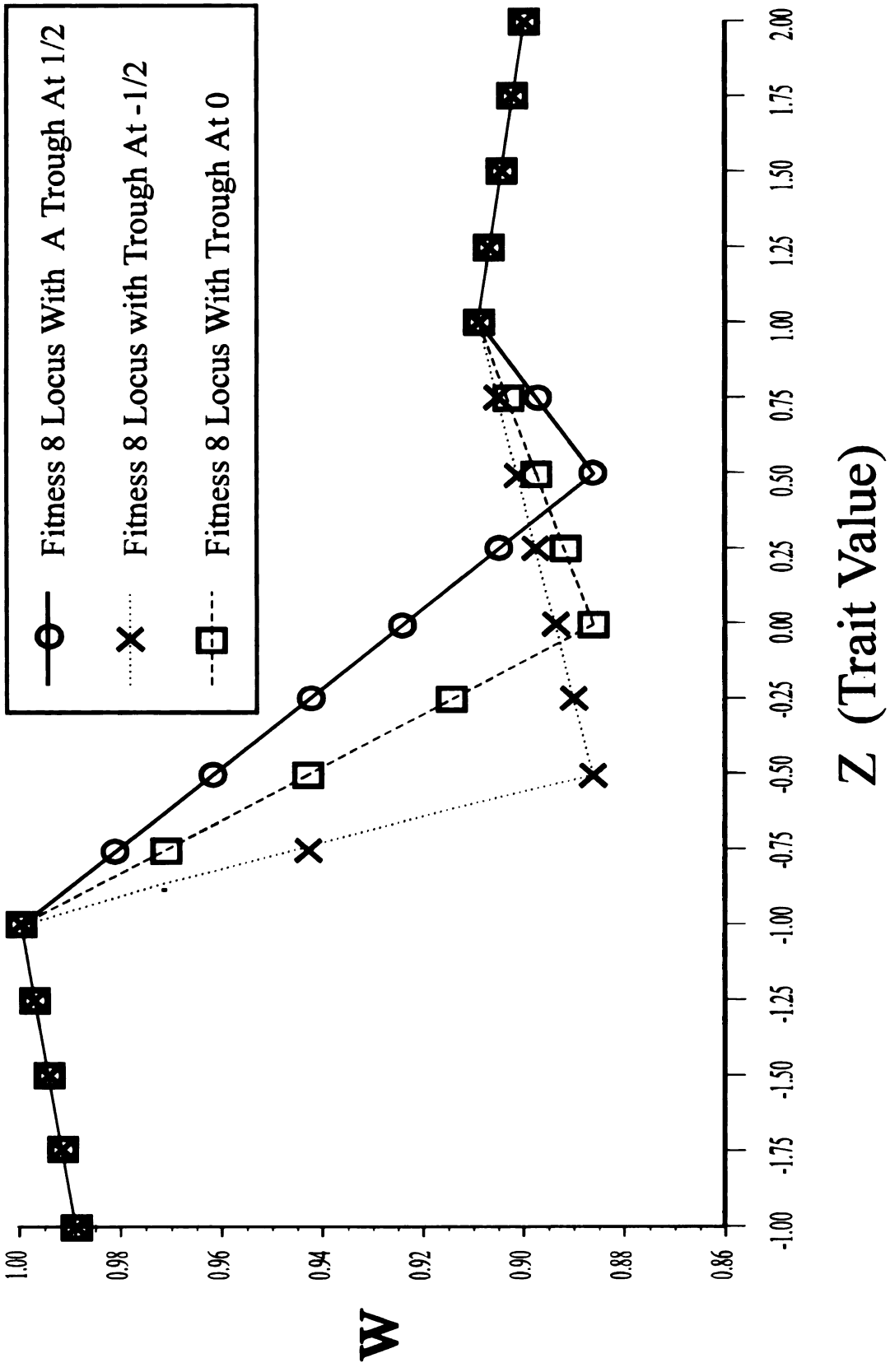

Fitness 4 Locus With A Trough At 1/2
Fitness 4 Locus with Trough At -1/2
Fitness 4 Locus With Trough At 0
W
1.00
0.98
0.96
0.94
0.92
0.90
0.88
0.86
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
Z (Trait Value)

Figure 4.3 - Phenotypic fitness surface for the 8 locus models.

Individual fitness is plotted against trait value for 8 locus simulations with trough locations at Z = 1/2, 0 and -1/2.

Figure 4.3


Fitness 8 Locus With A Trough At 1/2
Fitness 8 Locus with Trough At -1/2
Fitness 8 Locus With Trough At 0
W
1.00
0.98
0.96
0.94
0.92
0.90
0.88
0.86
-1.00
-1.75
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
Z (Trait Value)

generations.

The eight locus models increase the number of loci at which mutation can occur relative to the four locus model. This may influence the rate at which variation between demes builds up. It should also increase the equilibrium variation between demes. These are potentially important factors in the SBP because when variation exists between demes immigrants may carry the new alleles necessary to push a deme into the domain of a new peak. The starting variation between demes in allele frequency may also influence the outcome of the process. This study therefore looked at a variety of different starting conditions.

In the eight locus models multiple genotypes were capable of producing each phenotypic optimum. Because there are multiple genotypic fitness peaks which are hidden in this type of phenotypic optima this will be referred to as 'a diffuse adaptive peak '. There are several different ways the simulations could start on or near the diffuse lower peak, each with possible ramifications for the efficacy of SBP. One simple model would start with the entire population fixed at Z=2, i.e. to the right of the right -most peak.. This would mean that the population started with no variation, but variation was allowed to arise between demes as different loci mutate in different populations and selection drives each of the demes to its individual genotypic optima. Because these models began with the population fixed at an extreme phenotype they will be referred to as the ' phenotypic extreme' models and are labeled as the eight locus 'A' models. Fifty runs were made for each of three trough locations (Z = 1/2, Z = 0, Z = -1/2) as in all other eight locus models.

Another simple model would have the population start fixed at Z = 1 with all

demes fixed for the same alleles. This means that there will be no allelic or phenotypic variation at the start and that selection will tend to keep it that way. Because this model starts at the lower optima and there is no genotypic variance at the start of the trials this model is referred to as the 'no variance' model and labeled the eight locus 'B' model. Runs were performed under the no variance model using the same set of trough locations as in the phenotypic extreme model. An important contrast exists between the phenotypic extreme (A) and the no variance (B) models. In the phenotypic extreme models mutation and selection should act to increase the genetic variance between demes, in the no variance model selection should act to decrease genetic variation between demes.

In the eight locus phenotypic extreme model the time required for the phenotype to evolve to the vicinity of the lower peak will reduce the time available for movement between peaks relative to the no variance model. For this reason simulations were run where all individuals began with a phenotype of two and the mean phenotypic value of the population was monitored. When the mean phenotypic value of the population approached the lower peak the 12000 generation trial was started. No demes shifted to the higher peak until the 12000 generation trial was begun. This allowed variation between demes to arise by the combined action of selection and mutation without including the time necessary to find the lower peaks in the 12000 generations of the run. The first generation in these simulations began when the mean trait value was reduced to $Z = 5/4$. Some demes in these cases could start the trial at or near the phenotypic trough. Demes never, however, started the trial in the domain of the higher peak. Because these trials allowed variance to build up before the start of a trail they are referred to as the 'high variance' models, and are labeled the eight locus 'C' models.

The eight locus 'Skewed variance' (D) model was run with the same starting assumptions as the high variance model but in order to avoid the biasing effect of starting the simulation with some demes on or near the trough no individual deme in these simulations was allowed to have a phenotypic mean any less than that of the lower peak (i.e. 1) at the start of a trial. This means that none of the populations started near the trough. This skews the phenotypic variation away from the troughs but also prevents the bias of the third model. This skewed distribution was created by allowing selection to drive each demes mean trait value towards Z = 1. Once any deme reached Z = 1 truncation selection eliminated all individuals in that deme whose trait value was lower than 1. The truncation selection was removed and the 12000 generation run was started once the population mean dropped from Z = 2 to Z = 5/4.

The final eight locus model started with each deme fixed at Z = 1 as in the no variance model. In this model, however, each deme was fixed for a random set of four loci which were chosen independently of the four loci which are chosen in any other deme. This is the same as allowing each deme to arrive at the lower peak independently (i.e. with out migrational input from other demes) but making sure there is no phenotypic variation at generation 0. Because these models maximize the amount of genetic variance between demes while each deme is fixed at the lower phenotypic optimum they are referred to as the 'maximum variance' (E) models. The different eight locus models are summarized in Table 4.1.

A history of evolutionary and ecological events determines the genetic structure of a population at any point in time. The starting point for each of the eight locus models represents a different set of assumptions about what that history has been. The extreme

fixation (A) model represents a population which has not reached an equilibrium near any peak. This is realistic if the population is experiencing a relatively novel environment. The extreme fixation model also begins with no genetic or phenotypic variation between demes. These two conditions may be fairly common in a population which has recently

Table 4.1 - Summary of the 8 and 16 locus models.

Each 8 and 16 locus model is described by a mnemonic and initial variation. Some natural factors which might induce the pattern of variation are listed. The expected change in genetic variation under the simulated conditions is also listed.

Model	Mnemonic	Initial variation	Possible causes of initial variation pattern	Change in variation
8 Locus A	Extreme Phenotype	None	New niche and range (founder effect)	+++
8 Locus B	No Variation	None	Old niche with new range (founder effect)	Slow Buildup
8 Locus C	High Variation	Moderate	Long term stabilizing selection with migration	- - -
8 Locus D	Skewed Variation	Low	Same as above but with truncating selection agent	- - -
8 Locus E	Maximum Variation	Highest possible	Long term stabilizing selection with no migration	- - -
16 Locus A	Extreme Phenotype	None	New niche and range (founder effect)	+ + +
16 Locus C	High Variation	Moderate	Long term stabilizing selection with migration	- - -
16 Locus E	Maximum Variation	Highest possible	Long term stabilizing selection with no migration	- - -

expanded it's range or niche. This in not an equilibrium state for any natural population, but might be quite common.

The no variance (B) model also starts with no variation between demes, but is at a phenotypic optimum. This is a model which could easily represent a population created by the rapid expansion of a small founding population . In this case the population is near to an equilibrium state for the alleles of interest. This may be a common circumstance when new patches of suitable habitat become available to a population.

The high variance (C) models also starts roughly centered around an equilibrial mean but with variance in both directions around that mean. This situation would result from relatively uniform stabilizing selection across a structured population and is probably a common situation in natural populations. The skewed variance model (D) begins with little variance either genetic or phenotypic and a mean phenotype near equilibrium. When a population has evolved under directional selection up to a truncating point it would temporarily resemble the skewed variance model if the source of truncation selection was suddenly removed exposing a new adaptive surface. This model might easily result when ecological stresses such as competitors, predators, drought or resource limitation are suddenly removed.

The maximum variance (E) model will exist whenever multiple demes are allowed to independently reach equilibrium under a stabilizing selection which is uniform across demes. A maximum amount of genetic variance between demes arises in this model given that all demes are fixed at the lower phenotypic optimum. The one feature in this model which is unlikely in natural populations is the lack of variation within demes as well as the lack of any phenotypic variation between demes. The omission of these types of initial variation will reduce the efficacy of the SBP but allow a separate investigation of the effects of inter-demic variation. The inter-demic variance in the E model represents a type

of variance that will arise under a relatively constant selective environment when demes have been isolated for long periods of time. This is therefore a model which reflects a sudden increase in migration rate. All of the eight locus models are reasonably close to conditions which might frequently arise in natural populations. If there is a fault in the realism of these models it is that they all restrict the variation in predetermined ways in order to increase understanding of the effects of variance.

Three sixteen locus models were run with each allele contributing either 1/8 or -1/8 and trough at 1/2. This preserved the general form of the eight locus models but doubled the number of allelic substitutions necessary to shift between peaks. The sixteen locus 'phenotypic extreme' model was started under the same condition as the eight locus phenotypic extreme model. A sixteen locus 'high variance' model was run which was equivalent to the eight locus 'high variance' model. In that model the 12000 generation run was begun once the population mean dropped to 9/8. The sixteen locus 'maximum variance' model was started under the same conditions as the eight locus maximum variance model. All demes were fixed for a specific allelic combination which resulted in a trait value of -1 but each deme was allowed to find this combination independently.

The propensity of a given deme to shift to a higher mean fitness peak is a measure of the combined efficacy of phases I and II of the SBP. The percentage of trials in which the population had at least one deme shift to the higher peak was therefore recorded in order to compare the efficacy of phases one and two across genetic models. For those trials which had at least one deme shift, the percentage which ended with the entire population having achieved the higher fitness peak (i.e. the tendency for phase 3 to occur once phases 1 and 2 have occurred) was determined for each genetic model. The

percentage of all trials which led to all demes shifting to the highest fitness peak is a direct measure of the efficacy of the SBP as a whole. The percentage of trials for each genetic model in which all demes shifted to the higher adaptive peak was therefore calculated.

Since fixation on the higher adaptive peaks is not expected in these models some standard method of determining when a deme had shifted peaks was needed. For the purposes of this study any deme whose mean fitness was higher than the fitness of a deme fixed on the lower fitness adaptive peak was considered to have shifted peaks.

For each genetic model at least 50 trials were run, each of which consisted of 1 population of 100 demes. Bootstrapped 95% confidence intervals were estimated by multiple resampling of the available trials. These confidence intervals were computed by bootstrapping 2000 random samples from the trials and excluding the highest and lowest 2.5 percent of the bootstraps. Any population with at least 95% of its demes fixed on the high peak was considered to have fixed on the high peak population wide.

Results

The percentage of trials which had at least one peak shift and the percentages of those shifts which spread through the population are listed for each model in table 4.2.

Two locus Models

All the two locus models were reasonably likely to have at least one deme shift to the higher peak within 12000 generations (figure 4.4). As the size of the domain of the higher peak increased the propensity for peak shifts also increased. When the trough was closest to the higher peak at $Z = -1/2$, the percentage of trails with at least one peak shift was 14%. When the trough was at $Z = 0$ this percentage was increased to 22%, and

Table 4.2 - Summary of results from the 2, 4, 8, and 16 locus models.

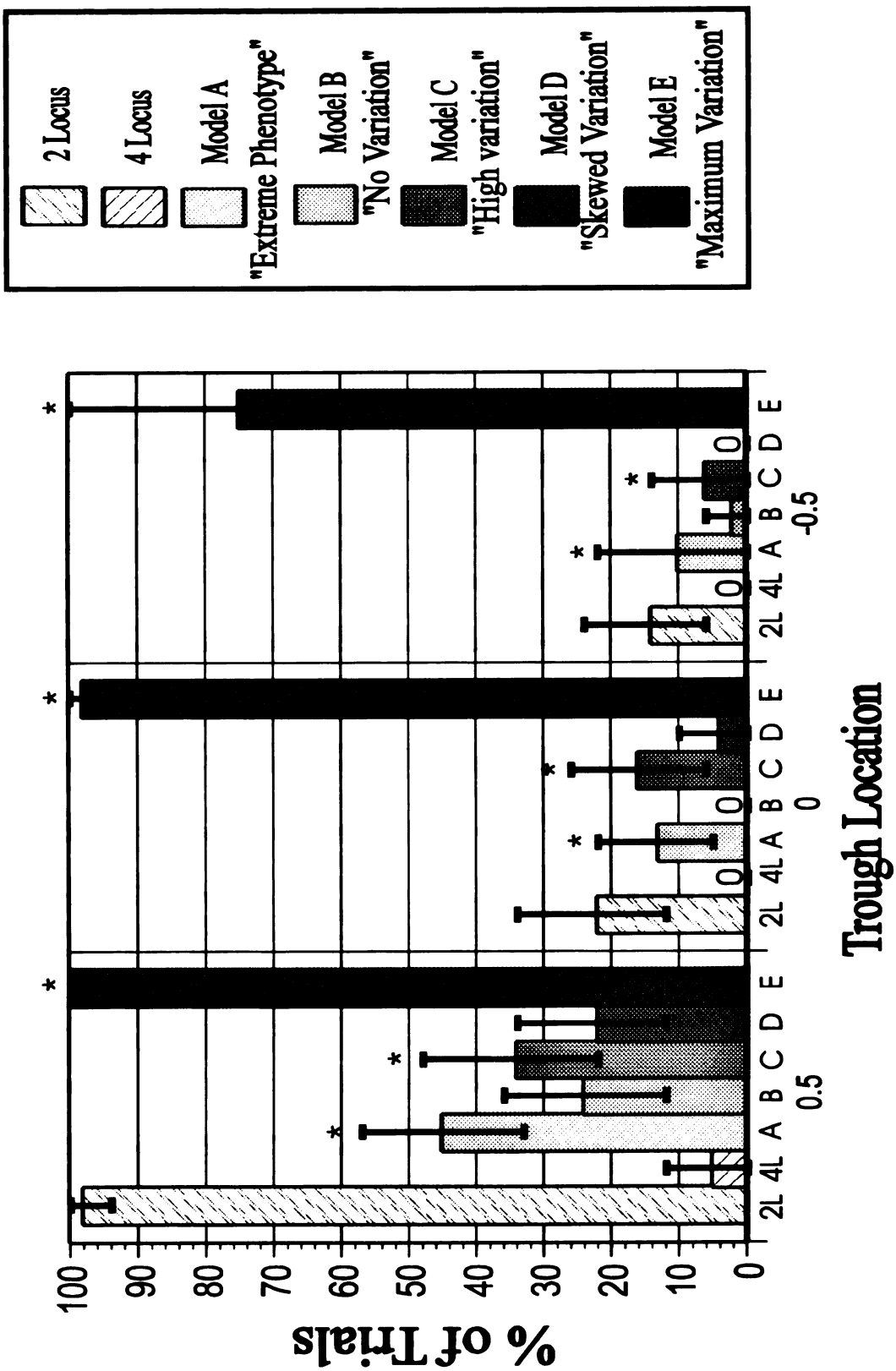
The percentage of trials with at least one shift (% with shift) and the percentage of trials which experienced a peak shift which then had that shift spread throughout the population (% shifts fixed) are listed for each model, and trough locations of Z = 1/2, 0, and -1/2. 16 locus models were only run with a trough location of Z = 1/2.

Model	Trough Location					
	Z = 1/2		Z = 0		Z = -1/2	
	% With a Shift	% Shifts Fixed	% With a Shift	% Shifts Fixed	% With a Shift	% Shifts Fixed
2 locus	98.0	94.0	22.0	64.0	14.0	72.0
4 locus	5.0	0.0	0.0	NA	0.0	NA
8 locus A	45.0	25.9	13.3	0.0	1.7	0.0
8 locus B	24.0	8.3	0.0	NA	2.0	0.0
8 locus C	34.0	64.7	16.0	50.0	6.0	100.0
8 locus D	22.0	36.4	4.0	0.0	0.0	NA
8 locus E	100.0	100.0	98	100.0	70.0	82.9
16 locus A	4.0	0.0	-	-	-	-
16 locus C	0.0	NA	-	-	-	-
16 locus E	20.0	40.0	-	-	-	-

Figure 4.4 - Percentage of trails in which at least one deme shifted.

Listing is by number of loci, variation model and trough location. Error bars represent 95% confidence intervals. Asterisks indicate high variance models.

Figure 4.4


2 Locus
4 Locus
Model A
"Extreme Phenotype"
Model B
"No Variation"
Model C
"High variation"
Model D
"Skewed Variation"
Model E
"Maximum Variation"
% of Trials
100
90
80
70
60
50
40
30
20
10
0
2L 4L A B C D E
0.5
0
-0.5
Trough Location

further increased to 98% when the trough was located at Z = 1/2.

The propensity for phase three to occur, once phase one and two had occurred, was highest (94%) when the trough was nearest to the lower peak at Z = 1/2. At trough locations of Z = 0 or Z = -1/2 the probability of a shift spreading dropped to 64% and 72% respectively. The difference between results when the trough was located at Z = 0 and Z = 1/2 is not significant (see figure 4.4).

Four Locus Models

Very few peak shifts occurred in the four locus models. When the domain of attraction of the higher peak was large (i.e. when the trough was at Z = 1/2) only 5% of trials resulted in a peak shift. On those occasions when there was a shift to the higher peak there was not a spread of that peak shift throughout the population. When the trough was located at Z< 1/2 there were no peak shifts at all.

Eight Locus Models

The eight locus models were generally more prone to peak shifts than the four locus models. This was true for all three trough locations. However, when the trough was at Z = -1/2 or 0 the ability to detect differences between models was poor due to the low number of trials in which shifts occurred. The exception to this was the eight locus maximum variance (E) model which consistently produced the highest number of peak shifts and a very high rate of fixation of those shifts.

The phenotypic extreme (A) and high variance (C) models were more prone to peak shifts at all trough locations than were the no variance (B) and skewed variance (D) models. The high variance (C) model was indistinguishable from the phenotypic extreme (A) model in this regard when the trough was located at 0 or -1/2, but was intermediate

between the phenotypic extreme (A) and the no variance (B) and skewed variance (D) models when the trough was at Z = 1/2 (see figure 4.4). As the trough location moves from 1/2 to -1/2 the probability of a peak shift decreases in all models. This occurred primarily as the trough is moved from Z = 1/2 to Z = 0 (figure 4.3).

Those models which produced many peak shifts were not necessarily the best at fixing those peak shifts (see figure 4.5). In the maximum variance (E), which had the highest percentage of peak shifts at every trough value, 100% of the peak shifts were fixed when the trough was at 1/2 and 0. When the trough was located at Z = -1/2 the percentage of peak shifts that spread throughout the population dropped to approximately 83%. The high variance (C) model, which was effective at producing shifts in all three trough locations, was the next most effective at fixing peak shifts. It fixed approximately 64% of all the peak shifts which occurred. The percentage of peak shifts which spread through the population for the high variance (C) model increased as the domain of the higher peak was reduced (i.e. when the trough was moved towards -1/2). The phenotypic extreme (A), no variance (B) and skewed variance (D) models were less likely to spread peak shifts than the high variance (C) and maximum variance (E) models, and did not result in any fixation across demes when the trough was less than 1/2.

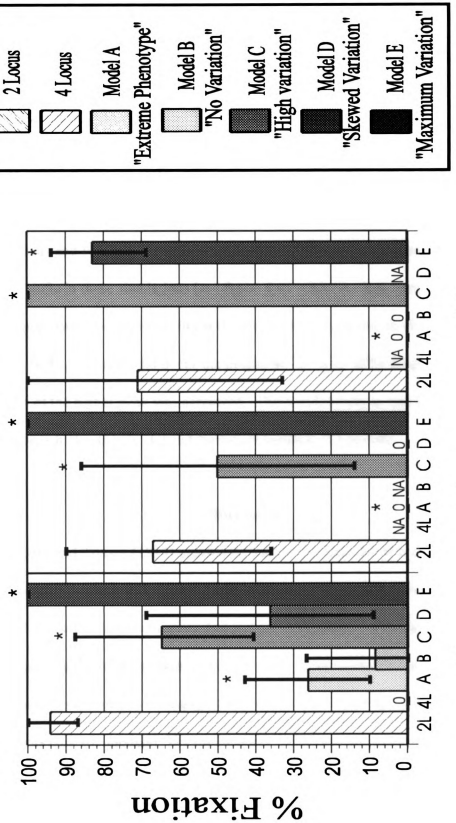
16 Locus Models

The sixteen locus model was much less likely to produce peak shifts than the equivalent eight locus models. The number of trials that produced a peak shift in the sixteen locus phenotypic extreme (A) model was so low (2) that it is impossible to determine whether it is any more or less prone to such shifts than the high variance (C) model in which no peak shifts occurred. The sixteen locus maximum variance (E) model

Figure 4.5 - Percentage of those trails with a deme shift that experienced a fixation of the highest fitness genotype.

Listing is by number of loci, variation model and trough location. Error bars represent 95% confidence intervals. Asterisks indicate high variance models.

Figure 4.5


2 Locus
4 Locus
Model A
"Extreme Phenotype"
Model B
"No Variation"
Model C
"High variation"
Model D
"Skewed Variation"
Model E
"Maximum Variation"
% Fixation
100
90
80
70
60
50
40
30
20
10
0
2L 4L A B C D E
2L 4L A B C D E
2L 4L A B C D E
0
NA 0 NA
0
NA 0 0
NA
0.5
0.0
-0.5
Trough Location

did show an appreciable number (20%) of peak shifts of which a large percentage were fixed (40%). Despite the respectable percentage of shifts fixed in the sixteen locus maximum variance (E) model it still performed poorly in this regard compared with eight locus E model (100% fixation.).

The Overall Efficacy of the SBP

The overall efficacy of the shifting balance process is best measured by the frequency with which the entire population is shifted to the highest peak. In general only the eight locus and two locus models were capable of producing detectable population wide peak shifts in these simulations (see figure 4.6). Only the high variance (E) model produced population wide peak shifts in the sixteen locus systems. In those models where population wide peak shifts did occur the propensity for such shifts dropped off rapidly as the domain of the higher peak was narrowed. This trend, however was less noticeable in the eight locus high variance (C) and maximum variance (E) models.

Discussion

Moore and Tonsor (1994) previously studied the behavior of a similar two locus two allele model across a wide range of migration rates. The epistatic model used by Moore and Tonsor included complete dominance of the alleles on the highest fitness peak. The two locus model with a trough located at $Z = 0$ in this study differs from the model of Moore and Tonsor only with respect to dominance (see figure 4.7 for a comparison of the two locus epistatic models). The no dominance model in this study successfully exported peak shifts only 64 percent of the time, while shifts were successfully exported 80 percent of the time in the Model of Moore and Tonsor. Phillips (1993) and Crow et

Figure 4.6 - The percentage of trials in which the highest fitness genotype was fixed throughout the entire population.

Listing is by number of loci, variation model and trough location. Error bars represent 95% confidence intervals. Asterisks indicate high variance models.

Figure 4.6

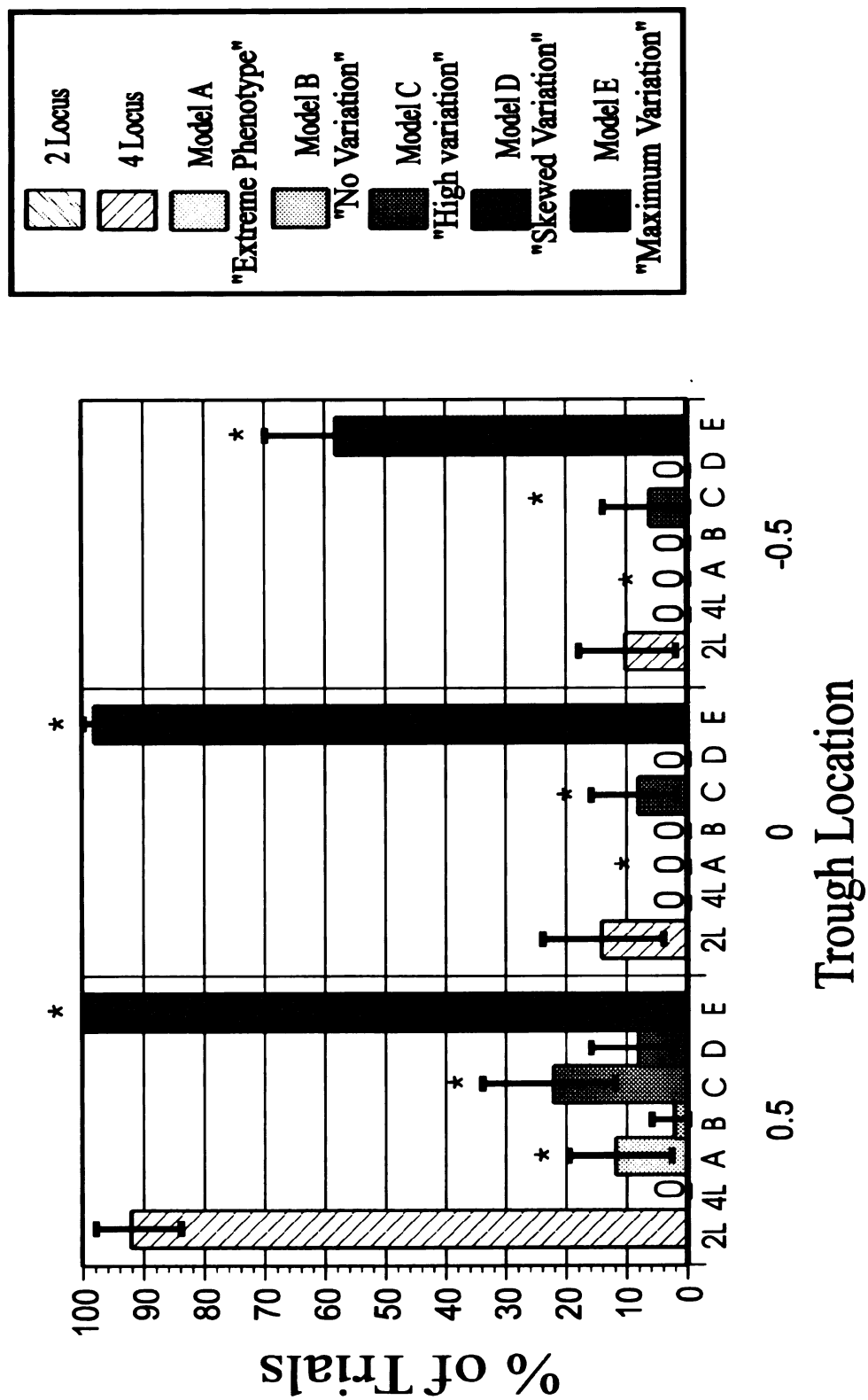

2 Locus
4 Locus
Model A
"Extreme Phenotype"
Model B
"No Variation"
Model C
"High variation"
Model D
"Skewed Variation"
Model E
"Maximum Variation"
% of Trials
100
90
80
70
60
50
40
30
20
10
0
2L 4L A B C D E
0.5
2L 4L A B C D E
0
2L 4L A B C D E
-0.5
Trough Location

Figure 4.7 - The fitness of each possible genotype in four different two locus two allele models.

The model of Moore and Tonsor (1994) is represented by 4.7a, 4.7b - 4.7d represent the models used in this study with troughs at Z = 1/2, 0 and -1/2 respectively.

Figure 4.7

Copies of B2	Copies of A2 = 1	2	3
1	1.00	.962	.925
2	.962	.925	.886
3	.925	.886	.909

Copies of B2	Copies of A2 = 1	2	3
1	1.00	.886	.894
2	.886	.894	.886
3	.894	.886	.909

Copies of B2	Copies of A2 = 1	2	3
1	1.00	1.00	.886
2	1.00	1.00	.886
3	.866	.866	.909

Copies of B2	Copies of A2 = 1	2	3
1	1.00	.943	.886
2	.943	.886	.897
3	.886	.897	.909

al. (1990) have determined that dominance of the alleles which produce the higher peak should lead to a greater propensity for the completion of phase three. This study bears out those findings. In addition an added probability of peak shifts within a deme is seen when dominance of the higher peak alleles is included (table 4.3).

The four locus models in this study were a great deal less likely to experience peak shifts than in the equivalent two locus models (figure 4.4). This is partially due to the increased genotypic drift required in order to enter the new domain of attraction. The two locus model with a trough at Z = -1/2 requires the same number of allelic substitutions as the four locus model with a trough at Z=1/2. The four locus model in that case still had significantly fewer shifts than the two locus model. This indicates that in addition to the slope of the fitness surface on either side of the trough, the number of allelic substitutions needed to push a deme into the domain of a new peak affects the probability of peak shifts. Because the phenotypic fitness surfaces compared between the two locus and the four locus models were exactly alike, the poor performance of the four locus models relative to the two locus models indicates that increasing the number of loci while decreasing the allelic effect on phenotype decreases the probability of peak shifts.

While it would be nice to draw general conclusions about the comparative efficacy of phase three across the two and four locus models the failure to produce peak shifts when the domain of the higher peak was not large (i.e. when the trough was at Z = 0 or less) prevented any exploration of this issue. The four locus model produced no population wide peak shifts when the trough was located at Z = 1/2 while the two locus model with the same trough location spread its peak shifts throughout the population 94 percent of the time. For these simulations the probability of adaptation of the entire

population via peak shifts dropped to zero in the change from the two to the four locus models. The number of allelic substitutions necessary in order to produce a peak shift was increased as the number of loci contributing to the trait increased in these models. The efficacy of the SBP clearly can be reduced by increasing the number of loci contributing to a trait in this situation.

Table 4.3 - The efficacy of the SBP in four different two locus models.

Four models are compared. The Moore and Tonsor (1994) (dominant favored) model is contrasted with the three two locus models in this study (Z = 1/2, 0 or -1/2). The percentage of trials with at least one peak shift (% with a shift), the percentage of peak shifts that then spread throughout the population (%of shifts fixed) and the percentage of trials which end in population wide peak shifts (% trials fixed) are presented for each model.

2 Locus Model	% With a Shift	% of Shifts Fixed	% of Trials Fixed
High Peak Dominant	80	32	26
Trough at Z = 1/2	98	94	92
Trough at Z = 0	22	64	14
Trough at Z = -1/2	14	71	10

The eight locus results indicate that increasing the number of loci that contribute to a trait does not necessarily reduce the efficiency with which the SBP proceeds. The eight locus models clearly were more effective than the four locus models in both producing peak shifts (figure 4.4) and in exporting those new combinations throughout the entire population (figure 4.5). In the eight locus models the relationship between peaks in terms of the number of mutant alleles which need to be substituted in order to affect a change in the domain is the same as in the four locus model. The phenotypic effect of any single

allelic substitution has remained constant between the eight locus and the four locus models. The number of loci contributing to the trait, however has doubled in the eight locus model. The number of loci at which mutations can occur has therefore been doubled. This increased rate at which mutations are introduced will increase the rate at which variation between demes is produced as well as the equilibrium level of variation within and between demes.

Unlike the four locus models, in the eight locus models there are multiple equally fit genetic peaks at the lower phenotypic peak. Selection may therefore maintain new variation as it arises in the 8 locus model. In the four locus models there is only one genetic peak at the lower phenotypic peak and selection will therefore swiftly remove variation between demes. This explains why the four locus models are less likely to experience peak shifts than the two locus, while the eight locus models are more likely to experience peak shifts than the four locus models. Whitlock (1995) has demonstrated that variance and changes in variance can be extremely important in the generation of peak shifts. The general increase in the probability for peak shifts in the eight locus models is probably attributable to this increased variation present.

In the four locus model there is only one most favored genotype within the domain of either peak. In this case selection will tend to reduce the variation between demes as well as within demes. This is not always the case in the eight locus models where there are multiple equally favored genotypes within the domain of either phenotypic peak. With these diffuse phenotypic peaks selection can act either to increase or to decrease the variance between demes. If a population consists of demes which are all close to the same genetic optimum then selection should push all those demes towards the same genetic

optimum. This tends to reduce the variance between demes. This model is the starting condition for the eight locus no variance (B) models in these simulations. If however the demes are uniformly fixed for the same genotype which is far from optimum, then selection will favor those beneficial allelic substitutions which arise locally and selection will increase the variance between demes. In the eight locus A, C, D and E models selection should tend to increase the between-deme genetic variance relative to the no variance (B) model. Because migration between demes homogenizes alleles across demes the lower the migration rate the more selection will tend to increase the variance between demes. The eight locus maximum variance (E) simulations model the highest genetic variance between demes since all demes rest on independent genetic optima at the beginning of the simulation. This is the expectation for populations which have adapted without migration between demes.

The A, C and D models should have lower variance between demes because migration is always homogenizing the variance across demes. The high variance (C) and skewed variance (D) models restrict access to the higher peak until the entire population's mean is near the lower peak. This allows migration to reduce the between demes genetic variance so that these models have lower expected genetic variance at generation 1 than the maximum variance (E) model. Because of the restrictions on phenotypic variance the skewed variance (D) models require more generations to reach their starting conditions. The genetic variance between demes should therefore be lower in those models than in the high variance (C) models.

Ultimately the difference between the phenotypic extreme (A) models and both the high variance (C) and skewed variance (D) models is what happens during migration. In

all three models the migration events homogenize the alleles across demes. In the high variance (C) and skewed variance (D) models migration when the lower peaks are being found only homogenizes demes. Any phenotypic variation beyond the lower peak and towards the higher peak which is generated is removed by truncation selection. The higher peak only exists after the entire population mean reaches the lower peak in the high variance (C) and skewed variance (D) models. In the phenotypic extreme (A) models migration between demes will always create favored genotypes if hybrid individuals fall far enough into the domain of the higher peak. This seems to be a realistic model and it allows for greater variance than the high variance (C) and skewed variance (D) models. However the phenotypic extreme (A) model allows very little time for the exploration of new peaks. The maximum variance (E) model should have the highest between-deme variance initially, followed by the high variance (C) and skewed variance (D) models respectively. The phenotypic extreme (A) and no variance (B) models both begin with no genetic variance between demes. The phenotypic extreme (A) model, however, should generate higher levels of variance than even the high variance (C) model eventually. The no variance (B) model should remain low in genetic variance relative to all the other eight locus models throughout each 12000 generation run.

Migration between demes can introduce new alleles to demes. When the genetic variance between demes is high this effect is much more important in creating new allelic combinations than is the introduction of new alleles via mutation. Only at very small migration rates is mutation likely to dominate over migration in creating new allelic combinations. The effect of these new allelic combinations is to increase phenotypic and genetic variance temporarily within a deme. These periods of higher phenotypic variance

are when peak shifts are most likely to occur (Whitlock 1995). The eight locus models, which had the highest expected variance were the ones most likely to produce peak shifts. The probability was highest for the maximum variance (E) models followed by the phenotypic extreme (A) and high variance (C) models with the no genetic variance (B) and skewed variance (D) models both producing relatively few shifts (figure 4.4). These simulations therefore confirm the importance of variance induced peak shifts (Whitlock 1995) in the SBP.

Of the three models that were most effective at producing peak shifts (E, A, C) the phenotypic extreme (A) model proved the least effective at phase three of the SBP. The generations needed to create variation in this model most likely do not leave enough time for phase three to be completed. The rate of phase three has been shown to depend on the number of loci involved (Crow. et al. 1990). With eight loci and many generations passing before a peak shift occurs the phenotypic extreme (A) model may often be unable to successfully reach the higher peak throughout the population. When peak shifts do actually occur the phenotypic extreme (A) models are however, still significantly more effective at spreading peak shifts throughout the population than the no variance (B) models (see figure 4.4). The maximum variance models (E) were almost always successful at spreading peak shifts.

The sixteen locus models were run with all parameters exactly the same as their corresponding eight locus models except that each allelic substitution had half as much phenotypic effect as it did in the eight locus models. The sixteen locus models were dramatically less likely to produce peak shifts and to have those shifts propagate throughout the population (see table 4.2). These results indicate that the number of loci is

important in determining the probability of a peak shift occurring in a given amount of time. While this result mirrors the comparison of the two and four locus models it is much more surprising. Unlike the two and four locus models which have only two genetic optima the eight and sixteen locus models both contain many genetic optima. The sixteen locus models used allow genetic variance to build up between demes using exactly the same mechanisms to generate that variance as in the eight locus models. Despite this the sixteen locus model was much less effective in finding the optimal phenotype in the 12000 generations of these simulations. It therefore may be that in general, with a given fitness function, increasing the number of loci contributing to a trait may reduce the probability of a peak shift.

Barton and Rouhani (1987) analytically compared the behavior of single locus models and additive polygenic models of the SBP. They found that two types of models had similar peak shift probabilities when the per population mutation rates were high ($N\mu >> 1/4$) but not when they were low. In the present study two through sixteen locus models of the SBP with a high mutation rate indicate that the efficacy of the process is highly dependent on the particular model. The probability of peak shifts seems to be dependent on both the number of loci involved and the amount of genetic variance which is likely to be generated within and between demes. Of the factors investigated by Barton and Rouhani (1987) peak shifts depended mainly on the depth of the adaptive valley. These simulations, in which the depth of the valley was not varied, indicate that the relative size of the domains of the higher and lower peaks also can strongly influence the probability of peak shifts. Models with troughs that were closer to the lower peak were in general much more likely to experience peak shifts (see table 4.2). Rouhani and Barton

(1987) found that in a polygenic character peak shifts that require crossing a trough that is more than a few times the square root of the additive genetic variance of the parent population may be unlikely in founder populations. In these simulations the affect of allelic substitution is clearly a factor in the balance between the distance to a new domain and the average amount of variation.

Previous analysis of phase three by Crow et al. (1990) predicts that the rate at which phase three occurs is increased as the number of loci is increased. The trend in these simulations generally fits those predictions. Dominance of the higher fitness alleles improves the rate of the third phase in the simulations of Moore and Tonsor (1994) relative to these simulations. This agrees with the predictions of Phillips (1993) and Crow et al. (1990). In addition the dominance effects seem to be part of a generally increased efficacy of the third phase when the domain of attraction for the higher fitness peak is increased. In this study models with troughs closer to the low peak in general were more effective at spreading peak shifts (see figure 4.4). However, for those eight locus simulations where the probability of peak shifts was highest (models E and C) the effectiveness of phase three remained constant or even increased as the domain of the higher peak was reduced.

In comparing single locus and polygenic models of the SBP Barton and Rouhani (1993) concluded that the most favorable conditions for the SBP probably remain constant across genetic systems. This conclusion is reaffirmed by the two locus model of Moore and Tonsor (1994). It is important to note, however, that while the optimal population structure for most genetic systems may be relatively consistent, the actual effectiveness of the process may vary widely between genetic models. In these simulations the efficacy of

the SBP as a whole was highly variable between models (figure 4.5).

The genetic variation which was present at the beginning of each 12000 generation trial seems to have had a large effect on the probability of a global peak shift. Despite this, probabilities of global peak shifts ranged from 0.0% to 92.1% when there was no initial genetic variance. The shape of the fitness surface is therefore important in determining the probability of a global peak shift. The phenotypic effect of each allelic substitution in the four and eight locus models was equivalent. The only difference between these models was the capability for the production of phenotypes which are not intermediate between the optima. A comparison of the four locus and eight locus models demonstrates that models of disruptive selection may be much more conducive to the SBP when the optima are not on the phenotypic extremes. The eight locus models, where the optima are not on the phenotypic extremes, allow the generation of greater variation between demes which increases the probability of peak shifts.

As predicted by Barton and Rouhani (1993), as models moved from several discrete loci towards a polygenic trait the probability of population wide peak shifts decreases if all other factors are held constant. Clearly the shape of the fitness function alone does not determine the probability of a peak shift. Not surprisingly, however, models with larger domains of attraction for the higher peak had higher probabilities of a peak shift in these simulations when all other factors were held constant. When all other factors were not held constant some systems of sixteen loci produced global peak shifts readily as did some models in which the domain of attraction for the higher peak was small. Many models produced peak shifts in the 12000 generations that were simulated.

The eight locus models were intended to investigate the effect of different amounts

of initial variance on the SBP. A comparison of the maximum variance (E) model with the other models also gives some insight into the effect of variable migration rates on the SBP. In effect the maximum variance (E) model represents an extreme model where total lack of migration allows each deme to independently find the lower adaptive peak, and subsequent increases in migration rate allow mixing of alleles. It has previously been suggested that variable migration rates can increase the effectiveness of the SBP by segregating the first and second phase which occur best at very low migration rates from the third phase which occurs only at higher migration rates (Moore and Tonsor 1994). The results of the maximum variance (E) model when compared to the other eight locus models suggest that even when phase 1 and 2 have not occurred during periods of very low migration, the variance between demes which results from low gene flow may be critical. When migration between the differentiated demes is reinitiated it creates new gene combinations which seem to trigger peak shifts with a very high frequency as predicted by Whitlock (1993). Ultimately, high variance is only needed for brief periods in order to trigger peak shifts. Variable migration rates allow variance to build between demes during low migration periods and to appear within demes during periods of high migration.

While model E demonstrates how variation of migration rates might influence the probability of peak shifts, the extreme nature of the model seems limiting. The extreme variance model is, however, one of many realistic ecological scenarios. The amount of phenotypic variation within a population is a product of the isolation of local breeding units, the history of selection, and past colonization patterns. Such ecological factors in natural populations are dynamic. The ecological history of a lineage may result in a population which is in any of the circumstances listed in table 4.1. The evolutionary

consequences of that history extend into the future by influencing the probability of peak shifts between adaptive peaks (table 4.2).

In conclusion this study indicates that the overall efficacy of the SBP is not consistent across genetic models. Increasing the number of loci contributing to a trait with a specific fitness surface can decrease the rate at which the SBP progresses. This is only true, however, within a given fitness surface. The shape of the fitness surface itself, through its effect on variance, can override the changes in the number of loci acting on the trait. The variance within and between demes is determined by the selective surface and the phenotypic and genotypic starting point of the demes within a population. Higher genetic variance triggers peak shifts. Ecological conditions which produce periodic increases in variance increase the likelihood of adaptation via the SBP. Specifically the history of migration between demes alters the SBP. Overall the probability of peak shifts in these simulation was high enough to indicate that the SBP may often be an important evolutionary factor.

Chapter 5

FLUCTUATING MIGRATION AND THE SHIFTING BALANCE PROCESS

Introduction

Recent work on the shifting balance process (SBP) suggests that the process is effective at producing meta-populational shifts between adaptive peaks under certain circumstances (Barton and Rouhani 1993; Moore 1996 chapter 3; Moore and Tonsor 1994). The SBP requires a balance of factors that may severely restrict the conditions under which the process increases the rate of adaptive evolution. Specifically migration rates that are optimal for the spread of peak shifts are too high to allow many peak shifts to occur. Consequently the SBP only seems to be an effective means of adaptive evolution over a small range of N*m* values (Barton and Rouhani 1993; Moore and Tonsor 1994). However, it has been suggested that periodic changes in migration rates may greatly enhance the efficacy of the process by decoupling the first and third phases (Moore 1996 chapter 3; Moore and Tonsor 1994, Slatkin 1985).

Moore and Tonsor (1994) and Barton and Rouhani (1993) found that a N*m* of a little less than one provided the optimal level of population structure for the SBP. However, the probability of peak shifts within a deme increases dramatically when N*m* is decreased by several orders of magnitude below one (Moore and Tonsor 1994). At very low levels of gene flow demes can effectively drift into the domain of new peaks.

Subsequent periods of high migration should then allow the spread of favorable allele combinations throughout a population. In this way fluctuations in migration rate may decouple the first and third phases of the SBP.

Fluctuations in migration rate may also trigger peak shifts through its effect on the distribution of variance within and among demes. Increases in phenotypic variance are a potentially important factor in creating peak shifts (Whitlock 1995). Migration rates and effective population sizes determine the distribution of genetic variation within and among demes. Low migration rates allow the buildup of genetic variation among demes via drift. Subsequent increases in migration may then allow variation to be redistributed so that the variation within many demes is increased. Even when the mean phenotype of a deme is not altered by drift, genetic variation among demes can build up over time in multilocus models of optimizing selection. If sufficient genetic variation among demes develops, subsequent migration may then trigger peak shifts between phenotypic optima (Moore, 1996 chapter 3). If the migration rates remain high peak shifts spread readily between demes.

Stochastic variation around a mean migration rate has been incorporated in previous models of the SBP (Moore and Tonsor 1994, Barton and Rouhani 1993). Those models have not included large fluctuations in mean migration rates. Wright thought that the SBP was likely to occur over long periods (Wright 1982a; Wright 1982b). Biotic and abiotic factors can radically alter the distribution and movements of organisms both over a small number of generations and over geologic time. Because migration can change over geologic time (Cronin and Schneider 1990; Van der Spoel 1994) and because geologic time scales are involved in the SBP large changes in mean migration rate have the

potential to alter the efficacy of the SBP. This study includes fluctuations in migration rate on several time scales into a model of the SBP. The purpose of this study is two-fold. First it is intended to determine the extent to which fluctuations in migration might influence adaptive evolution by decoupling phase one from phase three of the SBP. The study also investigates the patterns of fluctuations in migration rate which allow such decoupling to take place.

Methods

In order to compare the SBP with fluctuating migration to the SBP with a constant expected migration rate Monte Carlo simulations were used. This study extends the models of Moore and Tonsor (1994). Both studies model a diploid, obligate sexual, semelparous species. Density independent mortality before migration and mating was based on genotype-dependent survival probabilities. The model tracked individual genotype, fitness and dispersal behavior. Variation in deme size (N) allowed variation in the absolute number of individuals emigrating from demes (Nm), without requiring differential per-capita migration rates (m) between demes.

As in Moore and Tonsor (1994) the simulations followed single meta-populations (hereafter called populations) for 12000 generations. Each population was composed of a 10 by 10 matrix of subpopulations (demes) which was arranged in a torus to reduce edge effects. The migration rate (m) between demes was the per capita probability of leaving the parent deme during a generation. Because of the probabilistic nature of the model there is expected to be some stochastic variation around m even in those models that had no intentional fluctuations. The probability of a given individual migrating to a location X

demes away was described by the gamma function: Prob(X) = $(m)^{X(1-m)}$. Any individual migrating X demes away was placed in a randomly chosen deme at that distance. Simulations were run with 9 different constant migration rates between m = 0.0005 and m = 0.05. These constant migration rate simulations provided a point of comparison for models with fluctuating migration rates.

It may take substantial time for demes to drift into the domain of a new peak. The drift phase is most likely to occur at low migration rates. Under subsequent high migration rates demes that have drifted will quickly return to the vicinity of a traditional peak. It was therefore important to look at the period of the high migration as well as the period of the low migration rate as possible factors influencing the adaptive efficiency of the SBP. In the fluctuating migration rate simulations the initial migration rate was always m = 0.0005. This migration rate was used because it produced no population wide peak shifts in the simulations of Moore and Tonsor (1994) despite allowing demes to experience peak shifts. After a fixed period the migration rate was increased to m = .05. A migration rate of m = 0.05 prevented peak shifts from occurring within demes in a previous study (Moore and Tonsor, 1994). Three different high migration rate models were used. High migration rates lasted for periods of 10, 100 or 1000 generations depending on the model. Each of those three models was run with several different periods of low migration rate. Migration rates cycled between the high and the low migration rates after the predefined periods described in table 5.1. Cycling continued until each 12,000 generation simulation was finished. Figure 5.1 diagrams examples of several of the different migration models used in these simulations.

The average number of migrants and the average migration rate calculations are

Table 5.1 - Summary of the fluctuating migration models.

Each row represents a different migration model. The first column lists the number of consecutive low migration rate generations the population experiences before a high migration period. The second column lists the number of generations of high migration rate that the population experiences before beginning a new cycle of low and then high migration. Column three lists the number of cycles in a given simulation. The mean migration rate across all 12,000 generations is listed in column four. Column five is the average number of migrants per deme per generation.

# of Low Migration Generations/Cycle	# of High Migration Generations/Cycle	Number of Cycles	Mean *m*	Mean N*m*
11000	1000	1	0.0046	0.1126
5000		2	0.0088	0.2131
3000		3	0.0129	0.3135
1000		6	0.0253	0..61484
11900	100	1	0.0009	0.0222
5900		2	0.0013	0.0323
3900		3	0.0017	0.0423
1900		6	0.003	0.0724
900		12	0.0055	0.1327
400		24	0.0104	0.2532
100		60	0.0253	0.6148
11990	10	1	0.0005	0.0132
5990		2	0.0006	0.0142
3990		3	0.0006	0.0152
1990		6	0.0008	0.0182
990		12	0.001	0.0242

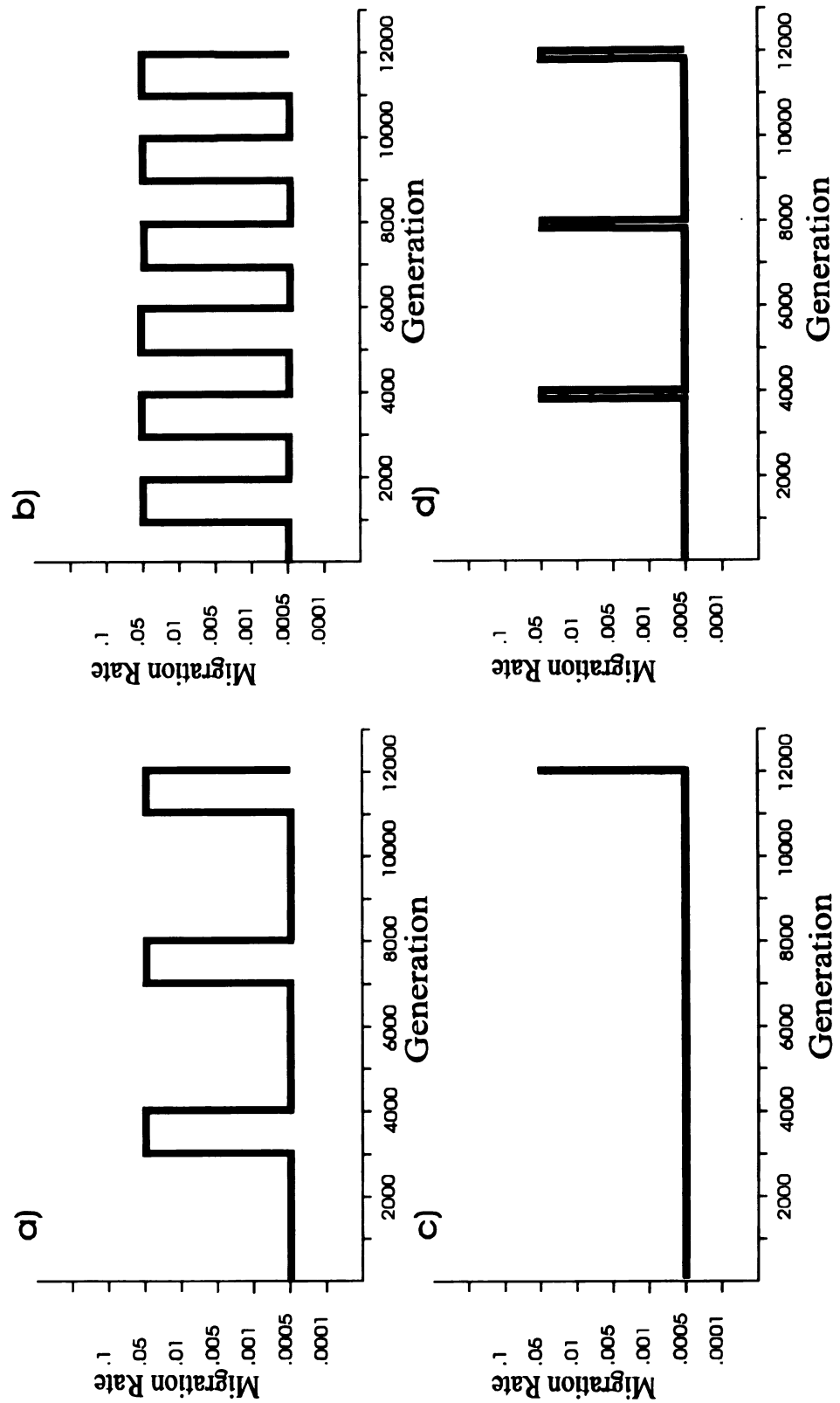
Table 5.1 (cont'd).

390	10	30	0.0017	0.0423
190		60	0.003	0.072
90		120	0.0055	0.1327
40		240	0.0104	0.2532
10		600	0.0253	0.6148
0 (Constant @ m = 0.00025)	0	0	0.0003	0.0061
0 (Constant @ m = 0.0005)	12000	0	0.0005	0.0122
0 (Constant @ m = 0.00075)	0	0	0.0008	0.0183
0 (Constant @ m = 0.001)	0	0	0.001	0.0244
0 (Constant @ m = 0.0025)	0	0	0.0025	0.0609
0 (Constant @ m = 0.005)	0	0	0.005	0.1218
0 (Constant @ m = 0.0075)	0	0	0.0075	0.1826
0 (Constant @ m = 0.01)	0	0	0.01	0.2435
0 (Constant @ m = 0.025)	0	0	0.025	0.6088
0 (Constant @ m = 0.05)	0	12000	0.05	1.2175

Figure 5.1 - Four examples of the type of migration rate cycles used in these simulations.

The migration rate is plotted against the number of generations since the start of the simulation. Two different 1000 Generation Periods of Higher Migration (GPHM) models are shown, one with a 4000 generation cycle (a), and one with a 2000 generation cycle (b). One 10 GPHM model with a 12000 generation cycle (c) is shown, and one 100 GPHM model with a cycle of 4000 generations (d) is also shown.

Figure 5.1


a)
b)
c)
d)
Migration Rate
.1
.05
.01
.005
.001
.0005
.0001
2000
4000
6000
8000
10000
12000
Generation

averages across all 12,000 generations. Because these simulations follow the SBP for only 12,000 generations the average N*m* which could be investigated with the 1000 Generation Period of High Migration (GPHM) model was 0.11262. Simulations of more than 12,000 generations would have been required to investigate lower N*m* values and those values would not have been comparable to the 12,000 generation models in this study.

A maximum deme size was imposed by incorporating a carrying capacity (K = 30), and intrinsic growth capabilities into a logistic function ($N_{(t+1)} = N_{(t)} + rN_{(t)}(K-N_{(t)})/K$, r = 1.1). This function determined the maximum number of individuals that could be born into that deme during the next generation ($N_{(t+1)}$). All demes had the same r and K, during each generation all demes therefore tended towards the same carrying capacity. Stochastic extinction of demes was allowed and recolonization occurred only when individuals of both sexes migrated into an extinct deme in the same generation.

Sexes were separate and mating was random within demes. All genetic variation was introduced via mutation. A mutation rate of 5×10^{-6} mutations per copy, per generation, per capita introduced mutants at each locus. This mutation rate was constant throughout all simulations. Forward and back mutation rates were identical.

Each phenotype had a predefined absolute juvenile survivorship. There was no mortality outside the juvenile phase. A two locus two allele model, identical to Moore and Tonsor's (1994), was used. The average absolute fitnesses of the genotypes were as follows: double homozygote wild type = 0.636, individuals that were heterozygous at one locus but homozygous wild type at the other = 0.620 and individuals that had at least one copy of the mutant allele at each locus = 0.700. These values yield average relative fitnesses of 0.909, 0.886 and 1.00 respectively. The fitness surface for individual

genotypes is shown in figure 5.2. All simulations were started with absolute fixation on the lower peak (all homozygous wild type).

At least 200 independent simulations (trials) were run for each fluctuating migration model. There were three variables of concern in these simulations. The first is a measure of the efficacy of phases one and two. It is the number of trials in which at least one deme shifted to the higher peak. The second is a measure of the effectiveness of the third phase. It is the percentage of trials that, after experiencing an initial peak shift within a deme (deme shift), then fixed that shift throughout the population. A population was considered to have fixed on the new peak when at least 95% of its extant demes had shifted to the new peak. The final measure is the number of all trials that end in fixation of the highest fitness genotype throughout the population. This represents the efficacy of the SBP as a whole. Confidence intervals (95%) on all measures were bootstrapped as in Moore and Tonsor (1994).

The N*m* values used in the results and discussion assume a mean deme size of 24.35 individuals at the time of migration. This value is based on deme sizes for 17,737 demes which had not shifted to the higher peak in Moore and Tonsor (1994). The parameters effecting deme size were exactly the same in this study and Moore and Tonsor (1994). The primary purpose of this study was to determine the conditions which lead to peak shifts, so the mean size of demes after peak shifts was not included.

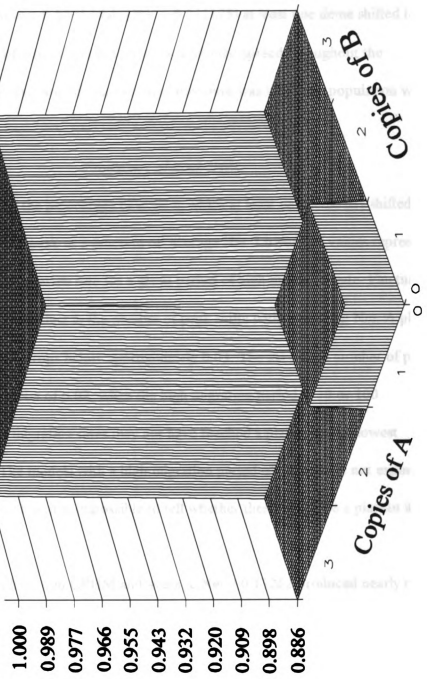
Results

The results for both the constant and fluctuating migration rate models are summarized in table 5.2.

Figure 5.2 - Genotypic fitness surface.

The surface is a plot of the fitness of an individual against the number of copies of mutant alleles as each of two loci.

Figure 5.2


W
1.000
0.989
0.977
0.966
0.955
0.943
0.932
0.920
0.909
0.898
0.886
Copies of A
Copies of B
0
1
2
3

Extreme Constant Migration Rates

No peak shifts occurred in the constant m = 0.05 simulations (N*m* ≈ 1.2175). In 44.2% of the constant *m* = 0.0005 trials (N*m* ≈ 0.012175) at least one deme shifted to the higher peak. In none of those cases did the peak shift then spread throughout the population. At neither extreme of constant migration rate was there any population wide peak shift.

Frequency of peak shifts

Figure 5.3 plots the percentage of trails in which at least one deme has shifted to the domain of the higher peak as a function of average N*m*. Lower N*m* values represent longer periods of low migration rate for a given period of high migration rate. Fluctuating models with N*m* > 0.03 decline in the number of peak shifts with increasing N*m*. A plateau seems to exist once N*m* drops below approximately 0.03. The maximum number of peak shifts is reached near a N*m* of 0.02, when the high migration period is 10 or 100 generations. Constant migration rates may not have reached a plateau at the lowest migration rates run. The models with a high migration period of 1000 were not examined for N*m* values below .11 so it is impossible to tell whether there would be a plateau in the N*m* = .03 region.

The model with a 1000 GPHM and average N*m* = 0.11262 produced nearly twice as many shifts as any other models with similar N*m*. The models with 100 generation periods of high migration produced fewer peak shifts than models with 10 GPHM. The 10 GPHM migration models were not consistently different from the static models with a similar N*m*. The 10 GPHM models tended towards higher peak shift rates than the

Table 5.2. Summary of results for the fluctuating and constant migration rate models.

Results are listed by the number of generations of high migration rate in each cycle (High Migration Periods) and the number of migrants expected each generation from each deme (Mean N*m*). The percentage of trials in which at least one peak shift occurred, the percentage of those trials which had a peak shift in which the shift spread throughout the population, and the percentage of all trials in which a population wide peak shift occurred are listed in columns 3, 4, and 5 respectively.

High Migration Periods (Generations)	Mean Nm	% of Trials with at Least One Shift	% of Shifts Fixed	% of Trials with Fixation
1000 GPHM	0.11262	51.5	100	51.5
	0.21306	37.5	98.7	37.0
	0.31351	23.0	100.0	23.0
	0..61484	2.0	100.0	2.0
100 GPHM	0.02222	39.0	0.0	0.0
	0.03226	42.5	7.1	3.0
	0.04231	38.0	39.5	15.0
	0.07244	27.0	70.4	19.0
	0.13271	11.5	91.3	10.5
	0.25324	2.0	100	2.0
	0.61484	1.5	100	1.5
10 GPHM	0.01318	44.5	0.0	0.0
	0.01418	49.0	0.0	0.0
	0.01519	34.5	0.0	0.0
	0.01820	51.0	0.0	0.0
	0.02423	49.5	7.1	3.5
	0.04231	43.0	52.3	22.5
	0.07244	34.5	81.2	28.0

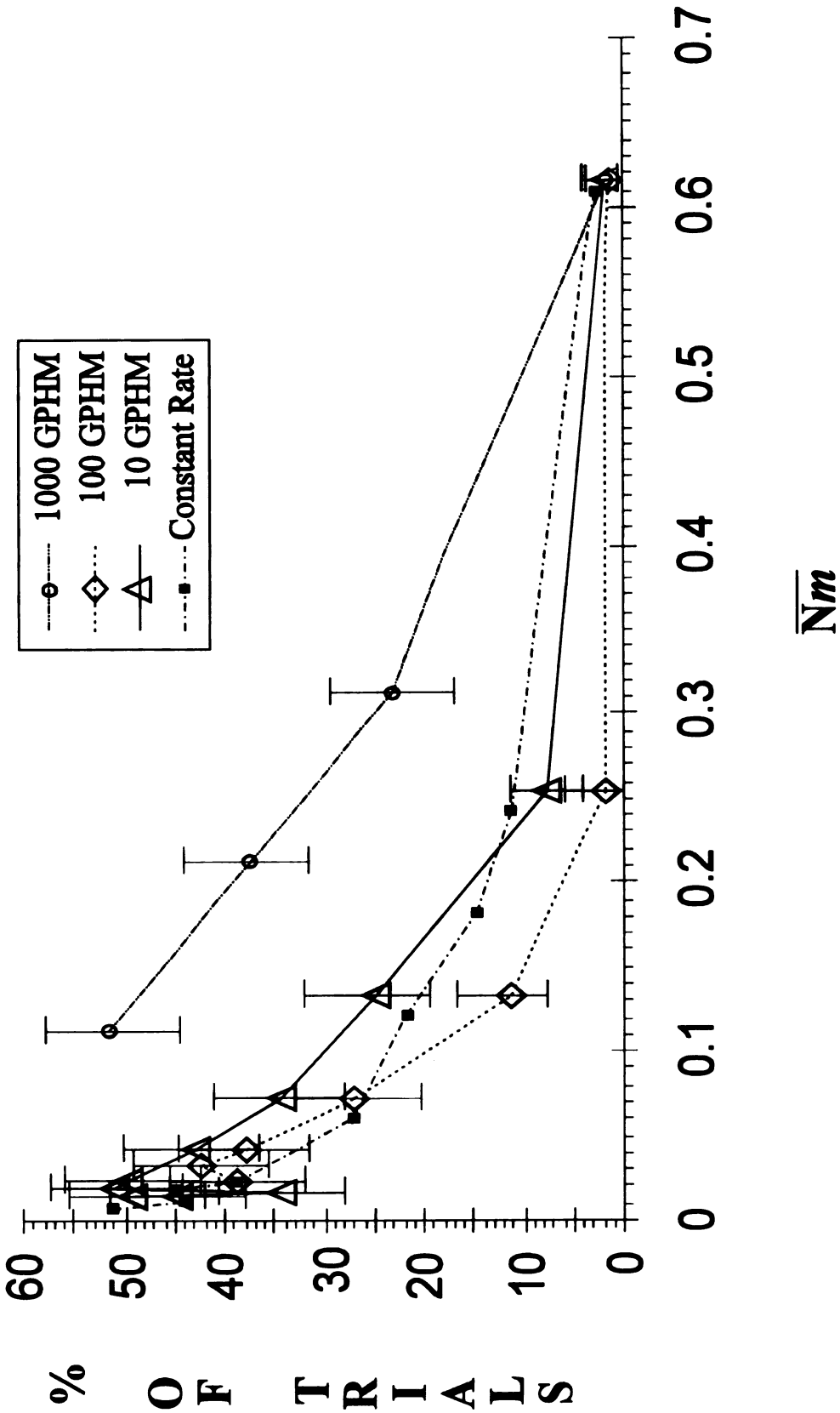
Table 5.2 (cont'd).

10 GPHM	0.13271	25.0	80.4	20.5
	0.25324	7.5	86.7	6.5
	0.61484	2.0	100	2.0
Constant @ m = 0.00025	0.00609	51	0.0	0.0
Constant @ m = 0.0005	0.01218	44.2	0.0	0.0
Constant @ m = 0.00075	0.01826	45	0.0	0.0
Constant @ m = 0.001	0.02435	38.5	0.0	0.0
Constant @ m = 0.0025	0.06088	27.0	22.2	6.0
Constant @ m = 0.005	0.12175	22.0	76.1	16.8
Constant @ m = 0.0075	0.18263	14.5	89.7	13.0
Constant @ m = 0.01	0.2435	11.0	77.3	85.0
Constant @ m = 0.025	0.60875	2.5	100.0	2.5
Constant @ m = 0.05	1.2175	0.0	NA	0.0

Figure 5.3 - Percentage of trials in which at least one deme shifted versus average N*m*.

Lines are plotted separately for constant rate, 10, 100 and 1000 Generation Periods of High Migration (GPHM). Error bars represent 95% confidence intervals. Error bars are not presented for constant migration rate simulations in order to reduce clutter.

Figure 5.3


1000 GPHM
100 GPHM
10 GPHM
Constant Rate
% OF TRIALS
0
10
20
30
40
50
60
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
Nm

constant models over an N*m* range of between 0.02 and 0.2. When N*m* was below 0.02 constant migration rate models were at least as prone to shifts as the 10 GPHM models. The 100 GPHM models produced fewer shifts than the 10 GPHM throughout the entire N*m* range except near 0.6. When N*m* was near 0.6 there was very little difference between any of the migration models.

Phase Three Propensity

Figure 5.4 plots the percentage of trials with a deme shift that then led to the fixation of the higher peak throughout the population (the tendency for phase three to occur once phases one and two had occurred) as a function of the arithmetic mean of N*m* over time. For the models with a 1000 GPHM virtually all peak shifts were fixed throughout the population. There were no trials run in the 1000 GPHM model which had a N*m* of less than 0.11262. In the other models phase three was unsuccessful when N*m* was less than approximately 0.02 and the propensity for phase three increased with increasing N*m*. At N*m* values higher than approximately 0.25 all models were nearly 100% efficient at exporting peak shifts throughout the population. In the range between 0.05 and 0.3 the 10 and 100 GPHM were usually more effective at spreading peak shifts than the constant migration models.

The SBP as a Whole

Figure 5.5 plots the percentage of trials in which there was population wide fixation of the highest fitness genotype (the efficacy of the process as a whole) as a function of mean N*m*. The 1000 GPHM models are significantly more effective than other models with equivalent average N*m*s with the exception of N*m* ≈ 0.6. The 100 GPHM model is less effective than the 10 GPHM model at N*m* values less than 0.6. At an N*m* of 0.6 the

Figure 5.4 - Percentage of those trials with a deme shift that experienced a fixation of the highest fitness genotype throughout the entire population versus average N*m*.

Lines are plotted separately for constant rate, 10, 100 and 1000 Generation periods of High Migration (GPHM). Error bars represent 95% confidence intervals. Error bars are not presented for constant migration rate simulations in order to reduce clutter.

Figure 5.4

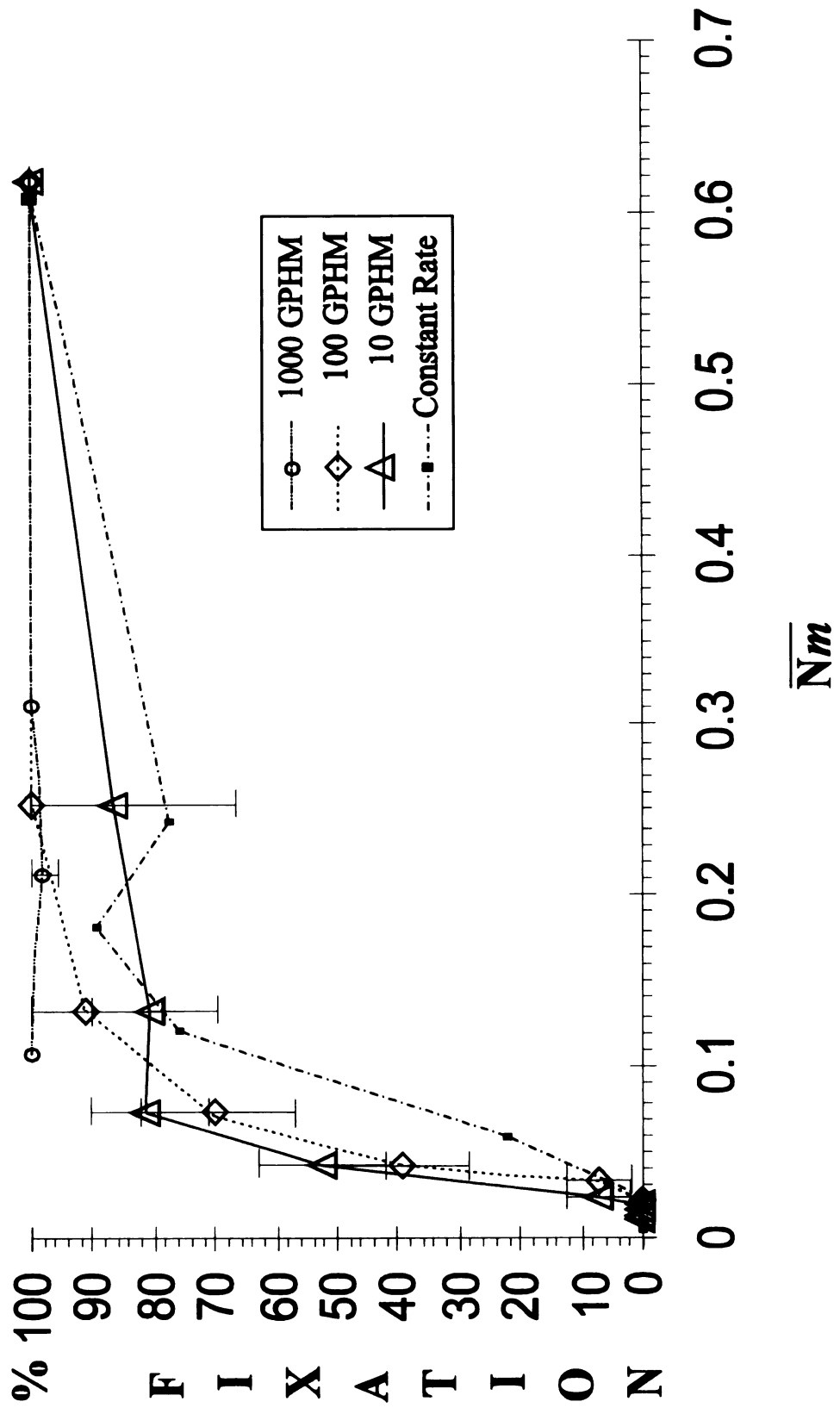
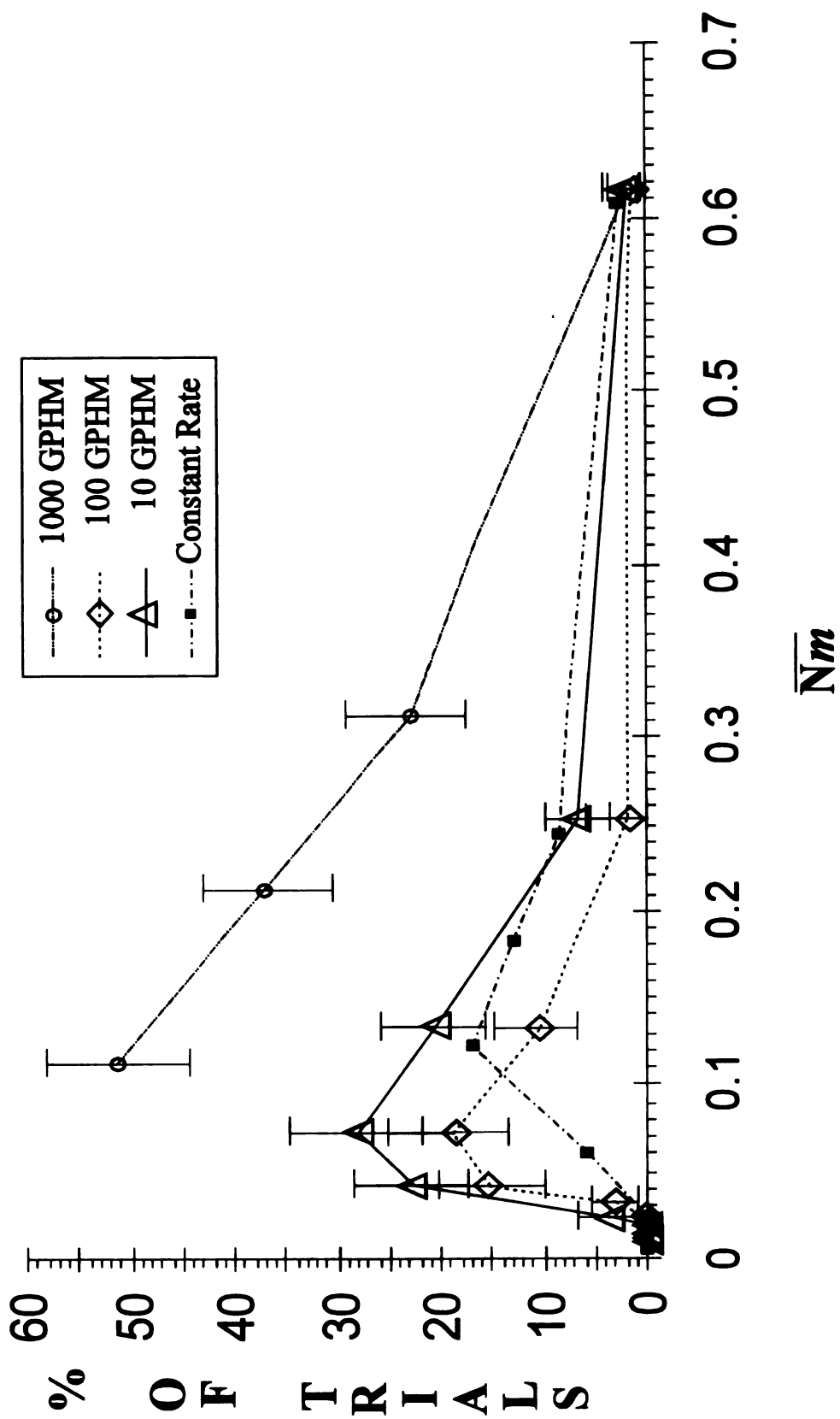

% FIXATION
100
90
80
70
60
50
40
30
20
10
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
Nm
1000 GPHM
100 GPHM
10 GPHM
Constant Rate

Figure 5.5 - Percentage of all trials in which the highest fitness genotype was fixed throughout the population versus average N*m*.

Lines are plotted separately for constant rate, 10, 100 and 1000 Generation Periods of Higher Migration Rate (GPHM). Error bars represent 95% confidence intervals. Error bars are not presented for constant migration rate simulations in order to reduce clutter.

Figure 5.5


1000 GPHM
100 GPHM
10 GPHM
Constant Rate
% OF TRIALS
0
10
20
30
40
50
60
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
$\overline{Nm}$

constant migration and the 10, 100 and 1000 GPHM models all converge towards the same low level of population wide peak shifts (~ 2%).

The optimum average N*m* varies between models. The optimum N*m* value for the completion of the SBP is in the vicinity of 0.07 for both the 10 and 100 GPHM models. The optimum N*m* for the constant migration rate model is in the vicinity of 1.2. The optimum N*m* for the 1000 GPHM model was not found in this study. When the average number of migrants is below 0.1 fluctuating models experience more population wide peak shifts than do constant migration rate models because the optimum migration rate for the fluctuating models is shifted towards lower N*m* values.

Discussion

Previous studies (Moore and Tonsor 1994; Barton and Rouhani 1993) have indicated that an optimal level of population structure exists for the SBP. Around this optimum the rate of evolution between adaptive peaks within a population is maximized. Moore and Tonsor (1994) found that N*m* in the vicinity of 0.1 produced reasonably high probabilities of population-wide peak shifts. Barton and Rouhani (1993) found that N*m* of just below 1 should provide the maximum number of population-wide peak shifts. The present study extends previous models by fluctuating the migration rates. The optimal average N*m* in this study agrees in general with the optimal N*m* of Barton and Rouhani, and with the optimal range of N*m* from Moore and Tonsor. The maximum rate of adaptive evolution occurs with an approximate average N*m* of between 0.043 and 0.122. The optimal migration rate appears to be lower when the period of high migration is either 10 or 100 generations than it is for a constant migration rate (figure 5.5).

The optimum average N*m* for adaptation via the SBP appears to be in the range of 0.07 when 10 to 100 generation periods of high migration are interspersed amongst low migration rate periods. When migration is constant the optimal N*m* for adaptation via the SBP increases slightly to approximately 0.12. Across fluctuating and non-fluctuating migration models the rate of population wide peak shifts at that optimum is not constant. This decrease in the optimal Nm for the SBP with 10 or 100 GPHM indicates that fluctuation in migration can disrupt the relationship between phase I and phase III. Longer periods of high migration rate are likely to completely decouple the two antagonistic phases.

The present study demonstrates that even though the optimal N*m* for adaptation in the SBP does not seem to be changed greatly by fluctuating migration, there is a substantial effect of fluctuating migration on the efficacy of the process. If fluctuations of high migration are of the correct period a significantly higher efficacy of the SBP is achieved than with any static migration rate. Fluctuation between very high and very low migration rates allow population wide peak shift propensities which are not possible with either the high or low rate. In addition, if the periods of the high and low fluctuations are of the right size it is possible to achieve higher populational peak shift rates than are attainable even with the most efficient static migration rate.

Most ecological process are studied on short time scales. Short periods of high migration (10 or 100 generations) are capable of producing population wide peak shift rates similar to static migration when the average migration rates were roughly equivalent. Ecological conditions are altered periodically on a geological time scale. Long period fluctuations of this geological scale allow much higher rates of population wide

peak shifts than static migration models or short period fluctuations. The 1000 GPHM models produced population wide peak shifts 51.5% of the time with an average N*m* of 0.11262 The static migration rate model with an approximate N*m* of 0.12175 produced population wide peak shifts in only 16.8% of trials. The three fold advantage in population wide peak shifts of the 1000 GPHM model indicates that the SBP is more important if long term fluctuations in migration rate occur than if migration rates remain stable around the optimum N*m* value.

The simulations with 100 GPHM produced significantly fewer population wide peak shifts than simulations with 10 GPHM. There are two phases that are affected by migration in the shifting balance process. The first is drift which requires small N*m* values. The second is interdemic selection which requires relatively high migration rates. As the period of high migration increases, the probability of successfully exporting peak shifts to new demes is increased and there is a concurrent reduction in drift. The 10 GPHM trials produce more peak shifts (figure 5.3) but are no more effective at exporting them (figure 5.4) than the 100 GPHM trials. It is possible that 100 generations of high migration allows mass selection to eliminate the majority of variation which had previously been protected from selection by fixation within demes. When only 10 generations of high migration occur mass selection should be much less effective at removing that variation. Apparently the 100 GPHM is long enough to severely retard the drift of demes into the domain of a new peak, but not long enough to export peak shifts throughout the population. A 10 GPHM does not apparently disrupt the exploration of adaptive landscapes.

A 1000 GPHM is clearly adequate for interdemic selection to take place when m = 0.05. Nearly all peak shifts were fixed throughout the population in the 1000 GPHM

(figure 5.4). Since even 3000 generations of low migration can produce a substantial number of peak shifts a noticeable fraction of trials result in population wide peak shifts during the 1000 GPHM trials even at very low average migration rates. Because the first and third phases have been decoupled in the 1000 GPHM the limiting parameter in determining the overall efficacy of the SBP with this model is probably the number of peak shifts which are likely to occur during the intervening periods of low migration. If 6000 GPHM models had been run it is predicted that high rates of populational peak shifts would have been detected even at an average N*m* of 0.6. This is expected because the period of low migration in that model would be adequate to provide a large number of deme shifts (Moore and Tonsor 1994) which would then be spread.

In addition to an exceptional ability to export peak shifts, the 1000 GPHM trials also produced more peak shifts than would be expected for an equivalent constant N*m* (figure 5.3). The increase in peak shifts is most likely a product of remixing of alleles between demes after many generations of independent drift. Demes which had drifted to fixation in the adaptive valley may suddenly be supplied with the allele necessary to push them into the domain of the higher peak once migration is increased. Increasing phenotypic variance even without any change in trait means can induce peak shifts in a deme experiencing disruptive selection (Whitlock 1995). Moore (1996, chapter 3) found that remixing of alleles in demes that have been isolated for long periods increases the propensity for peak shifts to occur. In the 1000 GPHM trials there was ample opportunity for variation to build up between demes as well as periods of mixing which allow that variation to produce novel phenotypes. The propensity for phase 1 to occur increased for a given N*m* in those models relative to the 10 or 100 GPHM models. The ability to export

those shifts was retained in those models as well. Clearly the conflicting requirements of the first and third phases of the SBP were decoupled in this model.

In this study periods of high migration equal to 1000 generations with N*m* values below 0.1 were not explored. As N*m* dropped to 0.11262 with a 1000 GPHM the number of population wide peak shifts continued to increase. This is the expected trend if the optimal average N*m* is in the vicinity of 0.07 or less. Indications from the 10 and 100 GPHM trials are that the average N*m* in a fluctuating migration model is interchangeable with N*m* for predicting what is the optimally adaptive migration rate between demes.

The decoupling of the first and third phases by long periods of high migration interspersed with long periods of low migration may lead to even greater populational peak shift probabilities than seen in this study. The 1000 GPHM model may have even higher rates of peak shifts if the average N*m* is dropped lower. Although the 12,000 generation run time for these simulations limits this study to an N*m* of 0.11262 or greater, real populations may go for even longer periods with a low average rate of migration. Longer cycles with lower N*m* would have provided more deme shifts which will inevitably be converted into populational shifts given long periods of high migration.

It is possible that given a different genetic model 1000 GPHM might be insufficient to increase the efficacy of the SBP. Epistatic fitness models with large numbers of interacting loci have been shown to proceed through phase three more slowly than models with only a few loci (Crow *et al.* 1990; Phillips 1993). This could increase the period of high migration necessary for the SBP to occur. It is also possible that under some models more favorable to the creation and maintenance of variation that 100 GPHM might be

more than sufficient to increase the efficacy of the SBP. Certain oligogenic models of disruptive selection are more effective at producing population wide peak shifts than some two locus models (Moore, 1996 chapter 3). This study primarily indicates that there are ways in which a slightly more complex model of the SBP can lead to a substantially higher global peak shift probability. The SBP is driven by events involving rare interactions of factors. Interacting ecological factors can occasionally create the correct environment for peak shifts in a population that is not normally likely to experience such shifts. If the SBP is occurring in natural systems it is likely to occur in an environment with considerably higher complexity than traditional models provide, and in most cases at higher rates than traditional models predict.

These results have ramifications for the interpretation of inter-demic migration rates measured in natural populations. Populations which seem to have stable and very low rates of gene flow between demes are likely to experience some peak shifts within demes. They are unlikely to have those shifts spread between demes. Over very long periods of time, however, intervening periods of high migration can substantially increase the efficacy of interdemic selection. In this scenario neither high nor low migration rates provides a necessary barrier to adaptation via the SBP. Instead the period of the high and low migrations rates and the average N*m* are important. Biotic and abiotic factors such as predator and competitor presence, resource availability, temperature, rainfall and sea level change over many temporal scales. Changes in these factors over annual and lunar periods may well affect the adaptive ability of some organisms with short generation times. Geologic processes such as glacial periodicity, continental drift and uplift may influence evolution in other organisms through their effects on migration.

The measurement of gene flow in natural populations is difficult but some progress has been made in that area. Reliable N*m* values from natural populations range far above and below 1 (Slatkin 1985). Given a broad range of migration across species some species are likely to be near the optimum migration rate for the SBP. Measuring the level of gene flow between populations over the short term will, however, give little indication of whether the SBP is likely to be operating. Long periods of very low migration followed by long periods of high migration will produce the maximum rate of peak shifts throughout a population.

In conclusion, the most efficient average migration rate for adaptation via the SBP appears to be slight lower for some fluctuating migration rate models than it is for constant migration rate models. The decoupling of phases 1 and 3 via fluctuating migration rates can increase the range of average N*m* over which the SBP occurs. This decoupling is also capable of greatly increasing the rate of population wide peak shifts within that range of average N*m*. What is most important to note is that short term studies of population structure in a given species probably give little evidence of whether the SBP is a common mode of adaptive evolution.

Summary

A review of literature on the presence of adaptive peaks indicates that adaptive peaks are ubiquitous but that detailed descriptions of fitness surfaces are nearly nonexistent. Several novel theoretical results are presented in this dissertation. A simulation study in chapter three is among the first to show that under certain circumstances the shifting balance process is viable. Chapter four indicates that efficacy of the process is not uniform across models. Chapter five shows that ecological complexity may also alter the efficacy of the shifting balance process. Models of the shifting balance process that include fluctuations in migration rate may be more likely to produce adaptive peak shifts throughout a population than models with fixed migration rates. The models presented in this dissertation otherwise agree with the findings of previous theoretical works on the shifting balance process which indicate that the optimal number of migrants for adaptation via the shifting balance is slightly below 1.0 and that the generation of variance between and within demes is a critical factor in the process.

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