A GENERALIZATION OF THEORY
ON THE EVOLUTION OF MODIFIER GENES

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Dedicated to the memory of two dear people

who passed away in the course of this year,

my cousin, Marcella Zamostin,

and my friend, Brian Sayre.

Though the reader may see sadness,

it is because of the joy I knew from having these two friends

that I write these words.

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ABSTRACT

In evolutionary genetics models, some features of the population are normally taken as fixed, while others evolve within this fixed background by having heritable variation. Background features include sexual reproduction, mutation, recombination, migration, etc.. In order to study the evolution of these background features, models have been examined in which they are under the control of a modifier gene. Using the approach of Feldman (1972), Karlin and McGregor (1974) sought a general theory for the evolution of modifier genes, and conjectured a "Mean Fitness Principle". It holds for several cases but fails for others. A "reduction principle" has been offered by Feldman (1980) as an alternative where recombination, migration, and mutation are found to evolve under constant selection regimes to reduced rates. Other classes of models exist where reduction is not the only outcome, and other complex behavior can occur.

This thesis developes a new approach to the problem. The central idea is that besides selection, another basic process, transformation, is occurring in deterministic population genetics models. Transformation is any process that results in offspring being of different types from their parents. This idea is formalized as transition probabilities from parent types to offpring types. Phenomena such as genetic load in populations at equilibrium, gene frequency cycling, and decreasing mean fitness, are shown to result from the

presence of transformation. Modifier gene models concern the evolution of the transformations themselves.

By using a general formulation of transformations, modifiers are treated in a unified way, including modifiers of gene conversion, unequal crossing over, sexual reproduction, and cultural transmission. The reduction principle is explained, and extended (for tightly linked modifiers) to models with multiple alleles, arbitrary selection, including frequency and density dependence, and arbitrary processes being modified. A principle is offered to explain when it does not operate. The strength of selection induced on the modifier is found to range on the order of the genetic load. A general formula is shown for "viability-analogous" modifier polymorphisms, conjectured by Feldman (1980).

Finally, a new principle is offered to explain the evolution of transformations through modifier genes: rather than evolving to increase the mean fitness, modifiers that are not themselves undergoing transformation appear to evolve to decrease the genetic load.

A GENERALIZATION OF THEORY ON THE EVOLUTION OF MODIFIER GENES

INTRODUCTION

THE IDEA OF MODIFIER GENES

One of the ubiquitous features of models of evolution is that they do not model everything evolving at once. Some traits of the organisms being modeled are proposed to have heritable variation, and a model is constructed for the effects of these these traits on the reproductive cycle of the organism in order to examine what happens to the heritable variation over time. Other traits, however, are taken as a fixed background in which this evolution is to be occurring.

The traits whose evolution is being modeled are typically traits affecting physiology, resource utilization, interactions with other organisms and interactions with conspecifics-- traits which affect fitness. The heritable variation for these traits is posited to occur at genetic loci. Background features of the population include features such as sexual reproduction, the genetic and mating systems, mutation processes, and the population structure. Genetic and mating systems include features of reproduction that determine inheritance, such as meiosis, chromosome number, recombination, alternation of generations, gender, level of inbreeding, assortative mating, and so forth. These are usually taken as fixed and appear in the structure of the models. A

common task of the theoretician is to see how the evolutionary fate of the heritable variation is a function of the state of the background features of the population. Some classical examples of this are the question of how linkage affects the evolution of two loci, and how haplodiploidy affects the evolution of eusociality.

Although these background features are usually separated logically from those features in the model that are evolving under selection, in fact there is no necessary biological dividing line between them in real organisms. These background features comprise some of the most elaborate and interesting phenomena to be found in biology. Meiosis and sex require a long line of complex structures and processes, from chromosomal structures, to cell physiology, to morphology and behavior. On this basis alone one would believe that these features have been shaped by evolution, that they are not in fact fixed.

The purpose of modifier gene models is to study how these background features themselves might have evolved, and their approach is to ask what happens when there is heritable variation for these features. Many background features have the same biological origins as selected features. Genetic systems and mutation processes are mediated by enzymes, regulatory genes, and other cellular components for which genetic variation has been found. Similarly, morphological and behavioral features under genetic control may affect the mating systems and the spatial structure of a population through the same means that they can affect resource utilization, predator avoidance and other aspects of fitness.

There is ample documentation both of specific loci affecting features such as recombination (Catcheside, 1977) and mutation (e.g. Cox

and Gibson, 1974) and of phylogenetic variation and change of features such as sexual versus asexual reproduction (Templeton, 1982), mating systems (Bateson, 1983) and so forth. The requisite genetic variation therefore appears to exist for these features to evolve.

The first modifier model to gain attention was a model for the evolution of dominance proposed by Fisher (1928). However, forty years passed before this approach for traits affecting fitness was first applied, by Nei (1967), to one of the major background features not involved directly in fitness, recombination. In his model, there are two loci undergoing viability selection, and a neutral third locus, the modifier, which controls the rate of recombination between them.

Before the modifier gene approach was developed, the explanations for the evolution of non-fitness features paralleled the kind of "group selection" or optimization ideas in use to explain altruism and population regulation. The essence of these approaches was to examine some statistic of the population, adopted as a measure of its "success", such as mean fitness, genetic load, or response rates to selection, and see how differences in the non-fitness trait would affect it. These non-genetic approaches have been applied to the evolution of mutation rates (Kimura, 1960), recombination (Muller, 1964; Turner, 1967; Eshel and Feldman, 1970), and sexual reproduction (Fisher, 1930; Crow and Kimura, 1965; Eshel, 1971). Although these statistics were not incorporated into actual dynamic models of evolutionary change, they were a first attempt to understand how natural selection can gain a hold on features which have no intrinsic effect on an organism's fitness.

This is what may have delayed the formulation of modifier gene models-- control over these background features does not give modifier

alleles any intrinsic selective differences. In the absence of any pleiotropic effects, these are neutral genes which can be selected only by becoming associated with genes that are under selection, that is, through hitchhiking.

Since Nei's model was formulated, modifier gene models of a number of non-fitness features have been analyzed, including

recombination (Feldman, 1972; Feldman and Balkau, 1973; Karlin and McGregor, 1974; Felsenstein and Yokoyama, 1974; Christiansen and Feldman, 1975; Feldman and Krakauer, 1976; Teague, 1976; Feldman et al. 1980),

migration rates (Balkau and Feldman, 1973; Karlin and McGregor, 1974; Christiansen and Feldman, 1975; Teague, 1977; Gillespie, 1981 a; Asmussen, 1983),

mutation rates (Leigh, 1970; Karlin and McGregor, 1974; Gillespie, 1981 a,b; Holsinger and Feldman, 1983),

segregation distortion (Prout et al. 1973; Hartl, 1975; Thomson and Feldman, 1976; Liberman, 1976),

assortative mating (Karlin and McGregor, 1974),

inbreeding (Feldman and Christiansen, 1983), and

sex-ratio (Eshel and Feldman, 1982; Karlin and Lessard, 1983).

Some regularities emerge, but there are many complexities which have remained unexplained in the literature.

THE RESULTS OF MODIFIER THEORY

Models of modifier genes can be divided into two major classes, those dealing with populations that have reached equilibrium in their

genetic composition and those dealing with populations that are in transient phases, due to fluctuating selection, drift, or through the recent introduction of advantageous genes. I will describe mainly the results from the equilibrium models, which are the topic of this thesis. Some of the main results are summarized in Table 1 .

To understand the long term evolution of a given feature, one wants to know whether evolution will produce any inexorable trends toward certain phenotypes. Feldman (1972) first developed the theoretical methodology to investigate this question for the evolution of recombination. His approach was to ask whether, in Nei's (1967) modifier gene model, populations with a given rate of recombination were immune at equilibrium to the invasion of new modifier genes that changed the recombination rate, and what requirements were there on the recombination rate produced by the new modifier to enable it to invade the population. His result was that populations with linkage disequilibrium between the two selected loci could be invaded by new modifier alleles which reduced the recombination rate, and were immune to invasion by modifier alleles that increased the recombination rate.

Karlin and McGregor (1974) applied this approach to modifiers of a number of classical "background" features. In an attempt to offer a principle that would explain, in general, the evolution of modifier genes, they proposed that the initial increase in the population of a new modifier allele would be governed by a "mean fitness principle", which I paraphrase:

> If the effect of a new modifier allele, were it fixed in the population, would cause the population's equilibrium mean fitness to increase, then this new allele will increase in

> frequency when introduced into the population. If the effect would mean a decrease in the mean fitness, the allele would be excluded from the population.

What they were proposing, in effect, was that the intuitively appealing mean fitness statistic actually predicted the dynamic behavior of modifier genes in the population. This principle works in some cases, but unfortunately is violated in several cases that have been discovered subsequently, including the basic recombination modifier model (Feldman et al., 1980, for the examples in Karlin and Carmelli, 1975), and modifiers of segregation distortion (Thomson and Feldman, 1974). No one has offered any refinement to the principle that would explain these counterexamples.

Nevertheless, one regularity emerges from a number of modifier models. Karlin and McGregor (1974) noted that for modifiers of recombination, mutation, and migration, the modifier always evolves to reduce these processes in populations at equilibrium. Subsequent treatments of modifier models have found this property to generalize to arbitrary viability selection regimes in random mating populations at equilibrium, for modifiers of recombination (Feldman, et al., 1980), mutation (Holsinger and Feldman, 1983 b), and migration (Teague, 1977; Asmussen, 1983). The possibility that these cases manifest some sort of reduction principle has been conjectured by Feldman (Feldman et al., 1980). These cases are shown in Table 1.

TABLE 1

SOME MAIN RESULTS FROM MODIFIER THEORY

POPULATIONS AT EQUILIBRIUM under:	Requirement for INITIAL INCREASE of new modifier allele:
a. Random Mating, Viability Selection	
RECOMBINATION MODIFICATION	REDUCTION OF RECOMBINATION
MUTATION MODIFICATION	REDUCTION OF MUTATION
MIGRATION MODIFICATION	REDUCTION OF MIGRATION
SEGREGATION DISTORTION MODIFICATION	ANY CHANGE IN DISTORTION
b. Random Mating, Viability Selection, + MUTATION	
RECOMBINATION MODIFICATION	INCREASE some cases, REDUCTION some cases.
c. Random Mating, Viability Selection, + MIGRATION	
RECOMBINATION MODIFICATION	INCREASE some cases, REDUCTION some cases.
d. Random Mating, Viability Selection, + SEGREGATION DISTORTION	
RECOMBINATION MODIFICATION	COMPLEX: cases of increase, decrease, or any change
e. PARTIAL SELFING, Viability Selection	
RECOMBINATION MODIFICATION	COMPLEX: cases of increase, decrease, and optima.
f. COMPLETE SELFING, Viability Selection	
RECOMBINATION MODIFICATION	REDUCTION OF RECOMBINATION
MUTATION MODIFICATION	INCREASE some cases REDUCTION some cases

POPULATIONS IN TRANSIENT PHASE: Random Mating, Viability Selection; Transience due to DRIFT, FLUCTUATING SELECTION or NOVEL MUTANT;	
For each of:	EVOLUTION FAVORS:
RECOMBINATION, MUTATION, MIGRATION MODIFICATION	INCREASE some cases, REDUCTION some cases.

Modifiers not treated here:

Assortative mating, selfing, sex ratio, dominance.

From Table 1, we see that in quite a number of cases, the reduction principle cannot be operating. With recombination modifiers, an increase in recombination can evolve when mutation, migration, segregation distortion or partial selfing are added to the model. These are all results for equilibrium populations. For transient phase populations, increases or decreases in the modified process can evolve.

THE APPROACH OF THIS THESIS

In this thesis I develop a framework for population genetics models in which the models of modifier genes in the literature become special cases of a more general model. The essential idea is that processes incorporated in population genetics models can be dichotomized into selection processes and transformation processes, that is, changes in number and changes in kind.

Chapter 1 develops this idea. The way that recombination, mutation, migration and other non-fitness features can be seen to be transformation processes will be formalized. Within the dichotomy of selection and transformation, modifiers can be seen to be a natural complement to selected loci: they are loci for variation in transformation processes rather than selection processes.

In Chapter 2, I examine some very basic properties of population genetics models from the perspective of this dichotomy. The point of this chapter that is most important for the theory of modifier genes is that transformation processes allow a standing genetic variance in fitness in a population at a stable genetic equilibrium. Another way to put this is that the population can be made to bear a stable genetic load.

In Chapter 3, I explore what happens to variation in the population for transformation processes. The mathematical reason for the reduction principle- i.e., why the reduction of recombination, mutation, and migration is a common result in several models-- is shown for these and a more general class of transformation processes, and is extended to some models for modifiers of sexual reproduction and cultural transmission. The reason that recombination and mutation rate increases evolve in some models in the literature is found to reside in the nature of the variation in transformations. A concept of "affine" variation in transformations is developed, which accounts for these situations and predicts others where increases in transformation may evolve.

The "dark horse" among principles offered to explain the evolution of modifier genes must certainly be Kimura's (1960) "Principle of Minimum Genetic Load", which proposes that modifiers would evolve to minimize the total genetic load in the population, including mutational and substitutional loads. Kimura offerred this principle not as a result, but as a premise upon which he derived "optimum" degrees of dominance and optimal mutation rates, and he gave no justification for it. No one has ever pursued this principle further. Although genetic load arguments have often been invoked without justification, we will find that the results in this thesis lead one back to Kimura'a "Principle of Minimum Genetic Load" in a restricted form: how a modifier gene evolves depends on the nature of the variation it controls, but as long as it is not itself being transformed, it may be that inevitable effect is to reduce the equilibrium genetic load of the population.

Furthermore, we can address what is something of a myth about neutral modifier genes: that selection on them will be very weak, and that any intrinsic pleiotropic fitness effects will overwhelm the selection due to modifier effects (Wright, 1964). In Chapter 3, we will see that this is not a necessary property of modifier genes, but rather, that the strength of the induced selection acting on a neutral modifier can be on the order of the genetic variance in fitness in the population.

Chapter 4 is a discussion of these results in a general context. One point made is that models of genetic control of phenotype distributions, such as sex ratio, habitat preference, propensity to perform altruism, and so forth, bear a fundamental homology with modifier gene models, and I discuss some of the common features of both.

Although the results I obtain here generalize much about the theory of modifier genes, they comprise the bare surface of what is easily tractable within the broad scope of of "selection processes" and "transformation processes" which includes phenomena as diverse as sexual reproduction, cultural transmission, migration, and host shifts of organisms. The theory analyzed here will be restricted to infinite populations, near genetic equilibrium, in constant environments. Nevertheless, I hope that by describing the general scope of this framework, it may facilitate further extensions of the theory.

CHAPTER 1

SELECTION AND TRANSFORMATION

Darwin's theory of evolution through natural selection has been described by Lewontin (1970) as embodying three principles:

" 1. Different individuals in a population have different morphologies, physiologies, and behaviors (phenotypic variation).

2. Different phenotypes have different rates of survival and reproduction in different environments (differential fitness).

3. There is a correlation between parents and offspring in the contribution of each to future generations (fitness is heritable).

...While they hold, a population will undergo evolutionary change."

One of the major concerns of population genetics is with principle 3. : how do the mechanisms that determine the correlation between parent fitness and offspring fitness impact evolution? The incorporation of Mendelian genetics into models of natural selection is a major contribution of the "Synthetic Theory" of evolution. The mechanisms of heredity are important to evolution because they are the causal connection between the characteristics of organisms in one generation and the characteristics of those in the next.

In one sense, the major accomplishment of genetics is the discovery and understanding of how genes are transmitted during reproduction. But what makes genetics non-trivial for evolutionary theory, however, is not that genes are being passed on. Rather, it is the fact that through the mechanisms of transmission, offspring may be _different_ from their parents. Of course, at one extreme, if the characteristics of offspring had _nothing_ to do with those of their parents, then selection could leave no impact on the population, and Darwinian evolution would be impossible. But at the other extreme, were offspring _identical_ to their parents, the mechanisms of heredity would be irrelevant to the evolutionary process. Features of transmission such as segregation, recombination, mutation, and so forth, give certain regularities to the differences between parents and offpring and take a central position in population genetics models of evolution. Differences between parents and offspring are necessary not only to make the mechanisms of heredity important to evolution, but are the _sine qua non_ for the science of genetics itself, from Mendel's experiments with peas to the transformation of _Drosophila_.

I will refer to any processes contributing to changes between parents and offspring as TRANSFORMATION processes, to emphasize that it is changes during reproduction that make the mechanisms of genetic transmission important to evolution.

The way I would like to characterize population genetics models of evolution will not even refer to genes specifically. In its general form, a micro-evolutionary model concerns populations composed of individuals of different types in different numbers; changes in these numbers over time constitute evolution. An individual's type is

determined by, but not necessarily the same as, the types of its parents. Transformation processes determine the nature of differences between parents and offspring. Selection determines the relative proportion of the next generation that the offspring of a given individual comprise, and this proportion will be determined by the individual's type.

In the context of Darwin's theory of evolution, the importance of transformation is commonly thought to lie with Lewontin's principle 1., above: transformation is the supplier of variation, the "raw material" upon which the "force" of selection can act. But processes in transmission that cause transformations do not simply introduce variation and then disappear to let selection act alone on the population. They interact continually with selection to affect the composition of the population. In this respect they are also a "force" in evolution.

For example, consider a classical case of transformation, the production of overdominant or underdominant heterozygotes from different homozygous parents. The offspring can all be quite different, with respect to selection, from either of their two parents. In the case of a mating of two identical heterozygotes bearing balanced lethal genes, half of the offspring can have very different phenotypes from their parents. Sexual transmission in these cases will not simply introduce variation into the population, but will confound the result of selection on the previous generation by transforming the phenotype between the parents and their offspring. A classic consequence of this is the occurrence of protected polymorphisms when the fittest type is the heterozygote. If the heterozygote could reproduce clonally it would go

to fixation, but because heterozygotes keep producing homozygotes under sexual reproduction, selection is confounded and a polymorphism results.

In deterministic models of evolution, selection and transformation comprise a basic dichotomy of forces that can change the composition of the population. Selection affects the quantity of reproductive output, while transformation affects the content of reproductive output. In infinite populations, if neither selection nor transformation are occurring, the composition of the population will be static. When population sizes are finite, both the quantity and content of reproduction become stochastic, and drift comes in to play.

TRANSFORMATION - SELECTION BALANCES

One can imagine two extrema for the evolutionary processes acting on a population. We can imagine a complete absence of transformations, with all offspring identical to their parents. Here, constant selection will eventually fix the population on the types with the maximal fitness value, or in the case of frequency dependent selection, possible bring the population to a polymorphism where all the types have the same fitness. On the other hand, we can imagine a complete absence of selection, where only transformations can change the composition of the population. In general, we would not expect the composition of types that the population might attain at any equilibria to be the same in the two situations. In real populations, there will be a combination of selection, transformation and drift impacting on the composition of types. This thesis concerns the interaction of selection and transformation.

Adaptation is the phenomenon most usually considered as the main effect of selection. Transformation has no single effect. A number of familiar biological phenomena are evolutionary effects of transformation:

TABLE 2

EVOLUTIONARY EFFECTS OF SOME TRANSFORMATIONS

PHENOMENON	TRANSORMATION PROCESSES RESPONSIBLE
Hardy-Weinberg proportions of genotype frequencies	segregation and syngamy under random mating
Homozygosity in selfing plants	segregation and syngamy under selfing
Linkage equilibrium between loci	recombination
Concerted evolution of multiple copy genes	inter-locus gene conversion
The "molecular clock"	mutation
Wahlund's effect	migration

THE NATURE OF TYPES THAT CAN EVOLVE

The discussion of micro-evolutionary models thus far has referred only to genotypes as the types involved in evolution. But from the way

I have characterized the general micro-evolutionary model, any domain of information about an organism satisfying two criteria will be involved in evolution and should be considered a part of an individual's type. This information

1) must be determined by the organism's parents, and
2) must either affect the organism's fitness or help determine the types of its offspring.

Now, there are untold numbers of details in an individual organism's existence that determine what and how much it reproduces -- its genetic constitution, embryonic environment, mutations, cultural heritage, chance encounters with mates, predators, prey, pathogens, accidents, weather, and so forth. But only some of this information is both determined by its parents and will be transmitted to the offspring or affect its fitness.

Some important examples of non-genetic information satisfying these criteria include geographical, micro-habitat, and cultural information. An organism's location or micro-habitat can both affect its reproductive output and affect the location or micro-habitat of its offspring. An organism's cultural heritage is also a domain of information that can affect its reproductive output, and that can be transmitted to its offpring.

Transformation in these cases takes the form of migration or dispersal in the case of organismal location, or shifts in habitats, hosts or diet from parents to offspring in the case of micro-habitat. Changes in cultural traits during the process of learning are transformations. In each of these processes, the offspring types bear a relation to, but need not be identical with, the parental types.

THE EVOLUTION OF TRANSFORMATIONS

The main task of this thesis is to develop a theoretical framework for understanding how transformation processes have themselves evolved. The general modifier approach to this question is to extend the domain of types to include the transformation process itself as an aspect of an organism's type. Thus, within the actual type of the parents there will be information on how these types are to be changed in producing offspring. The evolutionary question becomes: what happens to variation for transformation types when it is introduced into the population? Variation in transformations need not directly alter an organism's fitness, but what is of interest is how selection can come to be induced on transformation types.

Within this framework, it is possible that transformations also act on the transformation types, or even that the transformation type controls its own transformation. This would be the case, for example, if a mutator gene caused itself to mutate into other mutator alleles. Such dynamics will profoundly alter the evolution of the transformation types. In this thesis, transformation will be excluded for the most part from acting on the transformation types themselves, so that the means by which selection can come to be induced on transformation types can be seen clearly.

A fundamental assumption of the treatment here is that the processes of selection and transformation do not happen simultaneously but occur during disjoint intervals of time during the life cycle. This allows the life cycle to be formalized as an alternating sequence of selection events and transformation events. This is the appropriate representation for processes such as reproduction, which occurs as

discrete events, but it is not as good for processes such as migration, which may be a continuous process concurrent with selection during an organsism's life.

FORMALIZING TRANSFORMATION PROCESSES

The basic model I will use for transformation processes will be that of a mapping from the parental types to the probabilities of producing each possible offspring type. For now, the "type", with its entire genetic and other information, will be represented by a single index: i, j, k, etc.. Instead of putting all the complexity of genetic, cultural or other information that satisfies the above two criteria into the specification of the individual's type, this information is embedded within the structure of the transformation probabilities. This will clarify the point in analysis when more of the structure of the mapping must be specified, and allows the exploration of generalities that would be foregone had the models been restricted too early.

It is difficult to obtain models that include the complete variety of life cycles of different organisms. A division must be made between asexual and sexual organisms, since the "topology of descent" is purely branching in asexual, but involves anastomosing in sexuals. In cultural transmission, more than two individuals may be involved in determining a given cultural trait of an individual. In this thesis I examine only pair mating, where two individuals determine another's type.

Actually, sexual organisms that are purely selfing or apomictic also have pure branching descent. Population genetics models are often classified as sexual vs. asexual, or haploid vs. diploid, but these classifications overlap in terms of topology of descent. This is shown below:

TABLE 3

Topology of Descent

	Pure Branching	Pair Mating
Reproduction:		
Asexual		
Haploid	x	
Diploid	x	
Sexual		
Diploid		
with outcrossing		x
pure selfing	x	
Haploid		x

It will be seen later that sexual haploid models are often subcases of diploid models, where special constraints have been placed on selection and transformation.

I will represent the transformations as matrices of probabilities, T, subscripted with the parental and offspring types, equaling the proportion of offspring of a given type among the offspring of each parental type. In pure branching descent, this mapping will be from a single parent type j to probabilities of offspring types i:

$$T_{j \to i} \quad \text{where} \sum_i T_{j \to i} = 1 \text{ and } T_{j \to i} > 0 \quad \forall\, j,i.$$

Pair-mating organisms have more potential for complexity in their life cycles. Reproduction may occur through monogamously mated diploid pairs, multiple matings, contribution to gamete pools, independent haploid generations, haplodiploidy, and other arrangements. The common denominator is that at some point, an individual is produced whose type i depends on the types of two individuals (j,k). We need to consider both how individuals are formed from pairs and how the pairs are formed.

TRANSFORMATION FROM PAIRS TO INDIVIDUALS

The probability that an offspring of a pair of types j and k is of type i will be written

$$T_{(j,k)\to i},$$

where

$$\sum_i T_{(j,k)\to i} = 1 \quad \text{and} \quad T_{(j,k)\to i} \geq 0 \quad \forall\, j,k,i .$$

For notational simplicity, I will omit the parentheses henceforth and use

$$T_{j,k\to i}.$$

If there is no real interaction between the types j and k in the transformation process, then T can be represented as a "quasi-asexual" mapping:

$$T_{k,j\to i} = \tfrac{1}{2}(Q_{k\to i} + Q_{j\to i}),$$

where Q is defined like T in the pure branching case.

The transformation matrices for pure branching and pair-mating descent have the forms

$$T = \| T_{j \to i} \| \quad i,j = 1 \text{ to } n \qquad \text{for pure branching descent,}$$

and

$$T = \| T_{j_1, j_2 \to i} \| \quad i, j_1, j_2 = 1 \text{ to } n \qquad \text{for pair-mating descent,}$$

where n is the number of types in the population.

The matrix for the pair-mating descent is an n by n^2 matrix. The tables of offspring frequencies which are found in "mating tables" (see the examples ahead) are actually transformation matrices, with the redundant entries taken out, and usually transposed with respect to how I have defined them above.

DEFINITION 1: PERFECT TRANSMISSION

The mapping where there is perfect transmission of the types, with no transformation occurring, can be represented as:

$$T_{j \to i} = \delta_{ij} \text{ for pure branching descent;}$$

$$T_{j,k \to i} = \frac{1}{2}(\delta_{ij} + \delta_{ik}) \text{ for pair mating descent;}$$

where

$$\delta_{ij} = \begin{cases} 0 \text{ if } i \neq j \\ 1 \text{ if } i = j \end{cases}.$$

In matrix form this is

$$T = I \text{ for pure branching descent,}$$

and

$$T = \frac{1}{2}\left(\underline{e}^T \otimes I + I \otimes \underline{e}^T \right) \text{ for pair mating descent,}$$

where

$$\underline{e}^T = (1 \ldots 1) \text{ is a vector of } n \text{ ones,}$$

and $\otimes$ is the tensor product (For a review of basic properties of tensor products, see Appendix A in Karlin (1982)). It means that each offspring is of the same type as one of its parents, with equal probability between the two parents.

DEFINITION 2: TRANSMISSION DISTORTION.

The case in pair mating descent where each offspring is the same type as one of its parents, but with unequal probability between the two parents depending on their types, constitutes a form of transformation I will call "transmission distortion" to generalize the notion of segregation distortion of chromosomes in diploids. The transformation probabilities when only transmission distortion is occurring are

$$T_{j,k \to i} = \beta_{jk}\delta_{ji} + \beta_{kj}\delta_{ki} ,$$

where

$$0 \leq \beta_{jk} \leq 1 \ , \text{ and } \beta_{jk} + \beta_{kj} = 1 \quad \forall \ j,k.$$

To illustrate, the transformation matrix for transmission distortion with two types is

$$T = \begin{pmatrix} \beta_{11} & \beta_{12} & 0 & 0 \\ 0 & 0 & \beta_{21} & \beta_{22} \end{pmatrix} + \begin{pmatrix} \beta_{11} & 0 & \beta_{12} & 0 \\ 0 & \beta_{21} & 0 & \beta_{22} \end{pmatrix} .$$

It has no simple tensor product form.

TRANSFORMATION FROM INDIVIDUALS TO PAIRS:

For pair-mating reproduction, we need, in addition, to specify the process by which the pairs (i,j) are formed. I will examine the two

simplest processes, random mating of diploids, and random union of gametes within a gamete pool, with some extensions. I will also make some assumptions on sex symmetry which avert having to keep track of the types among each sex. For more complicated reproductive cycles, there will be several classes of populations corresponding to different sexes and ploidies, and there will be reproductive transformations between these classes. To model, for example, the reproductive cycle of an insect species which had sexual selection, multiple mating, and sperm competition, we would need to define the following: three classes of population -- the male and female adults and the sperm within a female; two reproductive transformations -- between adult and gamete and between gamete and zygote; two levels of mating processes -- the formation of adult matings and the fertilization of eggs; and three levels of selection -- viability, fertility, and sperm displacement.

Let us examine the simple case where pair formation is through random encounter of individuals. Thus the frequency, $p_{i,j}$, of pair type (i,j) will be $z_i z_j$ where z_i and z_j are the frequencies of types i and j at the time before pair formation. Under sex symmetry, pair types (i,j) and (j,i) are indistinguishable, so if $j \neq i$, then the actual frequency of pair type (i,j) is $p_{i,j} + p_{j,i} = 2p_{i,j}$. Type dependent biases in pair formation or fertility will give as the fraction that pair (i,j) contributes to the next generation:

$$p_{j,i}^{(s)} = p_{i,j}^{(s)} = \frac{f_{ij} z_i z_j}{\bar{f}} \quad \text{where} \quad \bar{f} = \sum_{i,j} f_{ij} z_i z_j .$$

The assumption of sex symmetry gives $f_{ij} = f_{ji} \quad \forall\ i,j$.

MATING WITHIN DEMES

Mating within demes requires a special normalization. When deme is incorporated into the type, then if we let S_k be the set of all types that are of deme k, we have:

For $i,j \in S_k$,

$$p_{i,j} = \frac{z_i z_j}{\sum_{a \in S_k} z_a} .$$

For $i \in S_k$, $j \notin S_k$,

$$p_{i,j} = 0 .$$

An alternate representation of subdivided populations is to normalize the frequency of the types within each S_k, so that

$$\sum_{i \in S_k} z_i = 1 ,$$

where the fraction, f_k, that S_k composes of the whole population, must in addition be specified.

Then

$$p_{i,j} = z_i z_j \quad \text{for} \quad i,j \in S_k .$$

This will be the form used later.

EXAMPLES OF TRANSFORMATION PROCESSES

The following are some models of common transformation processes represented by their transformation probabilities:

TABLE 4

Diploid Sexual Reproduction: Segregation-Syngamy Transformation

Parental Genotypes	Offspring Genotypes $\frac{A_1}{A_1}$	$\frac{A_1}{A_2}$	$\frac{A_2}{A_2}$
$\frac{A_1}{A_1} \times \frac{A_1}{A_1}$	1	0	0
$\frac{A_1}{A_1} \times \frac{A_1}{A_2}$	$1/2$	$\frac{1}{2}$	0
$\frac{A_1}{A_1} \times \frac{A_2}{A_2}$	0	1	0
$\frac{A_1}{A_2} \times \frac{A_1}{A_2}$	$\frac{1}{4}$	$1/2$	$\frac{1}{4}$
$\frac{A_1}{A_2} \times \frac{A_2}{A_2}$	0	$\frac{1}{2}$	$\frac{1}{2}$
$\frac{A_2}{A_2} \times \frac{A_2}{A_2}$	0	0	1

transformation probabilities

TABLE 5

Mutation:

	Offspring Type	
Parental Type	A_1	A_2
A_1	$1 - m_1$	m_1
A_2	m_2	$1 - m_2$

transformation probabilities

TABLE 6

Recombination:

Parental Gamete types	Offspring Gamete types A_1B_1	A_1B_2	A_2B_1	A_2B_2
$A_1B_1 \times A_1B_1$	1	0	0	0
$A_1B_1 \times A_1B_2$	$\frac{1}{2}$	$\frac{1}{2}$	0	0
$A_1B_1 \times A_2B_1$	$\frac{1}{2}$	0	$\frac{1}{2}$	0
$A_1B_1 \times A_2B_2$	$\frac{1}{2}(1 - R)$	$\frac{1}{2}R$	$\frac{1}{2}R$	$\frac{1}{2}(1 - R)$
$A_1B_2 \times A_1B_2$	0	1	0	0
$A_1B_2 \times A_2B_1$	$\frac{1}{2}R$	$\frac{1}{2}(1 - R)$	$\frac{1}{2}(1 - R)$	$\frac{1}{2}R$
$A_1B_2 \times A_2B_2$	0	$\frac{1}{2}$	0	$\frac{1}{2}$
$A_2B_1 \times A_2B_1$	0	0	1	0
$A_2B_1 \times A_2B_2$	0	0	$\frac{1}{2}$	$\frac{1}{2}$
$A_2B_2 \times A_2B_2$	0	0	0	1

transformation probabilities

TABLE 7

Migration:

	Deme after migration	
	1	2
Deme of Origin		
1	$1 - m_1$	m_1
2	m_2	$1 - m_2$

transformation probabilities

TABLE 8

Segregation Distortion:

	Offspring Gamete types	
	A_1	A_2
Parental Gamete types		
$A_1 \times A_1$	1	0
$A_1 \times A_2$	$\frac{1}{2}(1 + k)$	$\frac{1}{2}(1 - k)$
$A_2 \times A_2$	0	1

transformation probabilities

TABLE 9

Sex Ratio:

Parental Sexes	Offspring Sex: Male	Offspring Sex: Female
Male x Male	(zero fertility)	
Male x Female	$\frac{1}{2}(1 + m)$	$\frac{1}{2}(1 - m)$
Female x Female	(zero fertility)	

transformation probabilities

TABLE 10

Unbiased Gene Conversion in 2 Loci:

a = rate of gene conversion at locus A, b = rate of gene conversion at locus B.

Parental Gamete types	Offspring Gamete types A_1B_1	A_1B_2	A_2B_1	A_2B_2
$A_1B_1 \times A_1B_1$	1	0	0	0
$A_1B_1 \times A_1B_2$	$\frac{1}{2}$	$\frac{1}{2}$	0	0
$A_1B_1 \times A_2B_1$	$\frac{1}{2}$	0	$\frac{1}{2}$	0
$A_1B_1 \times A_2B_2$	$\frac{1}{2}$ (1-a-b+2ab)	$\frac{1}{2}$ (a+b-2ab)	$\frac{1}{2}$ (a+b-2ab)	$\frac{1}{2}$ (1-a-b+2ab)
$A_1B_2 \times A_1B_2$	0	1	0	0
$A_1B_2 \times A_2B_1$	$\frac{1}{2}$ (a+b-2ab)	$\frac{1}{2}$ (1-a-b+2ab)	$\frac{1}{2}$ (1-a-b+2ab)	$\frac{1}{2}$ (a+b-2ab)
$A_1B_2 \times A_2B_2$	0	$1/2$	0	$1/2$
$A_2B_1 \times A_2B_1$	0	0	1	0
$A_2B_1 \times A_2B_2$	0	0	$1/2$	$1/2$
$A_2B_2 \times A_2B_2$	0	0	0	1

transformation probabilities

TABLE 11

Cultural Transmission:

Type is religious preference. C = Catholic, P = Protestant, J = Jewish, O = Other.

Parental Types			Offspring Types			
Father		Mother	C	J	P	O
C	x	C	.81	0	0	.19
C	x	J	no data			
C	x	P	no data			
C	x	O	0	0	.5	.5
J	x	C	1	0	0	0
J	x	J	0	.8	0	.2
J	x	P	0	0	1	0
J	x	O	0	0	0	1
P	x	C	1	0	0	0
P	x	J	0	0	0	1
P	x	P	.015	0	.63	.355
P	x	O	0	0	.1	.9
O	x	C	.67	.165	0	.165
O	x	J	no data			
O	x	P	0	0	.5	.5
O	x	O	0	0	.11	.89

transformation probabilities

(Adapted from Cavalli-Sforza and Feldman (1981) with permission)

An additional transformation that has been modelled is unequal crossing over (Ohta, 1980). Here, as a simple formulation, the haplotype of a chromosome will be defined as the number of copies of the repeated gene. A single crossover between chromosomes will occur at meiosis, with uniform probability of occurring within each gene on each chromosome. Then the transformation probabilities will be

$$T_{j,k \to i} = (1-R)\frac{1}{2}(\delta_{ji} + \delta_{ki}) + R\frac{1}{jk}\min(j,k,i,j+k-i) ,$$

where j,k,i are the number of copies of the gene on each chromosome, and R is the probability of recombination.

SITUATIONS RENDERING PERFECT TRANSMISSION UNATTAINABLE

In a number of biological situations, there is information that critically affects an individual's fitness, which was transmitted to it by its parents, but which is intrinsically non-transmissible to its offspring. The maternal effect is a classic example. An individual's fitness may be determined by some combination of its mother's genotype and it own genotype, but this <u>combined</u> information is not what is transmitted to its offspring. In examples of kin selection or brood selection, an individual's fitness may depend on the composition of its brood. Again, although this will be determined by the types of the individual's parents, it is not information which the individual can transmit to <u>its</u> offspring.

Since selection is distinguishing between individuals on the basis of this non-transmissible information, it is really an additional part of the individual's type. But in these cases, it is impossible to define perfect transmission, because this part of the type is not

transmitted. Brood selection has figured into arguments on the evolution of sex (Williams 1975), and the importance of the fact that perfect transmission cannot be defined in this case will be seen later.

FORMALIZING SELECTION

The action of the other basic force changing the frequencies of types in the population, selection, will be represented as type-dependent scalars, w_i, that have multiplied the frequency, z_i, of each type, i, between the beginning and end of time intervals between phases of transformation. These products are then normalized to frequencies by dividing by their sum, the mean fitness, $\bar{w}$, and will be represented by

$$z_i^{(s)}.$$

Thus,

$$z_i^{(s)} = z_i \frac{w_i}{\bar{w}}, \quad \text{where} \quad \bar{w} = \sum_i z_i w_i .$$

In pair-mating reproduction, selection may also act on the mated pair phase of the life cycle. Because the formation of the population of mated pairs requires a transformation between two different sets of types (individuals to pairs), mating processes, sexual selection, and fertility selection can all be incorporated in the mating mapping. Here, I will divide the process into a random pair formation, followed by biases of the frequencies of these pairs depending on their types, and then biases according to type in the portion of the next generation that are offspring of each pair. These two sources of pair-type specific bias will be lumped into a single set of scalars f_{ij}, which

multiply the fequencies $p_{i,j}$, of each mated pair of types i and j, giving

$$p_{i,j}^{(s)} = f_{ij}\frac{p_{i,j}}{\bar{f}} ,$$

with

$f_{ij} = f_{ji}$ by the assumption of sex symmetry,

where

$\bar{f} = \sum_{i,j} f_{ij}p_{i,j}$ is the mean "fertility" or pair fitness.

NORMALIZATION BY TYPES

One addition to this formulation of selection that should be discussed is normalization by types. This is when the frequencies after selection are normalized so that a given class of types is given a certain total frequency in the population independently of how selection has acted on the types withing this class. This is the essential feature of soft selection, a form of frequency dependent selection, where the proportion of the population in each deme (which is part of the type) is normalized to a constant value. It is also an essential feature of sexual selection, where in the case of pure female choice, the frequency of types among females in the whole female population is the same as among mated females, while for males this need not hold. The case of sexual selection breaks the assumption of sex symmetry I am sticking to here, and will not be considered. Soft selection will be analyzed in the section on migration modifiers later.

At this point, having formalized the ideas of selection and transformation, it will be possible to incorporate these processes in

models of the life cycles of different organisms. This will permit a formal analysis of how they evolve under the influence of these two processes. Throughout I will assume that the populations are constituted through infinite independent sampling, so that sampling variance and drift do not occur.

CHAPTER 2

EVOLUTION UNDER SELECTION AND TRANSFORMATION

I have described how selection and transformation can be viewed as the two fundamental processes that can cause changes in the composition of a population in deterministic models. Each of these forces will have its own effect on the population. What I wish to do in this chapter is examine some of the basic properties of the interaction of these two processes.

Without specifying the exact nature of the types in the population or the nature of the transformations or selection acting on them, we can nevertheless examine some general features of their evolution when both selection and transformation are occuring. In this chapter, I will model two basic life cycles, pure branching and pair-mating, where selection and transformation are occurring. By employing the formal representations of selection and transformation developed in the previous chapter, mathematical recursions will be developed giving the frequencies of types in terms of their frequencies in the previous generation, which will allow a rigorous analysis of the interaction of selection and transformation. These recursions will be framed for infinite populations, and selection and transformation will not be fluctuating in time. The results are summarized as follows:

Populations where no transformation is occurring have these properties:

1) The mean fitness of the population increases in time when fitnesses are frequency independent.
2) The frequencies converge to stable equilibrium points, or surfaces in which the population is neutral.
3) At equilibrium, the marginal frequencies of all types present are equal.

In contrast populations also undergoing transformation have the following properties:

1) The mean fitness of the population may decrease in time.
2) The frequencies of types may approach stable limit cycles.
3) The set of types present at stable equilibria or cycles may be different when there is transformation occurring from those present when only selection is acting.
4) Frequency dependence of the marginal fitnesses is not required to produce positive stability of equilibria.
5) The marginal fitnesses of the types present at an equilibrium need not be equal.

It is this last property that is the basic source of selection on transformation types.

1. THE RECURSIONS ON THE FREQUENCIES OF TYPES

(1) POPULATIONS WITH PURE BRANCHING DESCENT

The life cycle of an organism which reproduces by itself is

formally quite simple. When there is no transformation occurring, selection is the only mapping in the life cycle, so the recursion giving the new frequency z_i', of type i in terms of the old frequency, z_i, is:

$$z_i' = z_i^{(s)} = z_i \frac{w_i}{\bar{w}},$$

where

$$\bar{w} = \sum_i z_i w_i \text{ is the mean fitness.}$$

Or using vector notation,

$$\underline{z}' = \frac{1}{\bar{w}} W\underline{z},$$

where

$$\underline{z} = \begin{pmatrix} z_1 \\ \vdots \\ z_n \end{pmatrix}, \quad W = \text{diag}(w_i), \quad \underline{e} = \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix}, \quad \underline{e}^T = (1 \ldots 1) \text{ , , and } \bar{w} = \underline{e}^T W \underline{z}.$$

When a life cycle consists of selection followed by transformation, the recursion is now

$$z_i' = \sum_j z_j \frac{w_j}{\bar{w}} T_{j \to i},$$

or in vector form,

$$\underline{z}' = \frac{1}{\bar{w}} TW\underline{z} \tag{2.1}$$

where T is the matrix $T = \| T_{j \to i} \|_{i,j}$.

Here

$$\sum_i T_{j \to i} = 1, \text{ for all } j; \quad \text{i.e., } \underline{e}^T T = \underline{e}^T.$$

Thus T is stochastic in the column sense. Also note that

$$\bar{w} = \underline{e}^T W\underline{z} = \underline{e}^T TW\underline{z},$$

so transformation affects only the content, not the quantity, of the reproductive output of the population.

MULTIPLE SELECTIONS AND TRANSFORMATIONS

Recursions of the form (2.1) can be shown also to apply to populations where the organisms can undergo transformation several times during a life cycle, with the possibility that different selection regimes act after each transformation. Let k index each phase of transformation and selection. Then

$$\underline{z}' = \frac{\prod_k T_{(k)}W_{(k)}\underline{z}}{\underline{e}^T\left(\prod_k T_{(k)}W_{(k)}\right)\underline{z}} .$$

If we let

$$W = \operatorname{diag}\left(\underline{e}^T \prod_k T_{(k)}W_{(k)}\right)$$

and

$$T = \left(\prod_k T_{(k)}W_{(k)}\right) \operatorname{diag}\left(\underline{e}^T \prod_k T_{(k)}W_{(k)}\right)^{-1} ,$$

then $\underline{e}^T T = \underline{e}^T$ and

$$\underline{z}' = \frac{TW\underline{z}}{\underline{e}^T TW\underline{z}} .$$

Therefore, multiple transformations and selections can be lumped into the product of a single T and a single W, and do not require a separate treatment.

(2) POPULATIONS WITH PAIR-MATING DESCENT

The basic life cycle I will examine for organisms where offpring are produced from the mating of pairs will consist of:

1) individual selection,
2) transformation from individuals to reproductive pairs,
3) selection on these pairs,
4) production of offspring with possible reproductive transformation.

Let z_i be the frequency of type i just after reproduction.

$z_i^{(s)}$ will refer to the frequencies after individual selection has acted.

After random pair formation pair-types (k,j) will have frequencies $p_{k,j}$ (under sex symmetry, pair types (k,j) and (j,k) will be indistinguishable, so if $k \neq j$ the actual pair frequency is $2p_{j,k}$, but this is accounted for in the summations).

Pair or fertility selection will bias these frequencies to $p_{k,j}^{(s)}$.

Finally, reproduction will yield the individuals in the new generation at frequencies z_i'.

The relations between these are:

$$z_i^{(s)} = \frac{z_i s_i}{\sum_j z_i s_j}$$ where $s_i > 0$ is the individual fitness of type i.

$$p_{k,j} = z_k^{(s)} z_j^{(s)} .$$

$$p_{k,j}^{(s)} = \frac{p_{k,j} f_{kj}}{\sum_{ab} p_{a,b} f_{ab}} .$$

$$z_i' = \sum_{kj} p_{k,j}^{(s)} T_{k,j \to i} .$$ By sex symmetry $T_{k,j \to i} \equiv T_{j,k \to i}$ $\forall$ k,j,i .

This yields the recursion

$$z_i' = \frac{\sum_{kj} z_k z_j s_k s_j f_{kj} T_{k,j \to i}}{\sum_{kj} z_k z_j s_k s_j f_{kj}} .$$

This basic model subsumes within it a great range of the deterministic models in the population genetics literature. It is essentially an augmentation of the "multiple state trait" model of Cavalli-Sforza and Feldman (1981), with the addition of individual and pair selection.

One can adopt the notation of Cavalli-Sforza and Feldman (1981) to yield a vector representation of this recursion. Suppose there are n types possible. Let us express T as an n by n^2 matrix:

$$\| T_{j_1,j_2 \to i} \| \quad i,j_1,j_2 = 1 \ldots n$$

where the elements are indexed across a row by the ordered pairs (j_1,j_2), and down a column by i.

Similarly, let F be an n^2 by n^2 diagonal matrix

$$F = \text{diag}(f_{i_1 i_2}) ,$$

let S be an n by n diagonal matrix

$$S = \text{diag}(s_i)$$

and let $\underline{e}$ be the n long vector of 1's. Using tensor products:

$$\underline{z}' = \left[(\underline{e} \otimes \underline{e})^T F (S \otimes S)(\underline{z} \otimes \underline{z}) \right]^{-1} TF(S \otimes S)(\underline{z} \otimes \underline{z}) . \qquad (2.4)$$

The mean fitness of the population will be the product of the mean individual fitness

$$\bar{s} \triangleq \sum_i z_i s_i$$

and the mean pair fitness

$$\bar{f} \triangleq \sum_{jk} p_{j,k} f_{jk} :$$

$$\bar{w} = \bar{\bar{s}f} = \bar{s} \sum_{jk} z_j^{(s)} z_k^{(s)} f_{jk} = \bar{s} \sum_{jk} z_j z_k \frac{s_j s_k}{\bar{s}\,\bar{s}} f_{jk} = \frac{1}{\bar{s}} \sum_{jk} z_j z_k s_j s_k f_{jk} \quad .$$

It is possible to define a single fitness value that lumps both individual and pair selection.

Define the lumped fitness values $w_{kj} = \dfrac{s_j s_k f_{kj}}{\bar{s}}$.

Then

$$\bar{w} = \sum_{kj} z_j z_k w_{jk} \ , \quad \text{and} \quad z_i' = \frac{\sum_{kj} z_k z_j w_{kj} T_{k,j \to i}}{\sum_{kj} z_k z_j w_{kj}}$$

In vector form, defining $W \triangleq F(S \circledcirc S)$, which is a diagonal matrix, we get:

$$\underline{z}' = \left((\underline{e} \circledcirc \underline{e})^T W (\underline{z} \circledcirc \underline{z}) \right)^{-1} T W (\underline{z} \circledcirc \underline{z}) \ . \qquad (2.5)$$

An alternative vector form uses instead $W = W^T = \| w_{ij} \|$, giving

$$\underline{z}' = \frac{1}{\underline{z}^T W \underline{z}} \left\| \sum_k z_k w_{jk} T_{j,k \to i} \right\| \underline{z} \ , \qquad (2.6)$$

where $\bar{w} = \underline{z}^T W \underline{z}$.

DEFINITION 3: MARGINAL FITNESSES

An important but simple concept is the idea of the marginal fitness of a type. The marginal fitness w_i for each type i is defined as:

$$w_i = \sum_j z_j w_{ij} = (W\underline{z})_i \ .$$

This is just the average of the fitnesses of all the individuals and pairs in which type i occurs.

Use of the marginal fitnesses allows us to represent recursion (2.6) in a form like that for pure branching, where the recursion involves multiplication by a positive diagonal matrix and a stochastic matrix (now dependent on $\underline{z}$):

$$\underline{z}' = \frac{1}{(\underline{z}^T W \underline{z})} \left\| \sum_k z_k \frac{w_{jk}}{w_j} T_{j,k \to i} \right\| \operatorname{diag}(W\underline{z})\, \underline{z} .$$

Let us define the matrix

$$Y \triangleq \left\| \sum_k z_k \frac{w_{jk}}{w_j} T_{j,k \to i} \right\|_{i,j} . \tag{2.7}$$

Y is stochastic (in the column sense) since

1) $\sum_{ik} z_k \frac{w_{jk}}{w_j} T_{j,k \to i} = \sum_k \frac{z_k w_{jk}}{w_j} = \frac{w_j}{w_j} = 1$ or $\underline{e}^T Y = \underline{e}^T$.

2) $\sum_k z_k \frac{w_{jk}}{w_j} T_{j,k \to i} > 0 \quad \forall\, i,j$, or $Y > 0$.

This assumes, necessarily, that $w_i > 0$. The cases where some $w_i = 0$ present no problem, for in this case type i becomes irrelevent to the population:

$$\bar{w} = \sum_{hj} z_h z_j w_{hj} = \sum_{\substack{h \neq i \\ j \neq i}} z_h z_j w_{hj} ,$$

and for $h \neq i$,

$$\sum_{jk} z_k z_j w_{jk} T_{j,k \to h} = \sum_{\substack{j \neq i \\ k \neq i}} z_h z_j w_{jk} T_{j,k \to h} .$$

Thus no z_h' depend on z_i. So we simply eliminate type i from the model.

If T is quasi-asexual, where $T_{k,j \to i} = \frac{1}{2}(Q_{k \to i} + Q_{j \to i})$, then

$$z_i' = \frac{1}{2\underline{z}^T W \underline{z}} \sum_{jk} z_j z_k w_{jk} (Q_{k \to i} + Q_{j \to i}) = \frac{1}{\underline{z}^T W \underline{z}} \sum_{jk} z_j z_k w_{jk} Q_{k \to i}$$

$$= \frac{1}{\underline{z}^T W \underline{z}} \sum_{k} z_k w_k Q_{k \to i} ,$$

which looks much like the pure branching case, except that $\bar{w} = \underline{z}^T W \underline{z}$ instead of $\underline{e}^T W \underline{z}$, and w_k depends on $\underline{z}$.

If pair selection is eliminated, so that $f_{ij} = 1 \quad \forall \quad i,j$, then the pair mating model is identical to the pure branching model:

$$w_{ij} = \frac{s_j s_i}{\sum_k z_k s_k} ; \quad w_i = \sum_j z_j w_{ij} = \frac{\sum_j z_i s_i s_j}{\sum_k z_k s_k} = s_i , \quad \text{independent of } \underline{z};$$

$$\bar{w} = \sum_{ij} z_i z_j w_{ij} = \sum_i z_i w_i = \sum_i z_i s_i , \quad \text{and}$$

$$z_i' = \frac{1}{\bar{w}} \sum_j z_j s_j Q_{j \to i} .$$

A RELATION TO QUANTITATIVE GENETICS MODELS

The models of the evolution of continuous characters that have been developed (see Slatkin (1970), Cavalli-Sforza and Feldman (1976), and Karlin (1979)) are, in their most general form, continuous versions of (2.5). The "segregation kernel" is the continuous version of the transformation matrix. These models are analyzed, however, with only very special forms for the selection functions and segregation kernels. Slatkin (1970) posed the question of how the segregation kernel itself would be expected to evolve, which is the equivalent of

the question of how transformations would evolve. With the proper translation to continuous variables (for example, the expression for perfect transmission would use the Dirac delta function instead of the Kronecker delta function), and the use of Lebesgue integration, I suspect that most of the results of this thesis could be extended to continuous variation with general segregation kernels and selection functions.

A NOTE ON SEX SYMMETRY

The assumption of sex symmetry that I am making throughout this thesis for fitnesses and transformations is for the sake of simplicity and does not affect the basic results obtained here. In fact, I will show that recursions with asymmetry either in the fitnesses or in the parental role in reproductive transformations can be shown to be equivalent to systems with complete sex symmetry. An essential requirement, however, is that the frequency of types be the same in both sexes among the offspring.

We allow for sex asymmetry in the model as follows:

Let $\underline{v}$ be the vector of type frequencies among the males, and $\underline{x}$ be that for females.

Let the individual fitnesses of males of type i be m_i, and the individual fitness of females of type i be s_i. m_i need not equal s_i.

The pair fitness of a type j male and a type k female will be f_{jk}, and f_{jk} need not equal f_{kj}.

The frequency of offspring of type i from a pair with a male of type j and a female of type k will be $T_{j,k \to i}$.

Now, we no longer require that $T_{j,k\to i} = T_{k,j\to i}$.

We obtain the recursion

$$v_i' = x_i' = \left(\sum_{ab} v_a m_a x_b s_b f_{ab}\right)^{-1} \sum_{jk} v_j m_j x_k s_k f_{jk} T_{j,k\to i} .$$

Since after one generation, $\underline{x} = \underline{v}$, the system can be reduced to one vector of frequencies

$$\underline{x} = \underline{v} = \underline{z} .$$

Define the lumped fitnesses $w_{ij} = m_i s_j$.

Then the fitness matrix

$$W = \| w_{ij} \|$$

need no longer be symmetric.

Now we again obtain the form

$$z_i' = \left(\sum_{ab} z_a z_b w_{ab}\right)^{-1} \sum_{jk} z_j z_k w_{jk} T_{j,k\to i} .$$

Define the following <u>symmetric</u> fitnesses and transformation probabilities:

$$\tilde{W} \triangleq \frac{1}{2}\left(W + W^T\right) , \text{ and } \tilde{T}_{j,k\to i} = \frac{1}{2}\left(T_{j,k\to i} + T_{k,j\to i}\right) .$$

The expression for the mean fitness is unchanged by substituting $\tilde{W}$ for W :

$$\sum_{ab} z_a z_b \tilde{w}_{ab} = \frac{1}{2}\sum_{ab} z_a z_b (w_{ab} + w_{ba}) = \sum_{ab} z_a z_b w_{ab} .$$

Substitution of $\tilde{T}$ and $\tilde{W}$ changes the summation terms to

$$\sum_{jk} z_j z_k \tilde{w}_{jk} \tilde{T}_{j,k\to i} = \frac{1}{2}\sum_{jk} z_j z_k w_{jk}\left(T_{j,k\to i} + T_{k,j\to i}\right) .$$

From this the following result can be seen readily:

THEOREM 2.1.

If either the fitnesses have sex symmetry or the transformations have sex symmetry, then the system is equivalent to a system with complete sex symmetry which had fitness matrix $\tilde{W}$ and transformation matrix $\tilde{T}$.

That is, if

$$W = W^T \quad \underline{\text{or}} \quad T_{j,k \to i} = T_{k,j \to i} \quad \forall\ j,k,i\ ,$$

then

$$z_i' = \Big(\sum_{ab} z_a z_b \tilde{w}_{ab}\Big)^{-1} \sum_{jk} z_j z_k \tilde{w}_{jk} \tilde{T}_{j,k \to i}\ .$$

Feldman, Christiansen and Liberman (1983) have shown this result for fertility selection assuming equal recombination between the two sexes. Karlin and Liberman (1979) derive this result for multi-locus systems with random mating, and "generalized nonepistatic" viability selection regimes. The transformation in this case is recombination between the loci combined with segregation and syngamy. They consider cases where the recombination distributions may differ between the sexes, which occurs in Drosophila, and where the selection regimes may differ between the two sexes. Since Theorem 2.1 made no assumptions about the nature of the selection or transformation processes, it can be seen that the equivalence shown in Karlin and Liberman (1979) extends to arbitrary multilocus selection regimes, including fertility selection, and other transformation processes besides recombination, such as mutation and gene conversion.

A completely different way of dealing with gender is to include gender as a part of the type, and designate disjoint sets of indices for the two sexes. The function of gender is incorporated in the pair selection values: matings between individuals of the same sex are given pair fitnesses of zero. To exclude the effect of same sex pairs from the value of the mean fitness of the population, we define the mean fitness:

$$\bar{w} \triangleq \Big(2 \sum_{j \in \text{males}} z_j \sum_{j \in \text{females}} z_j\Big)^{-1} \sum_{jk} z_j z_k w_{jk} .$$

In this form, gender is represented in the indices and not their order, so $W = W^T$ and $T_{j,k \to i} = T_{k,j \to i}$ $\forall$ i,j,k . The form of the recursion is therefore symmetric even when each sex is produced with different frequencies of types. This treatment of gender is useful for analyzing modifiers of sex ratio.

EVOLUTION IN THESE MODELS REQUIRES EITHER SELECTION OR TRANSFORMATION

When there is neither selection nor transformation, it can be seen readily that no changes in the frequencies of types can occur in either the pure branching model or the pair-mating model. With no selection, and perfect transmission, the recursions become

$$\underline{z}' = I\underline{z} = \underline{z} \text{ for pure branching,}$$

and

$$\underline{z}' = \tfrac{1}{2}(\underline{e}^T \otimes I + I \otimes \underline{e}^T)(\underline{z} \otimes \underline{z}) = \tfrac{1}{2}(1 \otimes \underline{z} + \underline{z} \otimes 1) = \underline{z}$$

for pair mating,

where it can be seen that the frequencies of types remain at what ever values they begin with.

2. BASIC PROPERTIES OF THE RECURSIONS

(1) CHANGES IN THE MEAN FITNESS

The way the mean fitness of the population changes in time in the presence and absence of transformation will be considered for the two basic life cycles. This consideration will be for fitnesses that are not frequency dependent.

1. PURE BRANCHING DESCENT:

WITHOUT TRANSFORMATION

In the absence of transformation, the new mean fitness of the population is

$$\bar{w}' = \sum_i z_i' w_i = \sum_i \frac{z_i w_i^2}{\bar{w}} .$$

Thus

$$\bar{w}' - \bar{w} = \frac{1}{\bar{w}} \left(\sum_i z_i w_i^2 - \left(\sum_i z_i w_i \right)^2 \right) = \frac{1}{\bar{w}} \operatorname{var}(w_i) ,$$

or

$$\frac{\bar{w}'}{\bar{w}} = 1 + \operatorname{var}\left(\frac{w_i}{\bar{w}} \right) .$$

This is essentially Fisher's Fundamental Theorem : $\bar{w}$ increases in time by an amount equal to the variance in fitnesses. A locally stable equilibrium will therefore be a local maximum of $\bar{w}$.

WITH TRANSFORMATION

When transformation is acting,

$$\bar{w}' = \sum_i z_i' w_i = \sum_{ij} z_j \frac{w_j}{\bar{w}} T_{j \to i} w_i ,$$

and

$$\bar{w}' - \bar{w} = \sum_{ij} z_j w_j \frac{w_i}{\bar{w}} (T_{j \to i} - z_i) .$$

In this case, $\bar{w}$ need not always increase every generation; we can always choose $\underline{z}$ such that

$$\bar{w}' < \bar{w} .$$

For let $w_{j*} = \max_j(w_j)$, and choose $z_{j*} = 1$. Then $\bar{w} = w_{j*}$ and

$$\bar{w}' - \bar{w} = \sum_i w_{j*} \frac{w_i}{w_{j*}} (T_{j* \to i} - z_i) = \sum_i w_i (T_{j* \to i} - z_i)$$

$$= \sum_i (w_i - w_{j*}) T_{j* \to i} + w_{j*} \left(\sum_i T_{j* \to i} - z_{j*} \right)$$

$$= \sum_i (w_i - w_{j*}) T_{j* \to i} + w_{j*}(1 - 1)$$

$$= \sum_i (w_i - w_{j*}) T_{j* \to i} \leq 0 ,$$

since

$$w_{j*} \geq w_i \ \forall \ i .$$

$\bar{w}'$ will be strictly less than $\bar{w}$ unless all the types which $j*$ is transformed to happen to have identical fitness to $j*$. Thus if there is any transformation of the fittest types to types of lesser fitness, it is guaranteed that for some range of initial frequencies, the mean fitness will decrease between generations.

2. PAIR-MATING DESCENT:

WITHOUT TRANSFORMATION

In the general model with individual and pair selection, when there is no transformation occuring, or $T = T_{id}$,

then we have

$$z_i' = \frac{z_i w_i}{\underline{z}^T W \underline{z}}$$

or in vector form

$$\underline{z}' = \frac{1}{\underline{z}^T W \underline{z}} \operatorname{diag}(W\underline{z})\ \underline{z} \ .$$

This is identical to the classical model of viability selection acting on an autosomal locus in diploids. In that case, the pair which is "mating" is two haploid gametes. Since the alleles segregate without change, no transformation is occurring. The behavior of this system is well known, an important property being that the mean fitness, $\bar{w}$, increases every generation (see Kingman 1980, for a proof).

WITH TRANSFORMATION

When transformation is occurring, $\bar{w}$ need not always increase every generation. For example, if we set $\underline{z}$ to maximize $\underline{z}^T W \underline{z} = \bar{w}$ then $\bar{w}'$ will be less than $\bar{w}$ unless

$$\bar{w}' = \frac{1}{\bar{w}^2}\ \underline{z}^T A^T W A \underline{z} = \bar{w} \ ,$$

or

$$(\underline{z}^T W \underline{z})^3 = \underline{z}^T \| \sum_k z_k w_{kj} T_{k,j \to i} \|^T W \| \sum_k z_k w_{kj} T_{k,j \to i} \| \ \underline{z} \ ,$$

which it need not do for all T's.

The best known example where transformation causes the mean fitness of the population to decrease in time is recombination, which was pointed out by Moran (1964). Another example is the case of fertility selection, where the mean fitness may decrease in time (Hadeler and Liberman, 1975; Pollak, 1978). In this case, the transformation is segregation and syngamy, and why fertility selection makes a difference for this transformation is explained in section 3.(3) .

(2) THE CONVERGENCE BEHAVIOR

PURE BRANCHING DESCENT:

The recursion for pure branching descent is essentially a linear system:

$$\underline{z}' = \frac{1}{\underline{e}^T W \underline{z}} T W \underline{z} .$$

Therefore, the convergence behavior can be generally characterized.

WITHOUT TRANSFORMATION

In the absence of transformation, each type changes frequency by a factor equal to its relative fitness,

$$z_i' = z_i \frac{w_i}{\bar{w}} .$$

If the fitnesses are frequency independent, then any type whose fitness is greater than the mean fitness of the population increases monotonically until the mean fitness, which is increasing, overtakes its fitness, at which point it decreases in frequency monotonically. The only types remaining at equilibrium are those whose fitness is the maximum fitness of all the types present. The frequencies of these types with the maximum fitness when polymorphic will remain at whatever frequencies to which they are perturbed.

WITH TRANSFORMATION

In the presence of transformation, there are a number of possible outcomes:

1) The population may converge to an equilibrium of frequencies that is independent of the initial frequencies of types in the population, which is therefore stable to any perturbations. Such an outcome in the absence of frequency dependent selection is possible only when transformation is occurring.

2) The population may converge to an equilibrium that depends on the initial frequencies of types in the population. This dependency may be of two kinds, both of which may be present:
   a. The equilibrium frequencies are continuous functions of the inital frequencies.
   b. The equilibrium frequencies are discontinuous functions of the initial frequencies. In this case, the types can be placed in ranked classes. For each class there corresponds a

space of equilibrium frequencies. The population will converge to that equilibrium space corresponding to the highest ranking class represented initially with positive frequency. In this case, the population is stable to the introduction of types from that or any lower ranked class, and will respond either as in 1) or 2)a. to such perturbations, but is unstable to the introduction of types from any higher ranked class.

3) Instead of an equilibrium, the population may converge to a cycle. The statements of 2) apply to these cycles. In fact, both cycles and equilibria should be considered together in conditions of 2).

These results follow from the spectral properties of TW (see Karlin and Taylor, 1975 for a review). Outcome 1) will occur when T is a primitive matrix (that is, when for some power n, $(TW)^n$ is strictly positive, meaning that each type will have some finite probability of being transformed to each other type after enough generations). The vector of frequencies to which the population converges is the leading eigenvector of TW, which has all positive components, described in the Perron-Frobenius theorem (Gantmacher, 1959).

Outcomes 2) and 3) may occur when T is imprimitive. In general, TW will have a certain number of non-negative eigenvectors, which have non-negative eigenvalues. The rank of each class in 2)b. is by the magnitude of each of these eigenvalues, and the types in each

class are simply those which exist as positive component frequencies among the non-negative eigenvectors and principle vectors (Franklin, 1968) for each non-negative eigenvalue.

If a non-negative eigenvalue is non-simple, then there may be multiple invariant subspaces within one class, allowing behavior 2)a.. If there are negative or complex eigenvalues of the same modulus as one of the non-negative eigenvalues, and then there may be cycling within this class.

When individuals are introduced from a higher class than exists in the population, then the frequency vector will contain some component of a non-negative eigenvector with a larger eigenvalue, which will then come to dominate the population.

PAIR MATING DESCENT:

The recursions for pair mating descent are intrinsically non-linear and their convergence behavior cannot be generally stated when both selection and transformation are occurring. We know they include the behavior of the pure branching populations, since it is equivalent when the transformation is quasi-asexual and there is no pair selection.

In the absence of transformation, the general pair-mating model is of the same form as the classic one-locus, multiple allele selection model, which has been worked out in detail. In its convergence behavior, the space of frequency vectors will be divided up into domains of attraction. In the absence of frequency dependent selection, within each domain will be a single equilibrium point to which the population

will converge, or a surface of equilibria, within which perturbations are neutral, if certain relations between the fitness values occur. Cycling is impossible without frequency dependent selection.

Furthermore, in the absence of transformation or frequency dependent fitnesses, some kind of "overdominance" (Karlin, 1981) is necessary to keep a polymorphism stable against perturbations. In the presence of transformation this need not be true. A simple example is the case of unidirectional mutation toward a codominant, deleterious allele in a one locus, two allele system, where a mutation-selection balance is attained with positive frequency of the strictly deleterious allele.

In the presence of transformation, the one added feature is the possibility of cycling in the absence of frequency dependent selection. I will merely cite some examples, below:

Transformation Acting:	Type of Selection Acting	Reference
Recombination	Pair (diploid viability)	Hastings (1981)
Segregation Distortion or Cultural Transmission	None	Cavalli-Sforza and Feldman (1981)
Segregation and Syngamy	Pair (diploid pair fertility)	Hadeler and Liberman (1975), Pollak (1978)

(3) THE VARIANCE IN THE MARGINAL FITNESSES OF THE TYPES PRESENT AT AN EQUILIBRIUM

In the absence of transformation, the relative change in frequency of each type is proportional to its fitness (in the case of pure branching descent) or its marginal fitness (in pair-mating descent). In either case, the notation is the same and the change in the ratio $\frac{z_i}{z_j}$ is

$$\frac{z_i'}{z_j'} = \frac{z_i}{z_j}\frac{w_i}{w_j} .$$

Thus, at any equilibrium we must have

$$w_i = w_j = \bar{w} \quad \text{for all} \quad i,j : \quad z_i,\ z_j > 0.$$

This is true regardless of any frequency dependence of the w's.

With transformation,

$$\frac{z_i'}{z_j'} = \frac{\sum_k z_k w_k T_{k \to i}}{\sum_k z_k w_k T_{k \to j}} ,$$

which does not in general give $w_i = w_j$ for all $z_i, z_j > 0$ at an equilibrium.

The possible magnitude of the differences in the marginal fitnesses at equilibrium depends on the extent to which offspring are identical to their parents. We can capture this quantitatively by expressing T as

$$T = (1 - \alpha)\, T_{id} + \alpha P , \tag{2.8}$$

where for pure branching descent

$$\alpha = 1 - \min_i T_{i \to i} ,$$

and for pair mating descent

$$\alpha = 1 - \min_{k,i} \frac{1}{(1 + \delta_{ki})}\, T_{k,i \to i} .$$

So

$$T_{k,j\to i} = (1-\alpha)\frac{1}{2}(\delta_{ki} + \delta_{ji}) + \alpha\, P_{k,j\to i} \cdot$$

The value α is simply the maximal amount of transformation occurring among any of the types or pairs of types. This representation separates the matrix component T_{id} in T from the other non-negative matrix components of T, leaving a transformation matrix P having

$$P_{i\to i} = 0 \quad \text{for some } i \text{ for pure branching,}$$

or

$$P_{j,i\to i} = 0 \text{ for some j and i for pair mating.}$$

If $T \neq T_{id}$, then $\alpha > 0$.

In the pure branching case, P is stochastic because

1) $\underline{e}^T P = \underline{e}^T$, since $\underline{e}^T T = \underline{e}^T\left((1-\alpha)I + \alpha P\right) = (1-\alpha)\underline{e}^T + \alpha\underline{e}^T P = \underline{e}^T$, and

2) $P_{j\to i} \in [0,1]$ $\forall$ i,j since:

$\forall\, j \neq i$, $P_{j\to i} = \frac{1}{\alpha} T_{j\to i}$, and for j=i, $P_{i\to i} = 1 - \frac{(1 - T_{i\to i})}{\alpha}$.

Thus

$$\forall\, j \neq i, \quad 1 \geq T_{j\to i} + T_{i\to i} \cdot$$

Therefore

$$T_{j\to i} \leq 1 - T_{i\to i} \leq 1 - \min_k T_{k\to k} = \alpha \cdot$$

Thus

$$P_{j\to i} = \frac{1}{\alpha} T_{j\to i} \leq 1.$$

And $T_{j\to i} \geq 0$, so $P_{j\to i} \geq 0$.

For i=j, $1 - T_{i\to i} \leq \alpha$ therefore $P_{i\to i} \geq 0$.

And $T_{i\to i} \leq 1$ therefore $P_{i\to i} \leq 1$.

DERIVATION OF BOUNDS ON THE EQUILBRIUM FITNESSES

PURE BRANCHING DESCENT:

Using the representation (2.8) of T in the recursion, we obtain:

$$\underline{z}' = \frac{1}{(\underline{e}^T W \underline{z})} \left((1 - \alpha)\, I + \alpha P \right) W \underline{z} \, .$$

Suppose the population is at an equilibrium. Then, regardless of whether it is stable or not,

$$z_i' = \hat{z}_i = \frac{1}{\hat{\bar{w}}} \sum_j \hat{z}_j w_j T_{j \to i} = \frac{1}{\hat{\bar{w}}} \sum_j \hat{z}_j w_j \left((1 - \alpha)\delta_{ij} + \alpha P_{j \to i} \right)$$

$$= \frac{1}{\hat{\bar{w}}} \left(\hat{z}_i w_i (1 - \alpha) + \alpha \sum_j \hat{z}_j w_j P_{j \to i} \right)$$

or in vector form

$$\hat{z} = \frac{1}{(\underline{e}^T W \hat{\underline{z}})} \left((1-\alpha) I + \alpha P \right) W \hat{\underline{z}} \, . \tag{2.9}$$

This will be called the EQUILIBRIUM IDENTITY.

Rearranging, we get $\left(\hat{\bar{w}} - (1 - \alpha)\, w_i \right) \hat{z}_i = \alpha \sum_j \hat{z}_j w_j P_{j \to i}$.

Therefore,

$$\left(\hat{\bar{w}} - (1 - \alpha)\, w_i \right) \hat{z}_i \ \varepsilon \ [0, \alpha \hat{\bar{w}}] \, ,$$

because

1) $P_{j \to i} \leq 1$, so

$$\sum_j \hat{z}_j w_j P_{j \to i} \leq \sum_j \hat{z}_j w_j = \hat{\bar{w}} \, , \text{ and}$$

2) $P_{j \to i} \geq 0$, so

$$\sum_j z_j w_j P_{j \to i} \geq 0 \, .$$

From this we can see that when transformation is acting, the fitnesses of the different types present at equilibrium need no longer be the same.

For

$$\hat{z}_i > 0 \quad \text{we have } 0 \leq \hat{\bar{w}} - (1-\alpha)\, w_i \leq \frac{\alpha\, \hat{\bar{w}}}{\hat{z}_i}$$

Thus

$$\frac{1 - \frac{\alpha}{\hat{z}_i}}{1-\alpha} \leq \frac{w_i}{\hat{\bar{w}}} \leq \frac{1}{1-\alpha} \,. \tag{2.10}$$

As α approaches 1, which means that some types never remain untransformed, the possible spread in relative fitnesses (the fitnesses divided by the mean fitness) at an equilibrium becomes unbounded.

PAIR MATING DESCENT:

Using the reparameterization (2.8) of T, substituting in the expression for the matrix Y of (2.7):

$$Y = \| \sum_k z_k \frac{w_{jk}}{w_j} T_{k,j \to i} \| = \| \sum_k z_k \frac{w_{jk}}{w_j} (1-\alpha)\left(\frac{\delta_{ij}}{2} + \frac{\delta_{ki}}{2}\right) + \alpha\, P_{k,j \to i} \|$$

$$= \frac{1}{2}(1-\alpha)\left(\operatorname{diag}\left(\sum_k \frac{w_{ik}\, z_k}{w_i} \right) + \| z_i \frac{w_{ij}}{w_j} \| \right) + \alpha \| \sum_k z_k \frac{w_{kj}}{w_j} P_{k,j \to i} \|$$

$$= \frac{1}{2}(1-\alpha)\left(I + \| z_i \frac{w_{ij}}{w_j} \| \right) + \alpha \| \sum_k z_k \frac{w_{kj}}{w_j} P_{k,j \to i} \| \,.$$

Now define

$$C \overset{\Delta}{=} \| \sum_k z_k \frac{w_{kj}}{w_j} P_{k,j \to i} \|_{i,j} \,.$$

Then C is also stochastic (in the column sense) since, with $\alpha > 0$:

1) $\underline{e}^T C = \underline{e}^T$. Because

$$\sum_i T_{k,j\to i} = 1 = (1-\alpha) + \alpha \sum_i P_{k,j\to i}$$

therefore

$$\sum_i P_{k,j\to i} = 1 .$$

Thus

$$\sum_{ik} z_k \frac{w_{jk}}{w_j} P_{k,j\to i} = \sum_k z_k \frac{w_{jk}}{w_j} = \frac{w_j}{w_j} = 1 .$$

2) $C \geq 0$. Since $\alpha = 1 - \min_{k,i} \frac{2}{1+\delta_{ki}} T_{k,i\to i}$, then

$$1 - \alpha = \min_{k,i} \left(\frac{2}{1+\delta_{ki}}\right) \leq \frac{2}{1+\delta_{ki}} T_{k,i\to i} ,$$

so

$$P_{k,i\to i} = \frac{1}{\alpha}\left[T_{k,i\to i} - \frac{(1-\alpha)}{2}(1+\delta_{ki})\right] \geq \frac{1}{2}\left[T_{k,i\to i} - \frac{2(1+\delta_{ki})}{2(1+\delta_{ki})} T_{k,i\to i}\right] = 0 .$$

And for $k \neq i$, $j \neq i$,

$$P_{k,j\to i} = \frac{1}{\alpha} T_{k,j\to i} \geq 0 .$$

So $P_{k,j\to i} \geq 0 \quad \forall\, k,j,i$. Therefore, $\sum_k z_k \frac{w_{kj}}{w_j} P_{k,j\to i} \geq 0 \quad \forall\, j,i$.

Substituting into the recursion, noting the identity,

$\mathrm{diag}(M\underline{x})\underline{x} = \mathrm{diag}(\underline{x})M\underline{x}$ for all square matrices M and vectors $\underline{x}$:

$$\underline{z}' = \frac{1}{\underline{z}^T W \underline{z}} Y \operatorname{diag}(W\underline{z})\underline{z} = \frac{1}{\underline{z}^T W \underline{z}} \left[\frac{1}{2}(1-\alpha)\left(I + \| z_i \frac{w_{ij}}{w_j} \| \right) + \alpha\ C \right] \operatorname{diag}(W\underline{z})\underline{z}$$

$$= \frac{1}{\underline{z}^T W \underline{z}} \left[\frac{1}{2}(1-\alpha)\left(\operatorname{diag}(W\underline{z})\underline{z} + \operatorname{diag}(\underline{z})W\underline{z} \right) + \alpha\ C \operatorname{diag}(W\underline{z})\underline{z} \right]$$

$$= \frac{1}{\underline{z}^T W \underline{z}} \left[(1-\alpha)\ I + \alpha\ C \right] \operatorname{diag}(W\underline{z})\underline{z} .$$

At any equilibrium, regardless of its stability,

$$\hat{\underline{z}} = \frac{1}{\hat{\underline{z}}^T W \hat{\underline{z}}} \left[(1-\alpha)\ I + \alpha\ \hat{C} \right] \operatorname{diag}(W\hat{z})\ \hat{\underline{z}} . \tag{2.11}$$

This is the EQUILIBRIUM IDENTITY for the pair-mating case.

This yields

$$(\hat{\bar{w}} - (1-\alpha)\ \hat{w}_i)\ \hat{z}_i = \alpha \sum_{kj} \hat{z}_k \hat{z}_j w_{kj} P_{k,j \to i} .$$

Therefore

$$\left(\hat{\bar{w}} - (1-\alpha)\ \hat{w}_i \right) \hat{z}_i \in [0, \alpha\ \bar{w}] . \tag{2.12}$$

Again, with transformation acting, the equilibrium marginal fitnesses of each type present need no longer be the same:

For $\hat{z}_i > 0$ we have

$$\frac{1 - \frac{\alpha}{\hat{\bar{w}}}}{1-\alpha} z_i < \frac{\hat{w}_i}{\hat{\bar{w}}} < \frac{1}{1-\alpha} .$$

Again we see that as α increases, the maximum possible spread in the equilibrium marginal fitnesses increases without limit.

TRANSFORMATION AND GENETIC LOADS

Muller's (1950) concept of genetic load was broadened and given a quantitative definition by Crow (1958) as

$$\text{Genetic Load} \triangleq 1 - \frac{\bar{w}}{\max_i(w_i)} .$$

It can be seen from the discussion above that in populations at equilibrium, a positive genetic load is possible only in the presence of transformation. Sources of equilibrium genetic load have been identified by the kinds of transformation producing them: segregation load (Crow, 1958), mutation load (Muller, 1950; Crow, 1958), migration load (Wright, 1977), recombination load (Crow and Kimura, 1970), meiotic drive load (Crow and Kimura, 1970), and dysmetric load (Crow and Kimura, 1970) in which the transformation involves shifts in habitat.

From (2.10) and (2.12), it can be seen that the maximum equilibrium genetic load, for all these cases, is simply the value α derived from the transformation occurring in each case, independent of the fitnesses of the different types. The result that the genetic load in the case of mutation may be independent of the selective values, depending only on the mutation rate, is therefore not as unexpected.

In the evolution of modifier genes, this difference between the maximal fitness in the population and the marginal fitness will play a major role. I would like to define a measure of this that is slightly different from the genetic load as defined by Crow (1958), that I will call the FITNESS LOAD:

$$L \triangleq \frac{\max_i(w_i)}{\bar{w}} - 1 = \frac{1}{1-\bar{L}} ,$$

where $\bar{L}$ is the classical genetic load.

The upper bound to the equilibrium fitness load is

$$L \leq \frac{1}{1-\alpha} ,$$

which increases without limit as α increases toward 1, and goes to 0 as α decreases to 0. So while the classical genetic load can range from zero to one, this "fitness load" can range from zero to infinity.

My definition of fitness load corresponds to the anomalous definition of genetic load by Ewens (1979). I am defining this new term not only because it is different from the classical definition of genetic load, but because it does not necessarily refer to genes. Recall that the "types" considered here include culturally transmitted behavior, habitat, and location, each of which may influence an individual's reproductive output, and each of which may be handed down to offspring.

(4) THE TYPES PRESENT AT EQUILIBRIUM

It can be readily seen that transformation may change the set of types present at an equilibrium. In the case of pure branching descent, only those types with the maximal fitness can be present at equilibrium under perfect transmission, whereas, if T is primitive, all types will be present at equilibrium.

On the other hand, in a situation where there is irreversible mutation, the fittest types may not be present at any equilibrium if mutation decreased the frequency faster than their selective advantage could increase it. In the same way, selfing may eliminate heterozygotes from the population which nevertheless have the greatest fitness.

The effect of transformation on the equilibrium variation in the population therefore depends on the exact nature of the transformation and how it interacts with selection.

3. ADDITIONAL ASPECTS OF EVOLUTION UNDER SELECTION AND TRANSFORMATION

(1) THE MEAN FITNESS AT EQUILBRIUM

How does $\hat{\bar{w}}$ depend on the transformation processes occurring? From the theory of small parameters (Karlin & McGregor 1972), we know that the equilibrium vector is continuous with perturbations in the recursion, as long as the the gradient matrix on perturbations of the equilibrium vector has no eigenvalues of one. If the equilibrium is locally stable under first order analysis, this is always true. Making this assumption, we can implicitly differentiate the equilibrium identity expressions.

PURE BRANCHING DESCENT

Let us describe the transformation matrix T as a perturbation from a transformation matrix T_1 :

$$T = T_1 + \epsilon (T_2 - T_1) .$$

The partial derivitive will be with respect to ϵ . Assuming that

selection is frequency independent, we obtain

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} \hat{z}_i + \bar{w} \frac{\partial \hat{z}_i}{\partial \varepsilon} = \sum_j \frac{\partial \hat{z}_j}{\partial \varepsilon} w_j T_{j \to i} + \sum_j \hat{z}_j w_j \frac{\partial T_{j \to i}}{\partial \varepsilon}$$

Thus $\frac{\partial \hat{\bar{w}}}{\partial \varepsilon}$ depends upon $\underline{z}$, T_1, T_2, and W.

Let us examine the case where transformation is a perturbation of the perfect transmission matrix. Then $T_1 = I$.

Thus

$$\hat{\bar{w}} z_i = w_i \hat{z}_i \ \forall\ i, \text{ i.e. } \hat{\bar{w}} = w_i \text{ or } \hat{z}_i = 0.$$

Let T_2 be a matrix P. Thus

$$T = I + \varepsilon (P - I) = (1 - \varepsilon) I + \varepsilon P .$$

Then

$$\frac{\partial T_{j \to i}}{\partial \varepsilon} = P_{j \to i} - \delta_{ij} .$$

So

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} \hat{z}_i + \bar{w} \frac{\partial \hat{z}_i}{\partial \varepsilon} = -\hat{z}_i w_i + \sum_j \hat{z}_j w_j P_{j \to i} + \frac{\partial \hat{z}_i}{\partial \varepsilon} w_i,$$

or

$$(\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} + w_i) \hat{z}_i = (w_i - \bar{w}) \frac{\partial \hat{z}_i}{\partial \varepsilon} + \sum_j \hat{z}_j w_j P_{j \to i} .$$

Define $E = \{i: \hat{z}_i > 0\}$, so $w_i = \hat{\bar{w}}$ $\forall\ i \in E$.

Then

$$(\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} + \hat{\bar{w}}) \hat{z}_i = \sum_j \hat{z}_j w_j P_{j \to i}, \ \forall\ i \in E .$$

Summing over $i \in E$,

$$\frac{\partial \bar{w}}{\partial \varepsilon} + \bar{w} = \sum_j \hat{z}_j w_j \sum_{i \in E} P_{j \to i} \leq \sum_j \hat{z}_j w_j = \hat{\bar{w}} .$$

Therefore, $\frac{\partial \bar{w}}{\partial \varepsilon} \leq 0$ at $T = I$. We will have strict

inequality,

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} < 0 \text{ , if for some } k \notin E : P_{j \to k} > 0.$$

Otherwise,

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} = 0 .$$

In other words, when the transformation acting in the population is changed slightly from the perfect transmission matrix to give positive probability of producing types of lower fitness than the types already present, then the mean fitness of the population at the nearby equilibrium will be decreased.

PAIR MATING DESCENT

Let us describe the transformation matrix T again as a perturbation from a transformation matrix T_1 :

$$T = T_1 + \varepsilon (T_2 - T_1) .$$

Assuming selection is frequency independent, implicit differentiation with respect to ε yields

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} \hat{z}_i + \bar{w} \frac{\partial \hat{z}_i}{\partial \varepsilon} = \sum_{jk} \hat{z}_j \hat{z}_k w_{jk} \frac{\partial T_{j,k \to i}}{\partial \varepsilon} + 2 \sum_{jk} \hat{z}_j \frac{\partial \hat{z}_k}{\partial \varepsilon} w_{jk} T_{j,k \to i} .$$

Let us consider the case where the transformation is a perturbation of the perfect transmission matrix,

$$T = \frac{1}{2}(\underline{e}^T \circledast I + I \circledast \underline{e}^T) (1 - \varepsilon) + \varepsilon P$$

or

$$T_{j,k \to i} = (1 - \varepsilon)\left(\frac{\delta_{ji} + \delta_{ki}}{2}\right) + \varepsilon P_{j,k \to i} .$$

Thus

$$\frac{\partial T_{j,k \to i}}{\partial \varepsilon} = P_{j,k \to i} - \frac{\delta_{ji} + \delta_{ki}}{2} .$$

Now, at $\varepsilon = 0$,

$$\hat{\bar{w}}\hat{z}_i = \hat{w}_i\hat{z}_i \quad \forall\ i \ .$$

So

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon}\hat{z}_i + \hat{\bar{w}}\frac{\partial \hat{z}_i}{\partial \varepsilon} = \sum_{jk}\hat{z}_j\hat{z}_k w_{jk}P_{j,k\to i} - \hat{z}_i\sum_k \hat{z}_k w_{ik} + \hat{z}_i\sum_k \frac{\partial \hat{z}_k}{\partial \varepsilon}w_{ik} + \frac{\partial \hat{z}_i}{\partial \varepsilon}\sum_k \hat{z}_k w_{ik}$$

giving

$$(\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} + \hat{w}_i)\,\hat{z}_i = (\hat{w}_i - \hat{\bar{w}})\frac{\partial \hat{z}_i}{\partial \varepsilon} + \sum_{jk}\hat{z}_j\hat{z}_k w_{jk}P_{j,k\to i} + \hat{z}_i\sum_k \frac{\partial z_k}{\partial \varepsilon}w_{ki} \ .$$

Define $E = \{i : \hat{z}_i > 0\}$. Then $\hat{w}_i = \hat{\bar{w}}\ \forall\ i \in E$.

Thus

$$\forall\ i \in E, \quad (\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} + \hat{\bar{w}})\,\hat{z}_i = \sum_{jk}\hat{z}_j\hat{z}_k w_{jk}P_{j,k\to i} + z_i\sum_k \frac{\partial \hat{z}_k}{\partial \varepsilon}w_{ki} \ .$$

Summing over $i \in E$,

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} + \hat{\bar{w}} = \sum_{jk}\hat{z}_j\hat{z}_k w_{jk}\sum_{i\in E}P_{j,k\to i} + \frac{1}{2}\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} \ ,$$

since

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} = 2(\hat{\underline{z}}^T W\frac{\partial \hat{z}}{\partial \varepsilon}) \ .$$

Since

$$\sum_{i\in E}P_{j,k\to i} \leq 1 \ ,$$

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} = 2\sum_{jk}\hat{z}_j\hat{z}_k w_{jk}(\sum_{i\in E}P_{j,k\to i} - 1) \leq 0 \ .$$

There will be strict inequality,

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} < 0 \quad \text{, if for some } i \notin E,\ P_{j,k\to i} > 0 \ .$$

Otherwise,

$$\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} = 0 \ .$$

In other words, $\hat{\bar{w}}$ will be lower if the increment in the transformation now causes the production of types not present at equilibrium from the pairs of those present. The conditions for the implicit differentiation to apply are that $\hat{z}$ be locally stable to the introduction of the absent types. In the case where the increment in transformation does not introduce new types into the population, but acts on the types present, even though $\frac{\partial \hat{\bar{w}}}{\partial \varepsilon} = 0$, the equilibrium mean fitness will be lower. The mean fitness forms a parabolic surface over the frequency simplex of those types present at an equilibrium. When no transformation is acting, the population is always at a global maximum in that surface, with respect to the types present. Thus, the fact that for some $i \in E$, $\frac{\partial \hat{z}_i}{\partial \varepsilon} \neq 0$, means that the equilibrium mean fitness will be lower with some transformation.

(2) THE EVOLUTION OF TYPES CONTAINING CONSERVED "PARTICLES"

In many multi-locus models, the only transformation occurring is the recombination between loci. The alleles at each locus are themselves untransformed, and occur at the same frequencies among offspring as in their parents. Recombination affects only the combinations of alleles occurring together in each haplotype. Because the alleles are not transformed, their change in overall frequency will be determined by their marginal fitness. Other processes such as transposition (without change in copy number), unequal crossing over, and inversion also conserve the identity of alleles at a locus while changing their relation to the rest of the genotype.

In general, when there is a "particle" in the type which is conserved during transformation, its change in frequency is simply its relative marginal fitness. This is shown as follows:

Let C_b be the set of all types which contain the conserved particle b.

For pure branching descent:

if $i \in C_b$, $j \notin C_b$, then $T_{j \to i} = 0$;

if $j \in C_b$, then $\sum_{i \in C_b} T_{j \to i} = 1$.

For pair mating descent:

if $i \in C_b$, $j \notin C_b$, $k \notin C_b$, then $T_{j,k \to i} = 0$;

if $j \in C_b$, $k \in C_b$, then $\sum_{i \in C_b} T_{j,k \to i} = 1$;

if $j \in C_b$, $k \notin C_b$, then $\sum_{i \in C_b} T_{j,k \to i} = 1/2$ if there is no transmission distortion (as defined in Chapter 1).

The overall frequency of conserved particle b is

$$x_b \triangleq \sum_{i \in C_b} z_i .$$

The marginal fitness of particle b is

$$w_b \triangleq \frac{1}{x_b} \sum_{i \in C_b} z_i w_i .$$

The recursion on x_b is:

a) Pure branching descent:

$$x'_b = \sum_{i \in C_b} z'_i = \sum_{\substack{j \\ i \in C_b}} z_j \frac{w_j}{\bar{w}} T_{j \to i} = \sum_{i, j \in C_b} z_j \frac{w_j}{\bar{w}} T_{j \to i} = \sum_{j \in C_b} z_j \frac{w_j}{\bar{w}} .$$

So

$$x'_b = x_b \frac{w_b}{\bar{w}} .$$

b) Pair mating descent:

$$x'_b = \sum_{i \in C_b} z'_i = \sum_{i \in C_b} z_j z_k \frac{w_{jk}}{\bar{w}} T_{j,k \to i}$$

$$= \sum_{\substack{j, i \in C_b \\ k \notin C_b}} z_j z_k \frac{w_{jk}}{\bar{w}} T_{j,k \to i} + \sum_{\substack{k, i \in C_b \\ j \notin C_b}} z_j z_k \frac{w_{jk}}{\bar{w}} T_{j,k \to i} + \sum_{j,k, i \in C_b} z_j z_k \frac{w_{jk}}{\bar{w}} T_{j,k \to i}$$

$$= 2 \sum_{\substack{j, i \in C_b \\ k \notin C_b}} z_j z_k \frac{w_{jk}}{\bar{w}} T_{j,k \to i} + \sum_{j,k, i \in C_b} z_j z_k \frac{w_{jk}}{\bar{w}} T_{j,k \to i}$$

$$= 2 \sum_{\substack{j \in C_b \\ k \notin C_b}} z_j z_k \frac{w_{jk}}{\bar{w}} \frac{1}{2} + \sum_{j,k \in C_b} z_j z_k \frac{w_{jk}}{\bar{w}} = \sum_{j \in C_b} z_j \frac{w_j}{\bar{w}}$$

$$= x_b \frac{w_b}{\bar{w}} .$$

When the population is at an equilibrium, then the marginal fitnesses of all the conserved particles in the population must be equal to $\bar{w}$.

When there is transmission distortion between the particles in the pair mating case, i.e.:

$$\text{for some } j \in C_b \text{ , } k \notin C_b \text{ , } \sum_{i \in C_b} T_{j,k \to i} \triangleq \beta_{bjk} \neq 1/2 ,$$

then a form of transformation is acting, so that the change in frequency of a particle is not solely determined by its marginal fitness, and at an equilibrium there may be a variance in the marginal fitnesses of the particles.

Define $\gamma_{bjk} \triangleq \beta_{bjk} - 1/2$.

Then

$$x'_b = 2 \sum_{\substack{j \in C_b \\ k \notin C_b}} z_j z_k \frac{w_{jk} Y_{bjk}}{\bar{w}} + x_b \frac{w_b}{\bar{w}} ,$$

hence at equilibrium,

$$\hat{\bar{w}} - \hat{w}_b = \frac{2}{\hat{x}_b} \sum_{\substack{j \in C_b \\ k \notin C_b}} \hat{z}_j \hat{z}_k w_{jk} Y_{bjk} .$$

(3) DIPLOIDY AND THE SEGREGATION-SYNGAMY TRANSFORMATION

The process of meiosis which diploid organsisms normally undergo in their sexual reproduction gives a special structure to the reproductive transformations acting on them. It is when we describe the reproductive transformation from pairs of diploid individuals to their diploid offspring that diploidy and the processes of segregation and syngamy give a special form to the transformation. In organisms such as sea urchins, there is never any pairing of diploid individuals; rather, diploids contribute gametes to a pool in which syngamy occurs to form the new diploid individuals. The gamete itself can be considered the individual and the diploid the mated pair, since in the formulation I have used, any viability or fecundity selection on the diploid is represented under pair selection. In this case the transformation probability $T_{j,k \mapsto i}$ represents the frequency of haplotype i gametes produced by diploid parents with genotypes composed of haplotypes j and k.

In the case where the mated pair is actually a pair of diploid individuals, I wish to represent the type with a classic notation for

diploids. The genotype of a diploid that received haplotype j from one parent and haplotype k from the other parent will be represented as $\frac{j}{k}$.

During reproduction, each parent will contribute a haploid gamete toward the formation of the new zygote. The frequency of haplotype i gametes produced by diploid $\frac{j}{k}$ will be $T_{j,k \to i}$. The probability that diploid pair $(\frac{a}{b}, \frac{c}{d})$ produce diploid offspring $\frac{i}{j}$ is:

$$T^M{}_{\frac{a}{b},\frac{c}{d} \to \frac{i}{j}} = T_{\frac{a}{b} \to i} \; T_{\frac{c}{d} \to j} .$$

T^M of this form will be called a segregation-syngamy transformation. In matrix form,

$$T^M = T \otimes T ,$$

or

$$T^M = \| T_{\frac{j_1}{j_2} \to i_1} \; T_{\frac{j_3}{j_4} \to i_2} \| \quad j_1, j_2, j_3, j_4, i_1, i_2 = 1 \ldots n .$$

One comment should be made regarding the asymmetry of this form. Usually, diploid genotypes $\frac{j}{k}$ and $\frac{k}{j}$ would be considered indistinguishable. In my notation, however,

$$T^M{}_{\frac{a}{b},\frac{c}{d} \to \frac{i}{j}} \neq T^M{}_{\frac{a}{b},\frac{c}{d} \to \frac{j}{i}} .$$

For the sake of symmetry, one could use instead:

$$T^M{}_{\frac{a}{b},\frac{c}{d} \to \frac{i}{j}} = \tfrac{1}{2}\left(T_{\frac{a}{b} \to i} \; T_{\frac{c}{d} \to j} + T_{\frac{a}{b} \to j} \; T_{\frac{c}{d} \to i} \right) .$$

However, this will be seen to be unnecessary when T^M is used in the recursion on the types in the population, where symmetry is restored.

Let $g_{\frac{j}{k}}$ be the frequency of diploid genotype $\frac{j}{k}$ (if we call $\frac{j}{k}$ and

$\frac{k}{j}$ indistinguishable, then the frequency is $g^j_k + g^k_j$ if $k \neq j$). The frequency of haplotype j will be:

$$z_j = \sum_k g^j_k = \sum_k g^k_j \ .$$

To represent the diploid genotype frequencies in vector form, let (j,k) form ordered indices of pairs so that:

$$\underline{z} = (\underline{e}_1^T \otimes I_1)\underline{g} = (I_1 \otimes \underline{e}_1^T)\underline{g} \ ,$$

where $\underline{e}_1$ and I_1 are of dimension equal to the number of haplotypes, n, and $\underline{g}$ is of dimension n^2.

For the genotype frequencies to be in Hardy-Weinberg frequencies means that $\underline{g} = \underline{z} \otimes \underline{z}$.

When the reproductive transformation is a segregation-syngamy transformation, then the recursion (2.4) becomes:

$$\underline{g}' = \frac{1}{(\underline{e} \otimes \underline{e})^T F(S \otimes S)(\underline{g} \otimes \underline{g})} (T \otimes T)F(S \otimes S)(\underline{g} \otimes \underline{g}) \quad ,(2.13)$$

where

$$\underline{e} = \underline{e}_1 \otimes \underline{e}_1 \ .$$

Suppose that the pair selection F is multiplicative, that is, the pair fitnesses can be expressed as products of individual "fertilities":

$$f^{\frac{a}{b},\frac{c}{d}} = k^a_b \, k^c_d \ .$$

This gives

$$F = K \otimes K \ .$$

Then (2.13) becomes

$$\underline{g}' = \frac{1}{(\underline{e}^T KS\underline{g})^2} (TKS\underline{g}) \otimes (TKS\underline{g}) \ .$$

We can now lump K and S, defining $W \triangleq KS$. Then

$$\underline{g}' = \frac{1}{(\underline{e}^T W\underline{g})^2} (TW\underline{g}) \otimes (TW\underline{g}) \ .$$

By summing to obtain the new haplotype frequencies, using the fact that $\underline{e}^T T = \underline{e}^T$, we have

$$\underline{z}' = (\underline{e}_1^T \otimes I_1)\underline{g}' = \frac{1}{(\underline{e}^T W \underline{g})^2} (\underline{e}^T W \underline{g})\, TW\underline{g} = \frac{1}{\underline{e}^T W \underline{g}} TW\underline{g} .$$

Therefore, $\underline{g}' = \underline{z}' \otimes \underline{z}'$, so after one generation, the genotype frequencies are in Hardy-Weinberg proportions, and the entire system is thus defined by the recursion on the haplotype frequencies:

$$\underline{z}' = \frac{1}{(\underline{e}_1 \otimes \underline{e}_1)^T W(\underline{z} \otimes \underline{z})} TW(\underline{z} \otimes \underline{z}) \qquad (2.14)$$

Random mating and multiplicative pair selection have therefore allowed us to decompose the n^2 dimensional system with the segregation-syngamy transformation between diploids to an n dimensional system with transformation acting between haplotypes. The importance of being able to decompose systems with segregation-syngamy transformations in this way will be seen in the next chapter, when we examine what happens to variation for the transformations. Linear variations in T will result in non-linear variations in $T^M = T \otimes T$. Most importantly, if T is an identity mapping for dimension n , T^M will not, however, be the identity mapping, $\tilde{T}_{id}$, for dimension n^2 : Here, we let

$$T = T_{id} \triangleq \frac{1}{2} (\underline{e}_1^T \otimes I_1 + I_1 \otimes \underline{e}_1^T) .$$

Hence,

$$T^M = T_{id} \otimes T_{id}$$

$$= \frac{1}{4}(\underline{e}_1^T \otimes I_1 \otimes \underline{e}_1^T \otimes I_1 + \underline{e}_1^T \otimes I_1 \otimes I_1 \otimes \underline{e}_1^T + I_1 \otimes \underline{e}_1^T \otimes \underline{e}_1^T \otimes I_1 + I_1 \otimes \underline{e}_1^T \otimes I_1 \otimes \underline{e}_1^T)$$

$$\neq \tilde{T}_{id} = \frac{1}{2}(\underline{e}_1^T \otimes \underline{e}_1^T \otimes I_1 \otimes I_1 + I_1 \otimes I_1 \otimes \underline{e}_1^T \otimes \underline{e}_1^T) .$$

In fact, there is not even any component of the n^2 identity mapping $\tilde{T}_{id}$ in $T_{id} \otimes T_{id}$. The value α for the maximum amount of transformation occurring for some pair of genotypes is therefore 1, which embodies the fact that a pair of two different homozygotes produce no homozygous offspring, all being heterozygotes. From the considerations of section 2.(3), since $\alpha = 1$, the maximum ratio of the largest marginal genotype fitness to the mean fitness is infinite. For a one-locus, two allele model, this situation would be approached if the two homozygotes had the same fitness and the heterozygote had almost zero fitness, although the pertinent equilibrium would be unstable in the absence of frequency dependent selection.

If because of non-random mating or non-multiplicative pair selection, the decomposition cannot be made, then the nature of the transformation acting on the population will be quite different from that acting on the haplotypes.

In the basic one locus model of fertility selection (Bodmer, 1965) there is no transformation acting on the haplotypes; the alleles are transmitted without change. Even then, however, if non-multiplicative fertilities expose the segregation-syngamy transformation, the full range of phenomena which may occur in the presence of transformation that I listed may occur. From this point of view, the discoveries of stable cycling (Hadeler and Liberman, 1975; Pollak, 1978), of decreases in the mean fitness (Pollak, 1978) and of complex polymorphisms (Feldman et al., 1983) should be understood to be effects caused not so much by selection acting on mated pairs rather than individuals, but by reproduction involving the segregation-syngamy transformation.

(4) AN EXAMPLE OF NORMALIZATION BY TYPES: SUBDIVIDED POPULATIONS

Models of subdivided populations are a primary example in which normalization by type occurs. The subdivisions may be into different demes, different habitats, or different sites. I use "deme" to refer generally to population subdivisions. Two forms of normalization by type have been modelled.

First is the idea of soft selection, where the fraction of the population that is in a given deme is always normalized after selection, to an amount that is a constant property of that deme. In addition one might define "soft recruitment", where the size of the population of new recruits to a deme is always normalized to a constant amount before selection, reproduction, and migration occur.

The second kind of normalization is necessary in pair-mating models when mating occurs only between members of the same demes. This can be represented by making the pair-type selection values $f_{i,j} = 0$ for i and j in different demes, and then normalizing so that the total frequency of pairs for each deme is still equal to the total fraction of the population in the deme before mating.

Both of these situations will be represented as follows. The type will be indexed with two subscripts, the first being its deme, the second any other pertinent features. Transformation will be defined to include both changes in <u>deme</u> and changes in the other information in the type.

Define x_{ei} to be the portion of the population that is in deme e and is type i.

c_e^s is the portion of the population in deme e after selection.

c_e^m is the portion of the population in deme e after migration.

c_e^r is the portion of the population in deme e after recruitment.

$T_{fj \to ei}$ is the fraction of offspring of type j from deme f that is of type i in deme e, for pure branching descent.

w_{ei} is the individual selection on type i in deme e.

The recursion on the frequency of types for the pure branching population is

$$x'_{ei} = \frac{c_e^r}{c_e^m} \sum_{fj} \frac{x_{fj} w_{fj}}{x_f \bar{w}_f} c_f^s T_{fj \to ei} ,$$

where

$$x_f \triangleq \sum_k x_{fk} , \quad \bar{w}_f \triangleq \sum_k \frac{x_{fk}}{x_f} w_{fk} ,$$

$$c_e^m \triangleq \sum_f \frac{c_f^s}{x_f \bar{w}_f} \sum_{ji} x_{fj} w_{fj} T_{fj \to ei} ,$$

and

$$c_e^r = \begin{cases} c_e^m & \text{for hard recruitment} \\ \text{constant} & \text{for soft recruitment} \end{cases} ,$$

$$c_f^s = \begin{cases} \dfrac{x_f \bar{w}_f}{\sum_f x_f \bar{w}_f} & \text{for hard selection} \\ \text{constant} & \text{for soft selection} \end{cases} .$$

In vector form this is

$$\underline{x}' = (N^m \otimes I)\, T\, (N^s \otimes I)\, W\underline{x} \ , \text{ where}$$

$$W = \text{diag}(w_{i_1 i_2}) \ ,$$

and

$$N^m = \text{diag}\left(\frac{c_i^r}{c_i^m}\right) \text{ and } N^s = \text{diag}\left(\frac{c_i^s}{x_i \bar{s}_i}\right)$$

are the normalizing matrices.

Under hard selection and hard recruitment,

$$N^m = \bar{w}\, N^s = I \ ,$$

and the model is identical to the model without normalization by types (2.1). With soft selection or soft recruitment, the model becomes a form of (2.1) with frequency dependent selection.

Now, the fitness load is defined as

$$L \triangleq \max_{e,i} \left(\frac{c_e^r c_e^s}{c_e^m x_e} w_{ei}\right) - 1 \ ,$$

and again this is bounded above by $\frac{\alpha}{1-\alpha}$ for α defined as before.

For pair-mating descent, previous modeling of subdivided populations (e.g. see Christiansen and Feldman, 1975) usually use gene frequencies <u>within</u> each deme, along with deme size, to characterize the population. To use this form, we define the following:

z_{fi} is the frequency within deme f of type i .

n_f is the initial size of deme f.

n_f^s is the size of deme f after selection.

n_f^m is the size of deme f after migration.

n_f^r is the size of deme f after recruitment.

$T_{fj,gk \to ei}$ is the fraction of offspring from a mated pair with one parent of type j from deme f, and the other parent of type k from deme g, that end up as type i in deme e.

$w_{fj,fk}$ is the lumped individual fitness and pair fitness of a pair of types j and k in deme f.

$\bar{w}_f \triangleq \sum_{jk} z_{fj} z_{fk} w_{fj,fk}$ is the mean fitness of deme f.

A life cycle consisting of selction, migration, and random mating within demes yields the recursions:

$$z'_{ei} = \frac{1}{n_e^m} \sum_{fjk} z_{fj} z_{fk} \frac{w_{fj,fk}}{\bar{w}_f} n_f^s T_{fj,fk \to ei} .$$

$$\text{and } n_e' = n_e^r .$$

We have

$$n_e^m \triangleq \sum_{ijkf} z_{fj} z_{fk} \frac{w_{fj,fk}}{\bar{w}_f} n_f^s T_{fj,fk \to ei} .$$

$$n_f^s = \begin{cases} n_f \bar{w}_f & \text{for hard selection} \\ n_f & \text{for soft selection} \end{cases} .$$

$$n_f^r = \begin{cases} n_f^m & \text{for hard recruitment} \\ n_f & \text{for soft recruitment} \end{cases} .$$

The fitness load in this case is defined as

$$L \triangleq \max_{e,i} \left(\frac{n_e^s w_{ei}}{n_e^m \bar{w}_e} \right) - 1 ,$$

where $w_{ei} \triangleq \sum_j z_{ej} w_{ei,ej}$ is the marginal fitness of type i in deme e. This is bounded above by $\frac{\alpha}{1-\alpha}$ for α defined as before.

4. TRANSFORMATION AND "UNITS OF SELECTION" ARGUMENTS

In this chapter, transformation has been shown to play a distinct role in models of evolution, producing phenomena that selection alone does not produce. The mechanisms of genetic transmission make transformation an essential component of population processes. The dual importance of selection and transformation may be able to add some clarity to the "units of selection" arguments that have been continuing for many years. It seems to me that in many discussions of this question (Dawkins, 1982; Hull, 1981; Gregorius, 1982; Templeton et al., 1976) there is a fundamental flaw which lies in two assumptions:

1) Evolution occurs by selection acting on units of selection.
2) Only objects which are replicated untransformed can be units of selection.

In each of these arguments, it is assumed that fundamentally selection is the cause of evolution. The only way to avoid considering the role of transformation is to find levels at which transformation is not acting, where there are conserved "particles", so that selection alone can be held responsible for the evolution of these particles. This usually requires descending to the level of the gene, which is often being transmitted untransformed, as Dawkins (1982) has done, or finding instances where higher level objects such as chromosomes are

being maintained as units, as we see in the discussions of Franklin and Lewontin (1970) and Templeton et al. (1976). This in no way takes transformation out of the dynamics of the population; transformation is now to be found acting on the fitnesses of these untransformed units. As Sober and Lewontin (1982) have noted, to pose a model of evolution in terms of individual genes, the concept of selection has to be redefined to be the marginal fitnesses of those genes, which are indeterminate because of the interactions with the rest of the genome, which is not constant because transformations are acting on it. In doing so one loses sight of the phenotypes at level of whole organisms, mated pairs, or groups which form the basis of fitness.

An alternative view which can be taken from the framework developed here is that evolution can't be reduced to selection processes. Transformation processes play a fundamental and distinct role. Selection can then be considered to act on the phenotype, while transformation confounds this in its various ways and adds its own direction by changing phenotypes into other phenotypes, and the combination of the two determines the course of evolution.

SUMMARY

In this chapter I have developed a general formulation for the action of selection and transformation on the composition of types in a population for two basic life cycles. A great many of the deterministic models in population genetics are subsumed within these general formulations, including multiple locus, multiple allele models,

gametic-, viability-, and fertility-selection models, models with different selection regimes between the two sexes, models with different recombination distributions between the two sexes, models with mutation, gene conversion, segregation distortion, migration, habitat preference, cultural transmission, and so forth. The results I have obtained from the analysis of the formulations do not capture the detailed behavior of these different models, but were intended to circumscribe to some degree the possible behavior of these systems.

In particular, the analysis describes some relationships between general features of these systems. I have tried to show how a number of phenomena are the result of transformation acting in populations under selection, including decreases in mean fitness, the possibility of a variance in fitnesses at equilibrium, and stable cycling.

A brief discussion is given on "units of selection" arguments, and it is argued that the discussions of this topic in the literature attempt an impossible task-- to reduce the dynamics of evolution to selection processes. By incorporating transformation processes, there is no need to use artifactual and indeterminate definitions of fitness.

Finally, this framework will be the starting point for developing theory on how transformations themselves evolve.

CHAPTER 3

THE EVOLUTION OF TRANSFORMATIONS

In the previous sections I developed general formulations for the evolution of the frequencies of types in a population undergoing selection and transformation. In this chapter, the evolution of the transformations themselves will be explored, by including in the models transmissible variation for the transformations. Actually, this is not so much an augmentation of the models in the previous chapter as a structuring of the variation between different types. We must now define two, and sometimes three independent dimensions in the specification of an individual's type: the selection type, the transformation type, and the "structural" type.

The selection type determines the selection that acts on the individual. The transformation type determines the frequencies of different selection types among the offspring of the individual given its own selection type (or of the mated pair, given their two selection types). The additional dimension for which transmissible variation may exist is in how the transformation types may be co-transformed or associated with the selection types in the offspring; this is what I call the individual's "structural" type.

The classic modifier model requires each of these three kinds of information. In the modifier model, a new locus, the modifier, is added to a set of other genes under selection. Different alleles at the

modifier locus produce different parameters for the transformation processes acting on the selected loci. In diploid models, in order to know how the modifier alleles are associated with the newly transformed alleles at the selected loci, we need to know the linkage phase of the modifier alleles in the diploid. This is its structural type.

I will not attempt an analysis which deals in complete generality with the forms of the selection, transformation, and structural types. The models I will treat will for the most part assume that the transformation types themselves are not being transformed, but are faithfully transmitted. I will investigate the evolution of transformation types in populations with pure branching descent, and in several models of populations with pair-mating descent.

This formulation of types partitions the variation for fitness and transformation into two independent pieces of information about the organism. However, in the actual variation among organisms, this separation may be bridged by pleiotropy. Wright (1964), discussing his criticism of Fisher's (1928) modifier theory for the evolution of dominance, showed that very small intrinsic fitness differences between the modifier alleles due to pleiotropic effects would dominate over the selection on the modifier alleles due to their effects on dominance. If we were to include pleiotropic fitness effects in the transformation types and pleiotropic transformation effects in the selection types we might obtain a more realistic model, but it returns then to the general form for evolution under selection and transformation discussed in Chapter 2. Short of this, I will examine cases where there are intrinsic fitness differences between the transformation types, where these differences interact multiplicatively with the fitnesses

determined by the selection type. Thus some of the questions regarding the effects of pleiotropy of modifiers can be investigated. Transformation types which have no intrinsic fitness effects will be called neutral.

1. THE SELECTIVE FORCES ON TRANSFORMATION TYPES

When the transformation types are not being transformed, they constitute a "conserved particle" within the type, which was discussed in section 3.(2) of the last chapter. Their growth rate in the population will be determined by their marginal fitnesses relative to the mean fitness of the population. In the case where the transformation type is neutral, its marginal fitness will simply be the average of the fitnesses of the selected types with which it is associated.

These marginal fitnesses would clearly be the same for all of the transformation types if they were randomly associated with the selected types. In such a case, there would be no change in the overall frequencies of the transformation types in the population. The essential feature of transformation types that allows them to evolve is that, through their effects on transformation, they may be able to create a non-random association between themselves and the selected types. Those transformation types which have induced their marginal fitnesses to be greater that the mean fitness of the population by causing themselves to occur more frequently with the fitter types in the population, will increase in overall frequency. Hitchhiking, then, is

the essential mechanism by which neutral, perfectly transmitted transformation types evolve.

For evolution by hitchhiking, the nature of the dynamics is quite different between populations that are in a transient phase of their evolution and populations that have reached an equilibrium. In fact, one might expect that at an equilibrium, because there are no changes in the frequencies, there could be no hitchhiking effects at all. However, recall that when transformation is occurring, there may be differences in the marginal fitnesses among the types present, and that this requires a constant net "flow" by transformation from the fitter types to the less fit. By altering this "flow", a transformation type can come to be non-randomly associated with the selected types, and may therefore aquire a marginal fitness different from the mean of the population. We would expect, therefore, that a prerequisite for evolution to occur among transformation types when the population is at equilibrium is that there be a standing variance in the marginal fitnesses of the types present, and this will be seen to be true. To be more precise, in order for a transformation type to have a geometric, rather than algebraic, asymptotic rate of change in frequency, there must be a variance in the marginal fitnesses at equilibrium. When we consider situations where there is transformation acting on the transformation types, this no longer need be true, as will be seen in the case of modifiers of segregation distortion.

In the literature, a dichotomy can be drawn between studies of the evolution modifier genes where the population is allowed to converge to equilibrium, and conversely, where the population is continually placed back in a transient phase of its evolution by fluctuations in selection,

sampling error due to finite population size, or the introduction of novel, fitter types. Examples of modifier models with transient dynamics include Leigh (1970, 1973), Eshel (1973), Painter (1975), Strobeck et al. (1976), Felsenstein and Yokoyama (1976), Charlesworth (1976), Charlesworth et al. (1977), Gillespie (1981 a,b,c). This thesis will deal solely with the nature of modifier hitchhiking in populations near equilibrium.

Any features of the organism which affect the maintenance of association between the transformation types and the selected types would be expected to influence the evolutionary dynamics of modifier hitchhiking. This is why the structural type can play an important role, because it determines the association of transformation and selected types in the offspring. In modifier gene models, it is the recombination between the modifier gene and the selected loci that will play this role. In cultural transmission models, the structural type has no single embodiment. One would include any covariance in transmission of different independent traits. Boyd and Richerson (1985) have modeled an example of this, where several traits may be simultaneously acquired from individuals chosen as models, hence their particular association in an individual model will be passed on. We would expect that the less the associations are maintained, the weaker the selection on the transformation types will be. This will be seen to be true where analysis is possible.

2. THE NATURE OF THE VARIATIONS IN TRANSFORMATIONS

One of the major results that will be found is that the evolution of transformations depends greatly on how the underlying biological processes involved in transformation constrain the variation in the transformation probabilities. The variation in the transformation processes in nature that have been characterized, such as mutation, recombination, and migration, is usually conceived not as adjusting each transformation probability individually, but rather as changing parameters in underlying processes which generate the transformations. The variation therefore has much fewer degrees of freedom than the number of types in the population. In the cases of mutation, recombination, gene conversion or other changes in the genetic material, it is changes in the basic rates of the underlying processes due to variation in enzymes, concentrations or other conditions. In processes such as dispersal, where location is the type, behavioral variables or morphological differences change the overall migration probabilities.

UNIFORM VARIATION

The model which is frequently used for variation in transformations, and is fairly well justified when transformations consist of single events, is that the relative probabilities of each transformation event are changed uniformly by changes in a parameter of some underlying process generating the transformations. By this I mean that the matrix of transformation probabilities contains a term mT_1, where all the variation occurs in the parameter m, and T_1 is a fixed matrix of the relative transformation probabilities. To illustrate, T_1

could represent the probabilities that a gene, given that it mutates, changes from one allelic state to another, while m represents the base line chance that it will mutate.

The process that m and T_1 represent need not be the only process involved in transformation. How this process relates to any other transformation processes occurring will affect how m and T_1 are incorporated into the transformation matrix. Several possibilities are given below:

1) m controls the rate of the only transformation process occurring. Then

$$T = (1-m)T_{id} + mT_1 .$$

2) m controls transformations that interact additively with others that are occurring. Then

$$T = (1-\alpha-m)T_{id} + \alpha T_2 + mT_1 ,$$

where αT_2 represents the other processes.

3) m changes the relative probabilities of different transformations, but not the overall rate. Then

$$T = (1-\alpha)T_{id} + \alpha\left((1-m)T_2 + mT_1\right) .$$

4) m changes the relative probabilities and the overall rate of transformation. Then

$$T = (1-m)\left((1-\alpha_2)T_{id} + \alpha_1 T_2\right) + m\left((1-\alpha_1)T_{id} + \alpha_1 T_1\right) ,$$

with $\alpha_1 \neq \alpha_2$ and $T_1 \neq T_2$.

5) m controls the rate of one step in a sequence of transformations. Then

$$T = \left((1-\alpha_1)T_{id} + \alpha T_2 \right) \left((1-m)T_{id} + mT_1 \right) \left((1-\alpha_2)T_{id} + \alpha_2 T_3 \right) ,$$

where the two outside matrices represent the transformations occurring before and after the one controlled by m .

For this case, if one of the transformations is from mated pairs to individuals, the changes in dimension require that the matrices have the appropriate size.

6) m changes the rate of events which can occur independently multiple times. Then

$$T = \left((1-m)I + mT_1 \right)^n .$$

This case is not defined for transformations from mated pairs to individuals, but only for transformations within the same phase of the life cycle, which is why in this case, $T_{id} = I$.

I will make several definitions to characterize the variation in the transformations for these different cases.

DEFINITION 1: Case 1) is defined as LINEAR variation, because the transformation matrices form a line that intersects the perfect transmission matrix.

DEFINITION 2: Cases 2) through 5) are defined as AFFINE variation, because the transformation matrices form a line that does not intersect the perfect transmission matrix.

DEFINITION 3: LINEAR and AFFINE variation comprise what is defined as UNIFORM variation, that is, variation where the transformation matrices all lie on a line. In case 6), the transformation matrices do not lie on a line, so it is an example of NON-UNIFORM variation.

A general form for uniform variation is

$$T = T_{id} + A + mB \quad , \qquad (3.1)$$
$$\text{where } \underline{e}^T A = \underline{e}^T B = 0 \ .$$

When $A = 0$ it is linear, and when $A \neq 0$ it is affine, unless A is proportional to B, in which case the variation is really linear, where the variable parameter now is defined as $\tilde{m} = m + \gamma$ if $A = \gamma B$, giving

$$T = T_{id} + \tilde{m}B \ .$$

Under some special relations between T_1, T_2, and T_{id}, which can be readily derived, cases 2) through 5) are actually linear variation.

An alternative form for uniform variation is

$$T = (1-m)T_1 + mT_2 \ , \qquad (3.2)$$

where T_1 and T_2 are transformation matrices.

For the first form, m can range from 0 up to a value that depends on the scaling of B, which is arbitrary, which keeps T within the hull of stochastic matrices, and in the second form it depends in detail on the entries of the matrices T_1 and T_2, and may range below 0 or above 1 under some circumstances; I mention this only to avoid confusion later. It will be clear from the particular matrices used what the range of m is, and it does not enter into any of the results.

When the variation in transformations consists of a one parameter family of transformation matrices as it has been characterized here, then the phenotype of the transformation type is simply the value of m that it determines. When the transformation is in a pure branching phase of a life cycle, each transformation type a determines a parameter m_a. When the transformation is from mated pairs to individuals, then a pair of individuals of transformation types a and b will determine a parameter $m_{a,b}$.

In nearly all of the random mating models of recombination, mutation, and migration modifiers in the literature, the variation in transformations due to modifier genes is uniform. An exception is the model of a modifier acting on recombination between multiple loci by Charlesworth (1976) and Charlesworth and Charlesworth (1979a). In this case, as the basic recombination rate increases, the relative frequency of multiple recombinants increases faster than that of single recombinants. In the presence of complete interference in recombination between loci, recombination occurs as only a single event for each individual and the variation becomes uniform.

Examples of affine variation include the model of Feldman et al. (1980) where a modifier controls recombination between two selected loci which are also undergoing mutation, the model of Charlesworth and Charlesworth (1979b) where a modifier controls recombination in a population also undergoing migration, and the model of Christiansen and Feldman (1975) where a modifier controls either recombination or migration in a population undergoing recombination and migration.

In the analyses to follow, these distinctions in the nature of the variation in transformations will be found to be fundamental in determining the evolution of the transformations.

3. THE EVOLUTION OF TRANSFORMATION TYPES UNDER PURE BRANCHING DESCENT

The biological situations in which pure branching descent occurs include both asexual organisms and purely-selfing organisms, as shown in Table 2. In purely-selfing diploids, organisms heterozygous at a modifier locus will produce homozygous offspring, which constitutes a transformation on transformation types, which I am excluding from the present analysis. Hence, I shall be considering only asexual organisms here.

The full type of an asexual organism will be specified by its transformation type a, and its selection type, j. No structural type need be specified since all of a type a's offspring will be type a.

The transformation probabilities will be expressed as $T_{aj \to ai}$. The recursion on the frequencies, z_{ai}, of types (ai), after a life cycle of selection and transformation is:

$$z'_{ai} = \sum_j z_{aj} \frac{w_j}{\bar{w}} T_{aj \to ai}, \quad \text{where} \quad \bar{w} = \sum_{ai} z_{ai} w_i .$$

In vector form this is:

$$\underline{z}' = \frac{1}{\bar{w}} \tilde{\tilde{T}} \tilde{\tilde{W}} \underline{z},$$

where

$$\tilde{\tilde{T}} = \left\| \begin{array}{cccc} T_1 & & & 0 \\ & T_2 & & \\ & & \ddots & \\ 0 & & & \end{array} \right\|, \quad \text{with} \quad T_a = \| T_{aj \to ai} \|,$$

$$\tilde{\tilde{W}} = I_1 \otimes W, \quad \text{with} \quad W = \text{diag}(w_i),$$

$$\underline{z} = \begin{pmatrix} \underline{z}_1 \\ \underline{z}_2 \\ \vdots \end{pmatrix} \text{ , with } \underline{z}_a = \begin{pmatrix} z_{a1} \\ z_{a2} \\ \vdots \end{pmatrix} \text{ , and}$$

$$\bar{w} = \left(\underline{e}^T \otimes \underline{e}^T\right) \tilde{W} \underline{z} \ .$$

This is, therefore, a special case of the general model of evolution under selection and transformation (Chapter 2, Section 1.(1)) where the matrix $\tilde{T}\tilde{W}$ is completely decomposable into diagonal blocks T_aW. The recursion therefore can be separated into recursions on the vector of frequencies for each transformation type a:

$$\underline{z}'_a = \frac{1}{\bar{w}} T_a W \underline{z}_a \ .$$

(1) CONVERGENCE BEHAVIOR

From the considerations of Section 2.(2) of Chapter 2, the convergence behavior of the population may depend on the initial frequencies of the types. What is of interest is the long term evolution of transformations in the population, so I will assume that each transformation type eventually gets tested in the population in combination with each of the selected types. This means that eventually the frequency vector of types will contain some component of eigenvectors or their principal vectors whose eigenvalues are of modulus equal to the spectral radius of T_aW. Assuming that the fitnesses and transformations are frequency independent, the asymptotic marginal fitness of transformation type a will then be the spectral radius of T_aW. The population will then fix on the transformation type with the largest spectral radius. If several types have the maximal spectral

radius, then they can be present in a polymorphism. This polymorphism will be neutral, however. That is, the total frequency of each transformation type is unconstrained and will not resist perturbation to other values, regardless of how the frequencies of selected types associated with a given transformation type converge. The situation described in Chapter 2, section 2.(2) 2)a. applies here.

1. POPULATION LEVEL CONSEQUENCES: MEAN FITNESS AND FITNESS LOAD

Two consequences for the population can be derived from these results. Once the population is fixed on the transformation types yielding the maximal spectral radius, its mean fitness is simply this spectral radius. Therefore, if a new transformation type is to increase when introduced to the population, it must result in an eventual increase in the mean fitness of the population. This is the Mean Fitness Principle of Karlin and McGregor (1974). In the absence of frequency dependence, the Mean Fitness Principle therefore holds in the case of populations with asexual descent (pointed out to me by Kent Holsinger, personal communication).

Another consequence can be seen to directly follow from this. Because the fitnesses are constant and the eventual mean fitness increases, the eventual fitness load,

$$\frac{\max_i(w_i)}{\bar{w}} - 1 ,$$

must decrease after the substitution of any new transformation types.

In case of frequency independence, these two consequences coincide. However, in an example of frequency dependent selection

discussed later, these two will not coincide, and this will be the basis of a new principle I will conjecture about the evolution of transformations.

2. DETERMINANTS OF THE SPECTRAL RADIUS

Of primary importance then is the spectral radius of $T_a W$. If the fitnesses of all the selected types are equal, then $\frac{1}{\bar{w}} W = I$, and the spectral radii for all transformation types are equal to one. This yields the following result:

RESULT 3.1:

When there is no selection on selected types, there can be no selection on transformation types.

The frequencies of the transformation types will remain at their initial values thoughout, while concurrently the frequencies of the selected types associated with each transformation type a will converge to equilibria or cycles in the spectral radius space of T_a.

When the fitnesses of the selected types are different, so that $\frac{1}{\bar{w}} W \neq I$, then different transformation matrices will yield different spectral radii. It is not possible to say in general which of any two transformation matrices will yield the larger spectral radius. However, the following specific results can be shown:

1. The highest spectral radius occurs for transformation types yielding perfect transmission, and the spectral radius is the maximum fitness

of the selected types. The other transformations which have this maximal spectral radius are those for which no types with the maximal fitness are transformed to any types with lesser fitness.

2. For a set of matrices T_a that vary linearly away from perfect transmission, the spectral radius $\rho(T_aW)$ is non-increasing, and strictly decreasing if T_a is irreducible.

Result 1. can be seen to be a consequence of result 2., which is Theorem 5.2 in Karlin (1982). The implications of these results for the evolution of transformations makes us examine the nature of variation in transformations.

a. LINEAR VARIATION

As described above, if what is varying is the overall rate of single event transformations in the absence of any other transformation processes, then the variation in transformations is expected to be linear. The transformation matrices will be of the form

$$T_a = (1-m_a)I + m_aT_1 .$$

Theorem 5.2 of Karlin (1982) states that

$$\text{if } m_a < m_b \text{ then } \rho(T_aW) > \rho(T_bW) ,$$

and if T_1 is irreducible, then the the right hand inequality is strict. In this case, therefore, evolution toward perfect transmission is the evolutionary outcome.

EFFECT ON THE FITNESS LOAD

An upper bound on the fitness load is $\frac{m_a}{1-m_a}$; therefore, as

transformation types with succeedingly smaller values of m_a substitute in the population, the fitness load is forced to go to zero.

b. AFFINE VARIATION

If the variation is not linear, other evolutionary outcomes are possible. There is no theorem comparable to Karlin's for affine or non-uniform variation, but in one special case the local rate of change of the spectral radius can be calculated. This is for transformations with memoriless distributions, defined as follows:

DEFINITION 4: A transformation with a MEMORILESS DISTRIBUTION is one whose transformation matrix is of the form

$$T = (1-\beta)T_{id} + \beta T_1 ,$$

where for pure branching descent,

$$T_1 = \mathrm{diag}(t_i)U ,$$

U is a matrix of ones, and $\sum_i t_i = 1$.

Therefore, all types have the same probability of undergoing a transformation processes in which their former type has no influence on the type they become. This has been called "house of cards" mutation by Kingman (1980).

The general affine form for transformations incorporating memoriless distributions is

$$T_a = (1-m_a)\left[(1-\alpha)I + \alpha S\right] + m_a\left[(1-\beta)I + \beta P\right] ,$$

where S and P are the rank one matrices

$$S = \mathrm{diag}(s_i)U, \quad \text{and} \quad P = \mathrm{diag}(p_i)U .$$

THEOREM 3.2a:

Assume that the normalized leading eigenvector $\hat{\underline{v}}$ where $\hat{\rho}\hat{\underline{v}} = \hat{T}W\hat{\underline{v}}$, spans the eigenspace for the spectral radius $\hat{\rho} = \sum_i \hat{v}_i w_i$ and therefore is an isolated point, and satisfies the requirements for differentiability with respect to changes in T.

Then the spectral radius $\rho(T_a W)$ for m_a near $\hat{m}$ is approximately

1)

$$\tilde{\rho} = \hat{\rho} + (m_a - \hat{m}) \frac{\alpha - \beta}{1-(1-\hat{m})\alpha - \hat{m}\beta} \hat{\rho} ,$$

if for some i, $\alpha s_i = \beta p_i = 0$,

or otherwise,

2)

$$\tilde{\rho} = \hat{\rho} + (m_a - \hat{m})\Big(\sum_i \frac{1}{\gamma_i} \hat{v}_i^2 w_i\Big)^{-1} \frac{1}{\gamma^2} \cdot \Big[(\alpha-\beta)\sum_i \frac{1}{\gamma_i} \hat{v}_i^2 (w_i - \hat{\rho})^2 + \hat{\rho}\,\alpha\beta\Big((1-\gamma)\sum_i \hat{v}_i (w_i - \hat{\rho})\Big(\frac{p_i - s_i}{\gamma_i}\Big) + \gamma\ \mathrm{cov}\Big(w_i, \frac{p_i - s_i}{\gamma_i}\Big)\Big)\Big] ,$$

(3.4)

where $\gamma_i \overset{\Delta}{=} (1-\hat{m})\alpha s_i + \hat{m}\beta p_i$, and $\gamma \overset{\Delta}{=} \sum_i \gamma_i = (1-\hat{m})\alpha + \hat{m}\beta$.

The full derivation of these results is given later, under Theorem 3.2b in Section 4. (1) on diploid modifiers, where the same forms appear.

In 1), evolution proceeds in the direction lowering the overall rate of transformation $(1-m_a)\alpha + m_a\beta$.

In 2), three terms contribute to determining whether the spectral radius increases or decreases with m_a . The first term in the brackets is the contribution from lowering the overall rate of transformation. This term is zero if and only if the fitness load is zero, for then

$$\hat{\rho} = w_i \quad \forall\, i \qquad \text{and} \qquad \hat{v}_i = \frac{\gamma_i}{\gamma} \quad \forall\, i \,.$$

The second two terms in the brackets are the contribution from shifting the transformation probabilities toward the more fit types. This term is zero if the fitness load is zero or if the variation is linear, requiring $\alpha = 0, \beta = 0$, or $S = P$.

From this one can say that there are two "forces" acting on the evolution of transformations, one toward more perfect transmission, and one toward producing more of the fitter types. If α is close to β , then an increase in the overall transformation can evolve if it sufficiently increases the probability of transformations to the fitter types, which may result in the extinction of lesser fit types. When the fitness load is zero, then there is no more selective opportunity for the evolution of new transformation types, unless these can cause the creation of novel, fitter types.

(2) "BALANCED MIXTURE" TRANSFORMATION POLYMORPHISMS

In the absence of frequency dependent selection or transformation, it was seen that any polymorphisms in transformation types present in

the population will be essentially neutral. With frequency dependence however, transformation type polymorphisms which are stable to perturbation may be possible. I will not consider this question generally here, but will examine the case where the fitness of each selected type increases as the type become more rare, which is the kind of frequency dependence often proposed for situations with intraspecific competition.

Suppose that the fitness of each selected type strictly increases without bound, as it decreases in frequency. Then in the absence of transformation, there will be a unique, globally stable polymorphic equilibrium where all the fitnesses have equilibrated. Call the frequency vector of this equilibrium $\hat{\underline{v}}$. Whenever the frequency of the selected haplotypes equals $\hat{\underline{v}}$, the fitness matrix will be

$$W = \bar{w} I .$$

So at equilibrium,

$$T_a \hat{\underline{z}}_a = \hat{\underline{z}}_a .$$

Therefore, all transformation matrices will produce spectral radius one. However, the eigenvectors $\hat{\underline{z}}_a$ must satisfy

$$\sum_a \hat{z}_{ai} = \hat{v}_i \text{ , where } \sum_j T_{a\, j \to i} \hat{z}_{aj} = \hat{z}_{ai} .$$

(To avoid the complications of possible cycling, I will assume that each transformation matrix is primitive, yielding one strictly positive, unique eigenvector with eigenvalue 1 .)

Let us rewrite each eigenvector $\hat{\underline{z}}_a$ as

$$\hat{\underline{z}}_a = x_a \hat{\underline{v}}(a) ,$$

where x_a is the total frequency of transformation type a and $\hat{\underline{v}}(a)$ is the frequency of the selected types among that transformation type, simply $\hat{\underline{z}}_a$ normalized.

Then the equilibrium requirement is

$$\hat{\underline{v}} = \sum_a x_a \hat{\underline{v}}(a) .$$

Thus, $\hat{\underline{v}}$ must be a linear combination of the eigenvectors of each transformation matrix. If there are fewer transformation types than selected types, it is not even guaranteed that $\hat{\underline{v}}$ will be in the space spanned by $\{\hat{\underline{v}}(a)\}$. There must be as many different $\hat{\underline{v}}(a)$ as there are selected types to guarantee that any $\hat{\underline{v}}$ is in the space they span. But there is a further requirement, that the convex hull of $\{\hat{\underline{v}}(a)\}$ contain $\hat{\underline{v}}$. This restricts the possible sets of transformation matrices that can allow this equilibrium to be reached to various "balanced mixtures" of complementary sets. I will refer to these equilibria where all types have the same fitnesses as "balanced mixture" polymorphisms. It is important to note that these generally require that the variation in the transformations <u>not</u> be linear: when the variation is linear, there is only one eigenvector for all the transformations. If the set of transformation types is not sufficient to yield a balanced mixture polymorphism, then there will be a variance in fitnesses at equilibrium.

A NUMERICAL EXAMPLE: MIGRATION WITH SOFT SELECTION

I have not analyzed the stability of these "balanced mixture" polymorphisms in general for this situation. But I have examined numerically an example of this situation, where there are two demes and transformation consists of individuals changing demes. Soft selection resets each deme i to a constant proportion c_i of the total population. The fitness of an individual in deme i therefore is

$$w_i(\underline{v}) = \frac{c_i}{v_i} .$$

Three evolutionary outcomes seem possible:

1) If the resident transformation type has a migration matrix whose leading eigenvector is not $\underline{c} = (c_i)$, then there will be a fitness variance at equilibrium, and any new transformation type with linearly less migration will be able to invade and displace it.

2) In the same circumstance as 1), any new transformation type whose migration matrix has as its leading eigenvector $\underline{c}$ will be able to invade and displace the resident, regardless of the overall rate of migration it causes.

3) In the same circumstance as 1), where the resident transformation type yields matrix T^*, any new transformation type whose migration matrix, T, satisfies

$$c_1T_{1\to 2} > c_2T_{2\to 1} \quad \text{if} \quad c_1T^*_{1\to 2} < c_2T^*_{2\to 1} , \text{ or}$$
$$c_1T_{1\to 2} < c_2T_{2\to 1} \quad \text{if} \quad c_1T^*_{1\to 2} > c_2T^*_{2\to 1} ,$$

will be able to invade, and the two transformation types will go to a balanced mixture polymorphism where the portions of the population in the demes after migration are $\underline{c}$.

In each of these outcomes, the net effect is that the fitness load is decreased. How the transformations themselves evolve depends upon the nature of the variation in the transformations. This suggests the following conjecture:

CONJECTURE: THE FITNESS LOAD PRINCIPLE:

Transformation types that are not themselves being transformed evolve to reduce the equilibrium fitness load of the population.

If this principle seems vaguely familiar to the reader, it is because this basic idea was proposed 25 years ago by Kimura (1960) in a paper that considers the evolution of mutation rates and dominance. Offered not as a result but as a premise, he states

> "I now assume that, in the course of evolution, ...by the accumulation of modifiers ...[the mean fitness] will be maximized, or more strictly the total genetic load ...will be minimized. This is my view on the course of evolution, and I would like to call it the principle of minimum genetic load."

Whether or not this is true in general for asexual populations I have not determined. If it holds it would be remarkable because the fitness load depends only on the difference between the mean fitness of the population and the maximal fitness in the population. If such a principle is operating, it might instead depend on some function of the fitnesses weighted by their deviation from the upper bound on the fitness load, which is determined by the extent of transformation occurring.

4. THE EVOLUTION OF TRANSFORMATIONS UNDER PAIR-MATING DESCENT

In organisms where the life cycle involves pair mating, there are two points of transformation in the cycle, the transformation from individuals to pairs, and from pairs to individuals. There may be, in addition, transformations within the individual or pair phases. Modifier models for individual-to-pair transformations in the literature include modifiers of assortative mating (Karlin and McGregor, 1974), and selfing (Feldman and Christiansen (1983) and Holsinger and Feldman (1984)). I will not be investigating the evolution of pair-mating transformations here, but will concentrate on pair-to-individual transformations. Most of the modifier models in the literature concern the evolution of pair-to-individual transformations. These include recombination, mutation, segregation distortion, and sex ratio modifiers. Migration constitutes a transformation within the individual phase if the migrant is an individual, or within the pair phase if the migrant is a pair.

When there is pair-mating in producing offpsring, the full three dimensional specification of the type, its selection, transformation, and structural components, must be used. Introducing three indices, structural, transformation, and selection types, to the formulation (2.2) we obtain this general recursion on the population.

$$z'_{s_1 ai} = \sum_{\substack{s_2 s_3 \\ bcjk}} z_{s_2 cj}\, z_{s_3 bk}\, \frac{w_{jk}}{\bar{w}}\, T_{s_2 cj, s_3 bk \to s_1 ai}\,,$$

where

$$\bar{w} = \sum_{\substack{s_2 cj \\ s_3 bk}} z_{s_2 cj} z_{s_3 bk} w_{jk}\,.$$

With the assumption that the transformation types are not themselves transformed we obtain:

$$z'_{s_1ai} = 2\sum_{\substack{s_2s_3\\bjk}} z_{s_2aj}\, z_{s_3bk}\, \frac{w_{jk}}{\bar{w}}\, T_{s_2aj,s_3bk \to s_1ai}$$

$$-\sum_{\substack{s_2s_3\\jk}} z_{s_2aj}\, z_{s_3ak}\, \frac{w_{jk}}{\bar{w}}\, T_{s_2aj,s_3ak \to s_1ai} \cdot \qquad (3.6)$$

I will investigate a number of models which fit the form of (3.6):

The diploid modifier gene model, with random mating, viability selection or multiplicative fertility selection. The haploid modifier models in the literature are special cases of this.

A model for culturally transmitted selection types and transformation types.

The cases where the transformation type affects the frequencies of pairs formed will not be of the form (3.6). I will, however, examine one variant from (3.6),

A model of a modifier of sexual reproduction, in which pair mating frequencies are variable.

(1) THE DIPLOID MODIFIER GENE MODEL

When a gene in an organism determines the tranformation type, it will be called a modifier locus. In this section, the evolution of

modifier loci in diploid organsisms will be considered. Two aspects must first be addressed: the question of transformation of transformation types, and the nature of the selected types. I wish to exclude the transformation of transformation types from the model. So the alleles at the modifier locus will be transmitted without transformation. Nevertheless. from the consideration in the last chapter of the segregation-syngamy transformation acting in diploid sexual reproduction, we know that the modifier genotypes of some of the offspring of two diploids will not be identical to the parental genotypes (production of heterozygotes from homozygotes, and vice versa), which constitutes a transformation of the transformation types. But recall that the segregation-syngamy transformation decomposes when there is random mating and only multiplicative fertility selection. Assuming these conditions, the recursion can be expressed in terms of haploids and haploid pairs (i.e., diploids). The tranformation type will now be the modifier haplotype, which is inherited without being transformed, thus satisfying the requirement for the analysis here.

Secondly, the selected type undergoing transformation need not be a genotype. In models of recombination and mutation modifiers, the selected type is a genotype at a specific locus or set of loci. The modifier therefore controls intragenomic transformation. In migration modifier models, however, location is part of the selected type. There are models where genes affect the transmission of culturally transmitted traits that determine fitness (Feldman and Cavalli-Sforza, 1976). These models of genetic control over culturally transmitted traits have not previously been called modifier models. but in terms of selection and

transformation, what they are controlling are processes that may result in a transformation between parental and offspring cultural types. Models of genetic modifiers of cultural transmission are generally quite complex, because segregation and syngamy transform the modifier genotypes and because the association between modifier genotype and cultural type in the offspring is quite complex. The analysis therefore requires a more general consideration of structural types and transformation of transformation types. and will not be attempted here. Modifiers of intragenomic transformation and modifiers of migration are simpler and will be analyzed in this section.

I. INTRAGENOMIC TRANSFORMATION

In this section I will analyze the model where the transformation type is determined by a modifier locus, and the selection type is determined by another set of loci. This model includes as special cases the models of Charlesworth (1979 a), Feldman (1972), Feldman and Balkau (1972, 1973), Feldman et al. (1980), Feldman and Krakauer (1973, 1976), Leigh (1973), Liberman (1976), Prout et al. (1973), Teague (1976), Thomson and Feldman (1974, 1976) and others. In this case, the co-transmission of transformation and selection types is determined by the linkage between the modifier and selected loci. In terms of the full haplotypes being transmitted, recombination between the modifier and selected loci constitutes a transformation. This recombination is embedded in the T of (3.6). The transformation that is of interest, however, is the transformation acting just on the selected loci.

Therefore I will redefine T in terms of the recombination between modifier and selected loci and an additional set of T's which represent the transformation acting only on the selected loci. The recombination between modifier and selected loci is taken as a fixed feature of the population, outside the control of the modifier.

Two additional problems for this formulation turn out to have the same solution.

1) Interference between recombination events is a ubiquitous phenomenon for homologous recombination in eukaryotes. If the transformation acting on the selected loci is recombination, then recombination with the modifier locus may change the probabilities of recombinant selected haplotypes. To deal with interference generally, we define two new sets of T's: one for when no recombination occurs with the modifier, and one for when recombination does occur.

2) This specification also solves the problem of the modifier locus being linked in between two selected loci. In this situation, recombination with the modifier also may change the haplotype of the selected loci. But this change can be accounted for simply by defining a different set of T's for when recombination with the modifier occurs, as before.

The new sets of T's will be defined in a slightly different way from the previous definitions:

$$T_{bk}^{aj \to ai}$$

represents the probability that haplotype M_aA_j is transformed to haplotype M_aA_i given that the other haplotype in the diploid genotype is M_bA_k, and there is no recombination between M and A.

Conservation of the modifier allele implies that:

$$T_{\frac{bk}{}}^{\frac{aj}{}\rightarrow ci} = 0 \quad \text{for all } b,j,k,i \quad \text{if } c \neq a \ .$$

An assumption I will make throughout that is critical when recombination to the modifier locus is occurring is that there is no position effect of the modifier on the transformations acting on the selected loci. In other words, although the linkage phase will affect the association of modifier alleles with the selected haplotypes among the gamete offspring of an individual, it will not affect the frequencies of the selected haplotypes themselves. This assumption would be expected to hold whenever the modifier control of the transformations is mediated through trans acting gene products or other cellular activities. This is expressed as:

$$T_{\frac{bk}{}}^{\frac{aj}{}\rightarrow ai} = T_{\frac{ak}{}}^{\frac{bj}{}\rightarrow bi} \ .$$

With this assumption it will not matter whether transformation of the selected haplotypes occurs before recombination with the modifier, or whether recombination with the modifier occurs first.

When recombination with the modifier occurs, then

$$\tilde{T}_{\frac{bj}{}}^{\frac{ak}{}\rightarrow ai}$$

represents the probability that either:

1) haplotype M_aA_k is transformed to haplotype M_aA_i in genotype $M_aA_j // M_bA_k$ after recombination has occured between M and A ; or

2) haplotype M_bA_k is transformed to haplotype M_bA_i in genotype $M_aA_j // M_bA_k$ and then recombination occurs between M and A.

If for some a,b,j,k,i, $T_{\frac{bk}{}}^{\frac{aj}{}\rightarrow ai} \neq \tilde{T}_{\frac{bk}{}}^{\frac{aj}{}\rightarrow ai}$, then there is interference.

In this diploid modifier model, transmission distortion is simply segregation distortion. Assuming that there is no segregation distortion of the modifier alleles, then:

$$0 \leq T^{aj \to ai}_{bk} \leq 1 \text{ , and } \sum_i T^{aj \to ai}_{bk} = 1, \sum_i \tilde{T}^{aj \to ai}_{bk} = 1 .$$

The same applies for $\tilde{T}$.

If segregation distortion does occur on the modifier alleles then this assumption is relaxed to:

$$0 \leq T^{aj \to ai}_{bk} \leq 2 \text{ , and } \sum_i T^{aj \to ai}_{bk} + \sum_i T^{bk \to bi}_{aj} = 2 .$$

The same applies for $\tilde{T}$.

The T in (4.10) can now be defined in terms of the new sets of T's:

Let R be the frequency of recombination between M and A. Then,

$$T_{aj,bk \to ai} = (1-R)\, T^{aj \to ai}_{bk} + R\, \tilde{T}^{ak \to ai}_{bj} \quad \text{for } a \neq b ;$$

$$T_{aj,ak \to ai} = \tfrac{1}{2}(1-R)\left(T^{aj \to ai}_{ak} + T^{ak \to ai}_{aj} \right) + \tfrac{1}{2}R\left(\tilde{T}^{ak \to ai}_{aj} + \tilde{T}^{aj \to ai}_{ak} \right) \quad \text{for } j \neq k ;$$

$$T_{aj,aj \to ai} = (1-R)\, T^{aj \to ai}_{aj} + R\, \tilde{T}^{aj \to ai}_{aj} .$$

PERFECT TRANSMISSION:

If the selected haplotype is being perfectly transmitted with a given modifier genotype, then

$$T^{aj \to ai}_{bk} = \delta_{ij} = \begin{cases} 0 \text{ if } i \neq j \\ 1 \text{ if } i = j \end{cases} ,$$

and

$$\tilde{T}^{ak \to ai}_{bj} = \delta_{ki} .$$

Only if $R = 0$, however, will this this will constitute perfect transmission of the full haplotype.

FITNESSES:

I will also use the diploid genotype notation to index the fitnesses, so the fitness of genotype

$$\frac{M_aA_i}{M_bA_j} \text{ will be } w_k^j \text{ for all } a,b.$$

THE RECURSION:

Let z_{ai} represent the frequency of haplotype M_aA_i. Then equation (3.6) is the recursion on haplotype frequencies in the population with the substitutions for T and W. Thus we obtain:

$$z'_{ai} = \sum_{bjk} z_{aj}z_{bk}\frac{w_k^j}{\bar{w}}\left((1-R)T_{bk}^{aj\to ai} + RT_{bj}^{\tilde{a}k\to ai}\right) .$$

Because this is a non-linear system, it will not be possible to obtain general global convergence results. Instead, pursuing the approach developed for modifier theory by Feldman (1972), the nature of equilibria and their local stability, and the fate of new modifier alleles introduced to the population at stable equilibria will be explored.

THE EQUILIBRIUM IDENTITY

At any equilibrium for this system, the following identity must be satisfied:

$$\hat{z}_{bi} = \sum_{cjk} \hat{z}_{bj}\hat{z}_{ck}\frac{w_k^j}{\hat{\bar{w}}}\left((1-R)T_{ck}^{bj\to bi} + RT_{cj}^{\tilde{b}k\to bi}\right) \qquad (3.7)$$

This can be written in vector form as follows:

Define

$$\Omega_b \triangleq \| \sum_{ck} \hat{z}_{ck} \frac{w_k^j}{\hat{w}_j} \left((1-R)T_{ck}^{bj} + bi + RT_{cj}^{bk} + bi \right) \|_{i,j} ,$$

and

$$D \triangleq \operatorname{diag}\left(\frac{\hat{w}_i}{\hat{\underline{w}}}\right) = \left\| \begin{matrix} \frac{\hat{w}_1}{\hat{\underline{w}}} & & 0 \\ & \ddots & \\ 0 & & \frac{\hat{w}_n}{\hat{\underline{w}}} \end{matrix} \right\| ,$$

where

$$\hat{w}_i \triangleq \sum_{bj} \hat{z}_{bj} w_j^i .$$

D is the matrix of the relative marginal fitnesses of the selected haplotypes, and will reappear throughout the analyses. If there is no marginal fitness variance, then $D = I$.

The matrix Ω_b is a stochastic matrix, since $\underline{e}^T \Omega_b = \underline{e}^T$. The equilibrium identity becomes

$$\hat{\underline{z}}_b = \Omega_b D \hat{\underline{z}}_b ,$$

where

$$\underline{z}_b \triangleq \begin{pmatrix} z_{b1} \\ z_{b2} \\ \vdots \end{pmatrix} .$$

Therefore, at equilibrium the spectral radius

$$\rho(\Omega_b D) = 1 \text{ for each modifier allele } b .$$

The local stability of equilibria are analyzed by deriving the linearized recursions on perturbations away from the equilibrium. For a polymorphism to be a plausible state of the population at equilibrium, the equilibrium must be stable to perturbations among the types present, having what is called interior stability. This condition is described as follows:

Let $\hat{\underline{z}}$ be an equilibrium. The population is perturbed to new frequencies $\underline{z}$ where the difference $\underline{\varepsilon} \triangleq \underline{z} - \hat{\underline{z}}$ is small. Let the difference after one generation be defined $\underline{\varepsilon}' \triangleq \underline{z}' - \hat{\underline{z}}$. Then, ignoring terms on the order of $\|\underline{\varepsilon}\|^2$, the recursion relating $\underline{\varepsilon}'$ to $\underline{\varepsilon}$ is:

$$\underline{\varepsilon}' = \Gamma\underline{\varepsilon} ,$$

where Γ is the local stability matrix. The polymorphic equilibrium will be stable if the spectral radius $\rho(\Gamma) < 1$, and unstable if $\rho(\Gamma) > 1$. If $\rho(\Gamma) = 1$ then a second order analysis is required. In some cases, the technique developed by Lessard and Karlin (1982) might be useful for this analysis, but this is not pursued further here.

To investigate the long term evolutionary fate of the modifier locus, we wish to know characteristics of new modifier alleles that either allow them or prevent them from increasing in the population when introduced at an equilibrium.

Let a new modifier allele, M_a , be introduced to the population at an equilibrium $\hat{\underline{z}}$ at small frequencies $z_{ai} = \varepsilon_{ai}$. The linearized recursion on the ε_a 's, ignoring terms of order ε_a^2 , is:

$$\varepsilon_i' = \frac{1}{\bar{w}} \sum_{jk} \varepsilon_j \hat{z}_{bk} \frac{w_k^j}{\bar{w}} \left((1-R) T^{aj}_{bk \to ai} + R T^{\tilde{a}k}_{bj \to ai} \right) . \qquad (3.8)$$

With the introduction of the new modifier allele, the frequencies of the pre-existing haplotypes will also be perturbed, and this perturbation will be represented by the vector $\underline{\varepsilon}_r$. The total recursion on the perturbations is:

$$\begin{pmatrix} \underline{\varepsilon}_r' \\ \underline{\varepsilon}_a' \end{pmatrix} = \begin{vmatrix} \Gamma & \Theta \\ 0 & \Omega_a D \end{vmatrix} \begin{pmatrix} \underline{\varepsilon}_r \\ \underline{\varepsilon}_a \end{pmatrix} ,$$

with each entry representing blocks, where Ω_a is defined for M_a as in the equilibrium identity.

The matrix Θ is irrelevant to the stability because of the zero block. Thus the spectral radius of the entire stability matrix is

$$\rho = \max(\rho(\Gamma), \rho(\Omega_a D)) \ .$$

Since the equilibrium is assumed to have interior stability, $\rho(\Gamma) < 1$. Therefore, the stability of the entire system depends on whether the new modifier allele increases or not when introduced, that is, whether

$$\rho(\Omega_a D) > 1 \quad \text{or} \quad \rho(\Omega_a D) < 1 \ .$$

This is what is called the exterior stability of the equilibrium. This partition was first established for a selectively neutral recombination modifer by Feldman (1972). Since Ω_a is a stochastic matrix, the spectral radius cannot be different from one unless there is an variance in the marginal fitnesses of the selected haplotypes at equilibrium. This yields the following result:

RESULT 3.3:

SELECTION CANNOT ACT ON A NEW MODIFIER ALLELE TO CHANGE ITS FREQUENCY AT MORE THAN AN ALGEBRAIC RATE UNLESS THERE IS AN EQUILIBRIUM FITNESS LOAD.

This result assumes random mating, populations at equilibrium, discrete non-overlapping generations, and no transformation acting on the modifier, as will all the results for pair mating descent, except where noted.

A NOTE ON FREQUENCY DEPENDENCE

An important property of exterior stability, not shared by interior stability, is the following:

THEOREM 3.4:

The exterior stability of an equilibrium is not affected by frequency dependent selection or frequency dependent transformation given two assumptions:

1) $\rho(\Omega_a D) \neq 1$,

2) both fitnesses and transformations are continuous function of $\underline{z}$.

This is because perturbations in W or T appear as second order terms, which cannot change either inequality

$$\rho(\Omega_a D) < 1 \quad \text{or} \quad \rho(\Omega_a D) > 1 .$$

For the interior stability, however, perturbations in W or T appear as first order terms and alter the matrix Γ .

I.1. THE EXTERIOR STABILITY OF EQUILIBRIA

In this section I derive a number of results about the conditions that allow or prevent the initial increase of a new modifier allele introduced to the population at equilibrium. Although the assumption of the existence of the equilibria may implicitly require unknown constraints on the selection regimes and transformation probabilities, in none of the results do these constraints or closed form solutions of

the equilibrium frequencies appear. The only generic assumptions made are that there be polymorphism in the selected haplotypes, that each selected haplotype and each modifier allele in the recursions occur with positive frequency, and that the marginal fitness of each selected haplotype be greater that zero, since it can be disregarded otherwise.

DEFINITION 4: MODIFIER AND SELECTED HAPLOTYPE FREQUENCIES:

Under some circumstances the total frequencies of selected haplotype or of modifier alleles will appear.

The total frequency of each modifier allele is represented by

$$x_a \triangleq \sum_i z_{ai} .$$

The total frequency of each selected haplotype is represented by

$$v_i = \sum_a z_{ai} .$$

DEFINITION 5: TENSOR PRODUCT FREQUENCIES.

A situation in which the modifier and selected alleles are in linkage equilibrium is described by the frequency vectors of the complete haplotypes being a TENSOR PRODUCT of the respective modifier and selected haplotype frequency vectors:

$$\underline{z} = \underline{x} \otimes \underline{v} .$$

THEOREM 3.5:

A NEW MODIFIER ALLELE WHICH ELIMINATES TRANSFORMATION AT THE SELECTIED LOCI WILL ALWAYS INCREASE WHEN RARE, FOR ANY AMOUNT OF LINKAGE TO THESE LOCI, WHEN THE EQUILIBRIUM BEARS A TRANSFORMATION-INDUCED FITNESS VARIANCE.

PROOF:

Here $T^{aj \to ai}_{bk} = \tilde{T}^{aj \to ai}_{bk} = \delta_{ij}$ $\forall$ i,j,b,k . Therefore the recursion is:

$$\varepsilon'_{ai} = (1 - R)\varepsilon_{ai} \frac{\hat{w}_i}{\hat{\bar{w}}} + R\hat{v}_i \sum_j \varepsilon_{aj} \frac{w_j}{\hat{\bar{w}}} .$$

Define $Q \triangleq \text{diag}(\hat{\underline{v}})W \text{ diag}(\frac{1}{\hat{w}_i}) = \| \hat{v}_i \frac{w_j}{\hat{w}_j} \|$.

$$\text{Then } \underline{\varepsilon}' = \Omega_a D \underline{\varepsilon} = \left[(1 - R)I + RQ \right] D \underline{\varepsilon} .$$

I will prove that the spectral radius

$$\rho(\Omega_a D) = \rho\left(\left[(1 - R)I + RQ \right] D \right) > 1 , \quad \forall \ 0 \leq R \leq \frac{1}{2} .$$

Proof:

1) First it will be shown that $(1-R)I + RQ$ is symmetrizable to a positive semi-definite matrix.

Let us call $\text{diag}(\hat{\underline{v}}) \triangleq D_1$, and $\text{diag}(\frac{1}{\hat{w}_i}) \triangleq D_2$. Thus $Q = D_1 W D_2$.

Since for the eigenvalues λ of Q,

$$\lambda(Q) = \lambda(D_1 W D_2) = \lambda\left((D_1 D_2)^{1/2} W (D_1 D_2)^{1/2} \right) ,$$

and the matrices W and $(D_1 D_2)^{1/2}$ are symmetric, all the eigenvalues of Q are real. Because Q is stochastic, its spectral radius is one, and thus all its eigenvalues are between -1 and 1.

Since $-1 \leq \lambda(Q) \leq 1$, then

$\lambda\left[(1-R)I + RQ\right] \in [(1-R)-R, (1-R)+R] = [1-2R, 1]$.

Therefore for $0 \leq R \leq \frac{1}{2}$, we have $0 \leq \lambda\left[(1-R)I + RQ\right] \leq 1$. All the eigenvalues are non-negative.

Defining $D_3 = D_1^{-\frac{1}{2}} D_2^{\frac{1}{2}}$, we have

$$\lambda\left[(1-R)I + RQ\right] = \lambda\left[D_3\left[(1-R)I + RQ\right]D_3^{-1}\right]$$

$$= \lambda\left[(D_1D_2)^{\frac{1}{2}}\left[(1-R)(D_1D_2)^{-1} + RW\right](D_1D_2)^{\frac{1}{2}}\right] \geq 0 .$$

The last matrix is non-negative and symmetric, with all non-negative eigenvalues, and is thus is positive semi-definite.

2) This enables us to use Theorem 5.1 Corollary F.2 of Karlin (1982), which states that $\rho(MD) \geq \sum_i \xi_i D_{(i)}$, where M is symmetrizable to a positive semi-definite matrix, $M\underline{\xi} = \underline{\xi}$, $\underline{e}^T M = \underline{e}^T$, and $\underline{e}^T\underline{\xi} = 1$.

Here, the eigenvector $\underline{\xi}$ is $\hat{D}\underline{v}$, since

$$\sum_j Q_{ij}(\hat{D}\underline{v})_j = \sum_j \hat{v}_i \frac{w_{ij}}{\hat{w}_j}\left(\frac{\hat{w}_j}{\tilde{w}}\hat{v}_j\right) = \hat{v}_i \sum_j \hat{v}_j \frac{w_{ij}}{\tilde{w}} = \hat{v}_i \frac{\hat{w}_i}{\tilde{w}} = (\hat{D}\underline{v})_i$$

$$\text{thus } \left[(1-R)I + RQ\right]\hat{D}\underline{v} = \hat{D}\underline{v} .$$

Therefore,

$$\rho(\Omega_a D) = \rho([(1-R)I + RQ]D) \geq \sum_i \hat{v}_i \frac{\hat{w}_i}{\bar{\hat{w}}} \frac{\hat{w}_i}{\bar{\hat{w}}} = \frac{1}{\bar{\hat{w}}^2} \sum_i \hat{v}_i (\hat{w}_i^2 - \bar{\hat{w}}^2) + 1$$

$$= 1 + \mathrm{var}\left(\frac{\hat{w}_i}{\bar{\hat{w}}}\right) \geq 1 .$$

Thus, if $\mathrm{var}(w_i) > 0$, then

$$\rho(\Omega_a D) = \rho([(1-R)I + RQ]D) > 1 ,$$

and the new modifier increases when rare.

The result that the new modifier allele can increase even when it is unlinked to the selected loci it is somewhat remarkable in light of the intuitive notions about hitchhiking. Hitchhiking is usually thought to be where an allele at one locus increases in frequency by being linked to an allele at another locus which is increasing in frequency due to selection. In this case, however, the locus that is hitchhiking is neither linked to the selected loci nor are the alleles at the selected loci changing frequency! The linkage disequilibrium between the modifier and the selected loci that is necessary for hitchhiking is generated by selection every generation, and even free recombination can no more than halve this disequilibrium by the next phase of selection.

RESULT 3.6:

The selective advantage of a new modifier allele eliminating transformation decreases with looser linkage to the selected haplotypes.

This is a direct result from Theorem 5.2 of Karlin (1982).

RESULT 3.7:

The fitness load is always greater than the fitness variance.

This is an incidental implication of Result 3.6, which gives

$$\rho(D) = \hat{L} = \max_i \left(\frac{\hat{w}_i}{\bar{w}} \right) > 1 + \mathrm{var}\left(\frac{\hat{w}_i}{\bar{w}} \right) .$$

This result does not require the fact that these are equilibrium values, hence this holds for populations in a transient phase of their convergence as well.

RESULT 3.8:

A VALUE CAN BE DERIVED FOR AN UPPER BOUND ON THE RATE OF TRANSFORMATION A NEW MODIFIER ALLELE ALLOWS THAT GUARANTEES IT WILL INCREASE WHEN INTRODUCED INTO A POPULATION WITH A MARGINAL FITNESS VARIANCE AT EQUILIBRIUM.

DERIVATION:

For a new modifier allele M_a, let us define

$$\tilde{m}_i \triangleq 1 - \min_{b,k} T^{ai \to ai}_{bk} ,$$

which is the maximal rate of transformation occurring for selected haplotype i in the presence of the new modifier allele.

From the recursion (3.8) on the new modifier allele, we obtain the inequality:

$$\varepsilon'_{ai} = \sum_{bjk} \varepsilon_{aj} \hat{z}_{bk} \frac{w_k^j}{\hat{\bar{w}}} \left((1-R) T_{bk}^{aj \to ai} + R \tilde{T}_{bj}^{ak \to ai} \right)$$

$$= (1 - R)\varepsilon_{ai} \sum_{bk} z_{bk} \frac{w_k^i}{\hat{\bar{w}}} T_{bk}^{ai \to ai} + R\varepsilon_{ai} \sum_{bk} \hat{z}_{bk} \frac{w_k^i}{\hat{\bar{w}}} \tilde{T}_{bi}^{ak \to ai}$$

$$+ (1 - R) \sum_{\substack{bjk \\ j \neq i}} \varepsilon_{aj} \hat{z}_{bk} \frac{w_k^j}{\hat{\bar{w}}} T_{bk}^{aj \to ai} + R \sum_{\substack{bjk \\ j \neq i}} \varepsilon_{aj} \hat{z}_{bk} \frac{w_k^j}{\hat{\bar{w}}} \tilde{T}_{bj}^{ak \to ai} \qquad (3.9)$$

$$\geq (1 - R)\varepsilon_{ai} \frac{\hat{w}_i}{\hat{\bar{w}}} (1 - \tilde{m}_i) .$$

Therefore, if

$$\tilde{m}_i < 1 - \frac{\hat{\bar{w}}}{(1 - R)\hat{w}_i} \quad \text{then} \quad \varepsilon'_{ai} > \varepsilon_{ai},$$

and haplotype $M_a A_i$ increases when introduced.

Thus whenever transformation induces a fitness variance at equilibrium, it is possible, at least when

$$0 \leq R \leq 1 - \frac{\hat{\bar{w}}}{\max_i(\hat{w}_i)},$$

for a new modifier that puts a certain upper bound on the amount of transformation to increase when introduced into the population. This occurs through hitchhiking with the fitter A haplotypes, by preserving their identity during reproduction.

This condition does not use the last three terms of (3.9); using the second term on the right hand side of (3.9) it can be sharpened so that if

$$0 \leq R < \max_i [(1 - \frac{\hat{\bar{w}}}{\hat{w}_i})(1 - \frac{\hat{v}_i w_i^i}{\hat{w}_i})^{-1}],$$

then the requirement for the initial increase of M_a is that there exist

$$\tilde{m}_i < 1 - \frac{\hat{\bar{w}}}{\hat{w}_i - R(\hat{w}_i - \hat{v}_i w_i^i)} .$$

This depends on $\hat{\underline{v}}$ however, so the improvement is undetermined without additional assumptions.

I.1a. THE EXTERIOR STABILITY OF FIXED MODIFIERS

Consider a population at a stable equilibrium where the modifier locus is fixed on one allele, M_1, yielding transformations T_1 and $\tilde{T}_1$. The selected haplotype frequencies must satisfy the identity

$$\hat{v}_i = \sum_{jk} \hat{v}_j \hat{v}_k \frac{w_k^i}{\hat{\bar{w}}} \left((1-R) T_{lk}^{lj \to i} + R T_{lj}^{lk \to i} \right) .$$

This can be represented in vector form as

$$\hat{\underline{v}} = \Omega_1 D\hat{\underline{v}} = \left((1-R) Y_1 + R\tilde{Y}_1 \right) D\hat{\underline{v}} ,$$

where

$$Y_1 \triangleq \| \sum_k \hat{v}_k \frac{w_k^j}{\hat{w}_j} T_{lk}^{lj \to i} \|_{i,j} , \qquad \tilde{Y}_1 \triangleq \| \sum_k \hat{v}_k \frac{w_k^j}{w_j} \tilde{T}_{lj}^{lk \to i} \|_{i,j} ,$$

and D is the diagonal matrix of relative marginal fitnesses. Y_1 and $\tilde{Y}_1$ are both stochastic matrices, since $\underline{e}^T Y_1 = \underline{e}^T \tilde{Y}_1 = \underline{e}^T$.

A new modifier allele, M_2, yielding transformations T_2 and $\tilde{T}_2$ as a heterozygote with M_1, is introduced into the population, and

the recursion on the frequencies of the new modifier allele is

$$\varepsilon'_i = \sum_{jk} \varepsilon_j \hat{v}_k \frac{w^j_k}{\hat{w}} \left((1-R) T^{2j \to 2i}_{1k} + R \tilde{T}^{2k \to 2i}_{1j} \right) .$$

This can be represented in vector form as

$$\underline{\varepsilon}' = \Omega_2 D \underline{\varepsilon} = \left((1-R) Y_2 + R \tilde{Y}_2 \right) D \underline{\varepsilon} ,$$

where

$$Y_2 \triangleq \| \sum_k \hat{v}_k \frac{w^j_k}{\hat{w}_j} T^{2j \to 2i}_{1k} \|_{i,j} \text{ and } \tilde{Y}_2 \triangleq \| \sum_k \hat{v}_k \frac{w^j_k}{\hat{w}_j} \tilde{T}^{2k \to 2i}_{1j} \|_{i,j} .$$

The matrices Y_2 and $\tilde{Y}_2$ are also stochastic.

What determines whether or not the new modifier allele will increase when rare is whether or not the spectral radius

$$\rho\left(\left[(1-R) Y_2 + R \tilde{Y}_2 \right] D \right) > 1 .$$

Note that the matrix for M_1, $\Omega_1 D$ has spectral radius equal to one,

$$\rho\left(\left[(1-R) Y_1 + R \tilde{Y}_1 \right] D \right) = 1 . \qquad (3.10)$$

This is known since the eigenvector $\hat{\underline{v}}$ is strictly positive by assumption, and the matrix $\Omega_1 D$ is non-negative: From Gantmacher (1959), non-negative matrices have a non-negative eigenvalue which is the spectral radius, and for which the corresponding eigenvector is non-negative. If $\hat{\underline{v}}$ in this case were not that vector, it would have to be orthogonal to it, being also an eigenvector. But being strictly positive, this is impossible. So $\hat{\underline{v}}$ is the eigenvector whose eigenvalue, 1, is the spectral radius of $\Omega_1 D$.

The question of the initial increase of the new modifier allele therefore reduces to the question of how changes from Ω_1 affects the spectral radius of that matrix when multiplied by D. At this point we need again to consider the nature of the variations in the transformations afforded by the modifier locus.

VARIATION IN DIPLOID INTRAGENOMIC TRANSFORMATIONS

Because there are only two transformation matrices involved here, the variation between them is necessarily uniform; what is of concern is whether the variation is linear or not. Suppose the variation is linear, where the relation between T_1 and T_2 is

$$T_{\overline{1k}}^{2j \to 2i} = (1-m_{\overline{1}}^{2})\delta_{ji} + m_{\overline{1}}^{2}\, T_{\overline{1k}}^{1j \to 1i} ,$$

and between $\tilde{T}_1$ and $\tilde{T}_2$ is

$$T_{\overline{1j}}^{2k \to 2i} = (1-m_{\overline{1}}^{2})\delta_{ki} + m_{\overline{1}}^{2}\, \tilde{T}_{\overline{1j}}^{1k \to 1i} ,$$

where $m_{\overline{1}}^{2}$ is a modifier parameter for modifier genotype $\frac{M_2}{M_1}$.

Then the following theorem holds:

THEOREM 3.9:

FOR A TIGHTLY LINKED MODIFIER LOCUS, WHEN A NEW MODIFIER ALLELE IS INTRODUCED TO A POPULATION AT EQUILIBRIUM, FIXED FOR THE MODIFIER, WITH A MARGINAL FITNESS VARIANCE FOR THE SELECTED

TYPES, THEN THE NEW MODIFIER ALLELE WILL INCREASE IF IT BRINGS THE TRANSFORMATION ON THE SELECTED LOCI UNIFORMLY CLOSER TO PERFECT TRANSMISSION, AND IT WILL BE EXCLUDED IF IT TAKES THE TRANSFORMATION UNIFORMLY FURTHER AWAY FROM PERFECT TRANSMISSION.

PROOF:

The recursion on the frequency of M_2 is

$$\underline{\varepsilon}' = \left[(1-m_1^2)(1-R)\| \sum_k \hat{v}_k \frac{w_k^j}{\hat{\bar{w}}} \delta_{ji} \| + R \| \sum_k \hat{v}_k \frac{w_k^j}{\hat{\bar{w}}} \delta_{ki} \| \right] \underline{\varepsilon}$$

$$+ \left[m_1^2 (1-R)\| \sum_k \hat{v}_k \frac{w_k^j}{\hat{\bar{w}}} T_{1k}^{1j \to 1i} \| + R \| \sum_k \hat{v}_k \frac{w_k^j}{\hat{\bar{w}}} \tilde{T}_{1j}^{1k \to 1i} \| \right] \underline{\varepsilon}$$

$$= \left[(1-m_1^2)\left((1-R)I + RQ \right) + m_1^2 \left((1-R)Y_1 + R\tilde{Y}_1 \right) \right] D\,\underline{\varepsilon} \,,$$

where Q, Y_1, $\tilde{Y}_1$ and D are defined as before.

If $m_1^2 = 0$ then we have the situation in Theorem 3.5, where the new modifier brings about perfect transmission, and which therefore increases for any R. If $R = 0$, then the recursion is

$$\underline{\varepsilon}' = \left[(1-m_1^2)I + m_1^2 Y_1 \right] D\,\underline{\varepsilon} \,,$$

and now,

$$\Omega_2 = Y_2 = (1-m_1^2)I + m_1^2 Y_1 \,.$$

In this case, Karlin (1982) Theorem 5.2 can be applied. From (3.10) with $R = 0$, we know that $\rho(Y_1 D) = 1$. Therefore, $\rho(\Omega_2 D) > 1$ if $m_1^2 < 1$ and $\rho(\Omega_2 D) < 1$ if $m_1^2 > 1$.

From the theory of small parameters (Karlin and McGregor, 1972) this holds also for some range of $R > 0$. I cannot determine whether it

holds for all R , however. A substitution of $\Omega_2 D$ into the proof of Karlin (1982) Theorem 5.2 ends with a term that requires additional analysis.

This theorem accounts for why the reduction principle works. In the modifier gene models where the reduction principle works, the transformation process controlled by the modifier, be it recombination, mutation or migration (which will be covered later) is the only transformation acting on the selected types and each transformation occurs as a single event. Therefore, the variation in the transformations is linear, so this theorem applies.

When the difference between the transformations determined by M_1 and M_2 is affine, the same results will be found to hold that held in the analysis of affine variation under asexual descent. The discussion of this is deferred until the next section. As will be seen shortly, this analysis of the exterior stability of fixed modifiers is actually a special case of the exterior stability of broad class of "viability analogous" modifier polymorphisms, and I shall continue the analysis in this broader context.

I.1b. MODIFIER POLYMORPHISMS AND THEIR STABILITY

From Theorem 3.8, it is clear that if the transformation determined by the modifier heterozygote is closer to perfect transmission than either homozygote, then as long as the marginal fitness variance at the equilibrium is not zero, the modifier locus has a protected

polymorphism. In previous work to be found on modifier polymorphisms, Feldman and Balkau (1973), Prout et al. (1973), Thomson and Feldman (1976), and Feldman and Krakauer (1976), two kinds of modifier polymorphisms have been discovered. One kind is distinguished by having zero linkage disequilibrium between the modifier and selected loci, while the other has linkage disequilibrium which can be quite high for tight linkage betweeen the modifier and selected loci. It has not proved possible to obtain explicit solutions generally to the equilibrium identity (3.7) with modifier polymorphisms and selected locus polymorphisms. In this section I will generalize the conditions on the existence of zero disequilibrium polymorphisms and analyze their exterior stability. No general results were obtainable for the polymorphisms with linkage disequilibrium. It will be shown that the "balanced mixture" modifier polymorphisms which were described in the asexual case cannot generally be characterized in diploids.

BALANCED MIXTURE MODIFIER POLYMORPHISMS

In diploids, the existence of balanced mixture polymorphisms cannot generally be shown. Even if we assume that the genotype fitnesses are all equal at equilibrium, the requirements for a balanced mixture modifier polymorphisms are not necessarily possible to satisfy. With equal fitnesses, we must have that

$$\hat{\underline{z}}_a = \left[(1-R)T_a + R\tilde{T}_a \right] \hat{\underline{z}}_a ,$$

where

$$T_a \triangleq \| \sum_{bk} \hat{z}_{bk} T^{aj \to ai}_{\underline{bk}} \|_{i,j}$$

and

$$\tilde{T}_a \triangleq \| \sum_{bk} \hat{z}_{bk} \tilde{T}^{ak \to ai}_{\underline{bk}} \|_{i,j} .$$

Because this is a system of quadratic equations, the set of transformation matrices that would satisfy the equilibrium cannot be characterized as in the asexual case.

MODIFIER POLYMORPHISMS WITH ZERO LINKAGE DISEQUILIBRIUM

The work in this thesis was initiated in investigating a conjecture by my major adviser, Dr. Feldman, which was a generalization of the results in Feldman and Krakauer (1976) on modifier polymorphisms with zero linkage disequilibrium between the modifier locus and selected loci. He noted that the equilibrium modifier allele frequencies in these cases had the same form as equilibria in two allele models of viability selection, with the modifier parameters in the place of fitnesses. In analogy to the marginal fitnesses in the case of viability selection at a single locus, this means that the marginal modifier parameters, $m_a \triangleq \sum_b x_b m_b^a$, for each modifier allele, M_a , are equal at equilibrium,

$$\hat{m}_a = m^* \quad \forall\, a \ ,$$

where x_b is the frequency of each modifier allele M_b . From this he made the following conjecture:

THEOREM 3.10:

FELDMAN'S THEOREM ON THE EXISTENCE OF VIABILITY-ANALOGOUS TENSOR PRODUCT MODIFIER POLYMORPHISMS:

When the parameter determined by the modifier locus enters linearly into the recursions on the frequency of selected types, then for any equilbrium where the modifier is fixed on an allele

yielding modifier parameter m^*, and the selected haplotype frequencies are $\hat{\underline{v}}$, there will also exist an equilibrium modifier polymorphism when each modifier allele has m^* as its marginal modifier parameter, with the modifier locus and selected haplotypes in linkage equilibrium, and the selected haplotypes at frequencies $\hat{\underline{v}}$.

Because the modifier locus and selected haplotypes are in linkage equilibrium, the vector for the complete haplotype frequencies can be expressed as the tensor product

$$\hat{\underline{z}} = \hat{\underline{x}} \otimes \hat{\underline{v}} ,$$

where $\hat{\underline{x}}$ is the vector of modifier allele frequencies (Feldman and Krakauer, 1976). Multi-locus haplotypes frequencies which are the product of single locus allele frequencies have been referred to as "central" or "multi-locus Hardy-Weinberg" equilibria (Karlin and Feldman, 1978; Karlin and Liberman, 1979). Here I will refer to such equilbria as "tensor product" equilibria to avoid ambiguity or confusion with populations at equilibria having Hardy-Weinberg proportions among the genotypes.

The property of the modifier parameter entering linearly into the recursions is a basic feature of parameters affecting transformation processes, but not selection, because changes in selection values usually enter in the mean fitness, which appears as a normalizer, so that they enter non-linearly in the recursions, whereas the transformation probabilities enter in linear transformations on the frequency vector. Although Feldman's theorem was framed for uniform

variation in the transformations, being for one parameter families of transformation matrices, the linearity of the recursions in each of the transformation probabilities allows the theorem to be extended to general variation in the transformations.

THEOREM 3.11:

CONDITIONS FOR THE EXISTENCE OF TENSOR-PRODUCT MODIFIER POLYMORPHISMS:

Consider a population where the modifier and selected haplotype frequencies are of a tensor product form:

$$\underline{z} = \underline{x} \otimes \underline{v} .$$

Then the recursion becomes

$$z'_{ai} = x_a \sum_{bjk} v_j v_k \frac{w^i_k}{\bar{w}} x_b \left((1-R) T^{aj \to ai}_{bk} + R \tilde{T}^{ak \to ai}_{bj} \right) .$$

At this point, we need to define the following analog to the marginal fitness of a selected haplotype:

DEFINITION 6: THE MARGINAL TRANSFORMATION OF A MODIFIER ALLELE

Define the marginal transformation of a modifier allele M_a as:

$$T a^{j \to i}_{k} \triangleq \sum_b x_b T^{aj \to ai}_{bk} \quad \text{and} \quad \tilde{T} a^{k \to i}_{j} \triangleq \sum_b x_b \tilde{T}^{ak \to ai}_{bj} .$$

Using this in the recursion gives

$$\underline{z}_a' = x_a \left[(1-R) \| \sum_k v_k \frac{w_k^j}{w_j} Ta_k^{j \to i} \| + R \| \sum_k v_k \frac{w_k^j}{w_j} \tilde{Ta}_j^{k \to i} \| \right] D\underline{v}$$

$$= x_a \left[(1-R)Y_a + R\tilde{Y}_a \right] D\underline{v} \quad ,$$

where $Y_a \overset{\Delta}{=} \| \sum_k v_k \frac{w_k^j}{w_j} Ta_k^{j \to i} \|$ and $\tilde{Y}_a \overset{\Delta}{=} \| \sum_k v_k \frac{w_k^j}{w_j} \tilde{Ta}_j^{k \to i} \|$. (3.11)

If for all modifier alleles M_a , and for some frequencies $\hat{\underline{x}}$ and $\hat{\underline{v}}$,

$$\left[(1-R)\hat{Y}_a + R\hat{\tilde{Y}}_a \right] \hat{D}\hat{\underline{v}} = \hat{\underline{v}} \quad , \tag{3.12}$$

then we have an equilibrium,

$$\underline{z}' = \hat{\underline{x}} \otimes \hat{\underline{v}} = \hat{\underline{z}} \quad .$$

The only requirement on the marginal transformations is that $\hat{\underline{v}}$ be a leading eigenvector of each matrix

$$\left[(1-R)Y_a + R\tilde{Y}_a \right] D$$

derived from the marginal transformations. So in particular, if all the marginal transformations are identical and $\hat{\underline{v}}$ satisfies (3.12), then the tensor product equilibrium obtains. Although there may be cases where (3.12) is satisfied even when the modifier alleles have different marginal transformations, I cannot generally characterize them.

"Viability-analogous" will refer to the marginal transformations all being equal, since this is the analog of the marginal fitnesses of multiple alleles all being equal at equilibrium under viability selection. In the case of uniform variation in transformations, the transformation are characterized by the modifier parameters. Therefore, in order for the marginal transformations to be identical, the marginal modifier parameters must be identical, which proves Feldman's theorem.

I will use V.A.T.P. as an abbreviation for "viability-analogous, tensor product".

When the variation in the transformations is non-uniform, as in the case of a modifier control recombination between several non-interfering loci, it will not in general be possible for the marginal transformations to be equal. Therefore, viability-analogous, tensor product equilibria should be thought of mainly as a feature of uniform variation in transformations.

I.1c. THE EXTERIOR STABILITY OF TENSOR-PRODUCT MODIFIER POLYMORPHISMS

Let the population be at a tensor product modifier polymorphism

$$\hat{\underline{z}} = \hat{\underline{x}} \otimes \hat{\underline{v}} ,$$

where the marginal transformation probabilities for each modifier allele are

$T^{*}\frac{j}{k} \rightarrow i$ and $\tilde{T}^{*}\frac{k}{j} \rightarrow i$, which yield matrices Y^{*} and $\tilde{Y}^{*}$ when substituted in (3.11).

Now we introduce a new modifier allele M_a which in a genotype containing modifier allele M_b yields transformation probabilities

$$T\frac{aj}{bk} \rightarrow ai \text{ and } \tilde{T}\frac{ak}{bj} \rightarrow ai .$$

The marginal transformations defined for the new modifier allele are

$$Ta\frac{j}{k} \rightarrow i = \sum_b \hat{x}_b T\frac{aj}{bk} \rightarrow ai \text{ and } \tilde{T}a\frac{k}{j} \rightarrow i = \sum_b \hat{x}_b \tilde{T}\frac{ak}{ai} \rightarrow ai .$$

The recursion on the frequencies of the haplotypes containing the new modifier allele is

$$\underline{\varepsilon}' = \left[(1-R) \left\| \sum_k \hat{v}_k \frac{w_k^j}{\hat{w}_j} Ta_{ik}^{j \to i} \right\| + R \left\| \sum_k \hat{v}_k \frac{w_k^j}{\hat{w}_j} \tilde{T}a_{jk}^{k \to i} \right\| \right] D\,\underline{\varepsilon}$$

$$= \left[(1-R)Y_a + R\tilde{Y}_a \right] D\underline{\varepsilon} = \Omega_a D\underline{\varepsilon} \quad .$$

RESULT 3.12:

An important point that can be seen here is that it is only the marginal transformation probabilities of the new modifier allele that are involved in its initial increase behavior. The different transformations it may produce with each of the existing modifier alleles do not appear except as contributions to an average.

RESULT 3.13:

The equilibrium frequencies that the selected haplotypes would reach under the marginal transformation of the new modifier allele must be different from the frequencies at the existing equilibrium for there to be selection for or against the new modifier allele that would change its frequency at a geometric rate. This can be seen by noting that if

$$\hat{\underline{v}} = \Omega_a D\hat{\underline{v}} \quad ,$$

satisfying the equilibrium identity with the same selected haplotype frequencies $\hat{\underline{v}}$, then

$$\rho(\Omega_a D) = 1 \quad ,$$

so the new modifier allele can change frequencies at no more that an algebraic rate.

The necessity for the variation in the transformation to appear in the equilibrium relations of the selected haplotypes in order for there to be selection on the modifier has been shown for recombination by Feldman (1972) and for migration by Christiansen and Feldman (1975). In these cases, since the variation in transformations is uniform, it is the modifier parameter that must appear in the equilibrium identity for there to be selection on the modifier.

VIABILITY-ANALOGOUS, TENSOR PRODUCT EQUILIBRIA

For viability-analogous tensor product equilibria, there is only one marginal transformation among the modifier alleles present at equilibrium. Therefore, the initial increase behavior of a new modifier allele depends only on the relation between the equilibrium marginal transformation and the marginal transformation of the new modifier allele. It is the same as if the new modifier allele were introduced to a population fixed on a modifier, where the fixed modifier homozygote yielded the equilbrium marginal transformation, and the new modifier allele yielded the new marginal transformation as a heterozygote.

So what must now be considered, regardless of the nature of the variation in transformations among the modifier genotypes present at equilibrium, is how the new marginal transformation compares with the equilibrium marginal transformation. When the new marginal transformation is uniformly closer to or further from perfect transmission, Karlin (1982) Theorem 5.2 again applies, so Theorem 3.9 can be extended to viability-analogous, tensor product modifier polymorphisms:

THEOREM 3.14:

FOR A TIGHTLY LINKED MODIFIER LOCUS, WHEN A NEW MODIFIER ALLELE IS INTRODUCED TO A POPULATION AT A STABLE VIABILITY-ANALOGOUS, TENSOR PRODUCT EQUILIBRIUM, WHERE THERE IS A VARIANCE IN THE MARGINAL FITNESS OF THE SELECTED TYPES PRESENT, THEN THE NEW MODIFIER ALLELE WILL INCREASE IF ITS MARGINAL TRANSFORMATION IS UNIFORMLY CLOSER TO PERFECT TRANSMISSION THAN THE EQUILIBRIUM MARGINAL TRANSFORMATION, AND IT WILL BE EXCLUDED IF ITS MARGINAL TRANSFORMATION IS UNIFORMLY FURTHER AWAY FROM PERFECT TRANSMISSION.

I.1d. THE EXTERIOR STABILITY OF VIABILITY-ANALOGOUS, TENSOR PRODUCT MODIFIER POLYMORPHISMS WITH RESPECT TO AFFINE VARIATION.

One of the crucial properties of affine variation in transformations is that Theorem 5.2 of Karlin (1982) no longer applies. When the variation in the transformations is not not simply a shifting of weight between perfect transmission and another transformation matrix, it is possible for an increase in the overall rate of transformation to evolve. This is shown in two examples in the literature where modifiers causing affine variation were studied. In the model by Charlesworth (1979 b), where a modifier controls recombination in a population also undergoing migration, and in the

models by Feldman et al. (1980), where a modifier controls recombination in a genes also undergoing mutation, increases in recombination were able to evolve. Although I cannot give any general condition for when increases in transformation will be able to evolve under affine variation, some limited results can nevertheless be obtained.

First I give an intuitive but trivial result. Suppose that with the new modifier allele, all the selected haplotypes are transformed to a selected haplotype h with probability one,

$$T\frac{aj}{bk}\to ai = \tilde{T}\frac{ak}{bj}\to ai = \delta_{ih} \quad \forall \ b,j,k,i \ .$$

Then the recursion on the haplotypes with the new modifier is

$$\varepsilon_h' = \sum_j \frac{\hat{w}_j}{\bar{\hat{w}}}\varepsilon_j \quad \text{and} \quad \varepsilon_i' = 0 \ \text{ for } \ i \neq h \ .$$

Therefore from the second generation on,

$$\varepsilon_h' = \frac{\hat{w}_h}{\bar{\hat{w}}}\varepsilon_h \ .$$

So this new modifier allele can increase when introduced only if selected haplotype h happens to have a marginal fitness greater than the mean fitness of the population. This extreme case serves as an example of a more general property that modifiers that cause an increased production of the fitter selected haplotypes can increase in the population, allowing the evolution of transformations to escape from the inexorable trend toward reduction in the overall amount of transformation which occurs under linear variation.

The balance between reduced transformation and increased production of the fitter types can be described quantitatively for affine variation within one class of transformations, those with memoriless

distributions, which include the "house of cards" mutation model of Kingman (1980). Here it is possible to calculate, for a tightly linked modifier, the amount of selection on new modifier allele as its marginal transformation deviates from the equilibrium marginal transformation.

A transformation with a memoriless distribution was defined (DEFINITION 4) to be one where all types have the same probability of undergoing a transformation process, and when they do, the type that they become has a distribution that is independent of their former type. Familiar examples in models of migration are the Wright island model, the Levene model, and the Deakin model (see Karlin, 1982). In the case of diploid genotypes, a transformation matrix with a memoriless distribution will have elements

$$T_{k}^{j \to i} = (1-\alpha)\,\delta_{ij} + \alpha\, t_i \quad \forall\, k \text{ , where } t_i \geq 0 \text{ and } \sum_i t_i = 1 \text{ .}$$

When there is uniform variation in the transformations, due to any of the reasons discussed in Section 2., the general form for the transformation matrix with a memoriless distribution is

$$T_{bk}^{aj \to ai} = (1-m_b^a)\left((1-\alpha)\delta_{ji} + \alpha s_i\right) + m_b^a\left((1-\beta)\delta_{ji} + \beta p_i\right) \text{ , } \quad (3.13)$$

where α and β are the overall transformation rates and s_i and p_i are probabilities of producing haplotype i given there is a transformation. The modifier may change, therefore, both the overall rate and the relative distribution of transformations. Here I have assumed there is no interference between recombination with the modifier and the transformation process.

THE RATE OF CHANGE IN THE SPECTRAL RADIUS OF THE STABILITY MATRIX FOR A NEW MODIFIER ALLELE

Suppose that the population is at a viability-analogous, tensor product equilibrium, with an equilibrium marginal modifier parameter of m^*. Substitution of (3.13) into (3.11) yields

$$Y^* = (1-m^*)\{(1-\alpha)I + \alpha S\} + m^*\{(1-\beta)I + \beta P\}, \qquad (3.14)$$

where $S = \text{diag}(\underline{s})U$, and $P = \text{diag}(\underline{p})U$.

Here, $\hat{\underline{v}}$ must solve the equilibrium identity:

$$\begin{aligned}\hat{\underline{v}} &= \left[\{(1-m^*)(1-\alpha) - m^*(1-\beta)\}I + (1-m^*)\alpha S + m^*\beta P\right]D\hat{\underline{v}} \qquad (3.15)\\ &= \{1 - (1-m^*)\alpha - m^*\beta\}D\hat{\underline{v}} + (1-m^*)\alpha\underline{s} + m^*\beta\underline{p},\end{aligned}$$

yielding

$$[I - \{1 - (1-m^*)\alpha - m^*\beta\}D]\hat{\underline{v}} = (1-m^*)\alpha\underline{s} + m^*\beta\underline{p}.$$

Suppose that a new modifier allele, M_a has been intoduced to the population, yielding a marginal modifier parameter m_a. The recursion on the frequencies of the haplotypes bearing M_a is

$$\underline{\varepsilon}' = Y_a[(1-R)I + RQ]D\underline{\varepsilon},$$

where m_a has been substituted for m^* in (3.14) to yield Y_a, and since there is assumed to be no interference, $\tilde{Y}_a = Y_aQ$. Then the following theorem applies:

THEOREM 3.2b:

CONSIDER THE CASE OF AFFINE VARIATION IN TRANSFORMATIONS WITH MEMORILESS DISTRIBUTIONS (3.14). FOR A TIGHTLY LINKED MODIFIER, THE SPECTRAL RADIUS OF THE STABILITY MATRIX FOR A NEW ALLELE WITH MARGINAL MODIFIER PARAMETER m_a NEAR m^* IS APPROXIMATELY

1.

$$\rho(Y_a D) \tilde{=} 1 + (m_a - m^*)\frac{\alpha-\beta}{1-\gamma} ,$$

if for some i , $\alpha s_i + \beta p_i = 0$,

or otherwise,

2.

$$\rho(Y_a D) \tilde{=} 1 + (m_a - m^*)\Big(\sum_i \frac{1}{\gamma_i}\hat{v}_i^2\hat{w}_i\Big)^{-1}\frac{1}{\gamma^2}$$
$$\cdot \Big[\frac{\alpha-\beta}{\tilde{w}}\sum_i \frac{1}{\gamma_i}\hat{v}_i^2(\hat{w}_i-\tilde{w})^2 + \alpha\beta\Big((1-\gamma)\sum_i \hat{v}_i(\hat{w}_i-\tilde{w})\Big(\frac{p_i-s_i}{\gamma_i}\Big) + \gamma\ \mathrm{cov}\Big(\hat{w}_i,\frac{p_i-s_i}{\gamma_i}\Big)\Big)\Big] ,$$

where

$$\gamma_i \triangleq (1-m^*)\alpha s_i + m^*\beta p_i \text{ , and } \gamma \triangleq (1-m^*)\alpha + m^*\beta .$$

PROOF:

Suppose that sufficient time has elapsed so that $\underline{\varepsilon}$ has converged to the leading eigenvector of the stability matrix $\Omega_a D$ The general relation for an eigenvector $\hat{\underline{\varepsilon}}$ associated with eigenvalue λ of $\Omega_a D$ is:

$$\lambda\hat{\underline{\varepsilon}} = \big[(1-m_a)\big((1-\alpha)I + \alpha S\big) + m_a\big((1-\beta)I + \beta P\big)\big]\ \big[(1-R)I + RQ\big]\ D\,\hat{\underline{\varepsilon}} . \quad (3.16)$$

Assume that the eigenvector is an isolated point, so that implicit

differentiation with respect to m_a is possible.

Define the partial derivitives

$$\overset{\circ}{\lambda} \triangleq \frac{\partial}{\partial m_a}\lambda \ , \qquad \overset{\circ}{\underline{\varepsilon}} \triangleq \frac{\partial}{\partial m_a}\hat{\underline{\varepsilon}} \ .$$

Then:

$$\begin{aligned}&\overset{\circ}{\lambda}\,\hat{\underline{\varepsilon}} + \lambda\,\overset{\circ}{\underline{\varepsilon}} \\ &\quad = \left[(\alpha-\beta)I - \alpha S + \beta P\right]\left[(1-R)I + RQ\right]D\hat{\underline{\varepsilon}} + Y_a\left[(1-R)I + RQ\right]D\overset{\circ}{\underline{\varepsilon}} \ . \end{aligned} \tag{3.17}$$

At $m_a = m^*$, $\hat{\underline{\varepsilon}} = \hat{\underline{v}}$, and $\lambda = \rho = 1$, these identities can be used:

1) $UD\hat{\underline{v}} = \underline{e}$ 2) $UD\overset{\circ}{\underline{\varepsilon}} = \overset{\circ}{\rho}\underline{e}$ 3) $UQD = UD$ 4) $QD\hat{\underline{v}} = D\hat{\underline{v}}$.

Hence

$$PQD\overset{\circ}{\underline{\varepsilon}} = PD\overset{\circ}{\underline{\varepsilon}} = \mathrm{diag}(\underline{p})UD\overset{\circ}{\underline{\varepsilon}} = \mathrm{diag}(\underline{p})\underline{e}\,\overset{\circ}{\rho} = \overset{\circ}{\rho}\underline{p} \ ,$$

and

$$PQD\hat{\underline{v}} = PD\hat{\underline{v}} = \underline{p}.$$

After substituting these in (3.17) and rearranging we have

$$\begin{aligned}&\overset{\circ}{\rho}(\underline{v} - (1-m^*)\alpha\underline{s} - m^*\beta\underline{p}) + \left[I - \left(1 - (1-m^*)\alpha - m^*\beta\right)D\right]\overset{\circ}{\underline{\varepsilon}} \\ &\qquad - R\left(1 - (1-m^*)\alpha - m^*\beta\right)\left[Q - I\right]D\overset{\circ}{\underline{\varepsilon}} \\ &\quad = \beta\underline{p} - \alpha\underline{s} + (\alpha-\beta)D\hat{\underline{v}} \ . \end{aligned}$$

Evaluating $\overset{\circ}{\rho}$ can be done only when $R=0$, which yields

$$\overset{\circ}{\rho}\left(\hat{\underline{v}} - (1-m^*)\alpha\underline{s} - m^*\beta\underline{p}\right) + \left[I - \left(1 - (1-m^*)\alpha - m^*\beta\right)D\right]\overset{\circ}{\underline{\varepsilon}} = \beta\underline{p} - \alpha\underline{s} + (\alpha-\beta)D\hat{\underline{v}} \tag{3.18}$$

Two cases must be considered:

CASE 1.

$$1 - \left(1 - (1-m^*)\alpha - m^*\beta\right)\frac{\hat{w}_h}{\hat{\underline{w}}} = 0 \quad \text{for some h.}$$

$$\text{Then} \quad (1-m^*)\alpha s_h + m^*\beta p_h = 0 \ .$$

Let us define

$$\gamma \triangleq (1-m^*)\alpha + m^*\beta \ ,$$

which is the overall transformation rate.

Then $\dfrac{\hat{w}_h}{\hat{\underline{w}}} = \dfrac{1}{1-\gamma}$ and

$$\overset{\circ}{\rho} = \frac{\beta p_h - \alpha s_h}{\hat{v}_h} + \frac{\alpha-\beta}{1-\gamma} \ .$$

1. $0 < m^* < 1$.

Then $\alpha s_i = \beta p_i = 0$, and $\overset{\circ}{\rho} = \dfrac{\alpha-\beta}{1-\gamma}$.

2. $m^* = 0$ or $m^* = 1$.

Then the requirements for differentiability may not satisfied.

For $m^* = 0$, this means $\alpha s_h = 0$, so

$$\overset{\circ}{\rho} = \beta\frac{p_h}{\hat{v}_h} + \frac{\alpha-\beta}{1-\gamma} \ .$$

Because v_h drops out of (3.15), and since $m^* = 0$, p_h does not appear in (3.15), so the value $\frac{p_h}{v_h}$ is not uniquely defined.

CASE 2.

$$1 - \left(1 - (1-m^*)\alpha - m^*\beta\right)\frac{\hat{w}_i}{\hat{w}} > 0 \qquad \forall\, i\ .$$

Then the matrix $I - \left(1 - (1-m^*)\alpha - m^*\beta\right)D$ is invertible.

Since

$$1 - \left(1 - (1-m^*)\alpha - m^*\beta\right)\frac{\hat{w}_i}{\hat{w}} = \frac{1}{\hat{v}_i}\left((1-m^*)\alpha s_i + m^*\beta p_i\right) \text{ from (3.15),}$$

then

$$\left[I - \left(1 - (1-m^*)\alpha - m^*\beta\right)D\right]^{-1} = \operatorname{diag}(\hat{\underline{v}})\left[(1-m^*)\alpha \operatorname{diag}(\underline{s}) + m^*\beta \operatorname{diag}(\underline{p})\right]^{-1}\ .$$

Define

$$D_2 \triangleq \left[(1-m^*)\alpha \operatorname{diag}(\underline{s}) + m^*\beta \operatorname{diag}(\underline{p})\right]^{-1}\ .$$

Then

$$\overset{\circ}{\rho}\left(\operatorname{diag}(\hat{\underline{v}})^2 D_2\underline{e} - \hat{\underline{v}}\right) + \overset{\circ}{\underline{\varepsilon}} = \operatorname{diag}(\hat{\underline{v}})\, D_2\left(\beta\underline{p} - \alpha\underline{s} + (\alpha-\beta)D\hat{\underline{v}}\right)\ . \tag{3.19}$$

By multiplying (3.19) by $\underline{e}^T D$, we can use the fact that $\overset{\circ}{\rho} = \underline{e}^T D\overset{\circ}{\underline{\varepsilon}}$ and $\underline{e}^T D\hat{\underline{v}} = 1$ to obtain

$$\overset{\circ}{\rho}\left(\underline{e}^T\operatorname{diag}(\hat{\underline{v}})^2 D D_2\underline{e}\right) = \underline{e}^T\operatorname{diag}(\hat{\underline{v}})D D_2\left(\beta\underline{p} - \alpha\underline{s} + (\alpha-\beta)D\hat{\underline{v}}\right)\ . \tag{3.20}$$

Now define $\gamma_i \triangleq (1-m^*)\alpha s_i + m^*\beta p_i = \left(D_2^{-1}\right)_{ii}$, so $\sum_i \gamma_i = \gamma$.

Then $\overset{\circ}{\rho}$ can be expressed

$$\overset{\circ}{\rho} = \left(\sum_i \frac{1}{\gamma_i} \hat{v}_i^2 \hat{w}_i\right)^{-1} \sum_i \frac{1}{\gamma_i} \hat{v}_i \hat{w}_i \left(\beta p_i - \alpha s_i + (\alpha - \beta) \frac{\hat{v}_i \hat{w}_i}{\hat{\bar{w}}}\right) \qquad (3.21)$$

Further evaluation is possible using the identity

$$\sum_i \frac{\hat{v}_i^2 \hat{w}_i^2}{\gamma_i} = \sum_i \frac{1}{\gamma_i} \left(\hat{v}_i \hat{w}_i - \frac{\gamma_i}{\gamma} \hat{\bar{w}}\right)^2 - \frac{\hat{\bar{w}}^2}{\gamma} + \frac{2\hat{\bar{w}}^2}{\gamma} .$$

Then

$$\sum_i \frac{1}{\gamma_i} \left((\alpha - \beta) \frac{v_i^2 w_i^2}{\hat{\bar{w}}} + \hat{v}_i \hat{w}_i (\beta p_i - \alpha s_i)\right)$$

$$= \frac{\alpha - \beta}{\hat{\bar{w}}} \sum_i \frac{1}{\gamma_i} \left(v_i w_i - \frac{\gamma_i}{\gamma} \hat{\bar{w}}\right)^2 + \sum_i \frac{1}{\gamma_i} \hat{v}_i \hat{w}_i \left(\beta p_i - \alpha s_i + \frac{\gamma_i}{\gamma} (\alpha - \beta)\right) .$$

The first term above can be rewritten:

The equilibrium identity

$$\hat{v}_i \left(1 - (1 - \gamma) \frac{\hat{w}_i}{\hat{\bar{w}}}\right) = \gamma_i ,$$

gives

$$\hat{v}_i (\hat{\bar{w}} - \hat{w}_i + \gamma \hat{w}_i) = \gamma_i \hat{\bar{w}} ,$$

thus

$$\hat{v}_i \hat{w}_i - \frac{\gamma_i}{\gamma} \hat{\bar{w}} = \frac{1}{\gamma} \hat{v}_i (\hat{w}_i - \hat{\bar{w}}) .$$

So

$$\sum_i \frac{1}{\gamma_i} \left(\hat{v}_i \hat{w}_i - \frac{\gamma_i}{\gamma} \hat{\bar{w}}\right)^2 = \frac{1}{\gamma^2} \sum_i \frac{1}{\gamma_i} \hat{v}_i^2 (\hat{w}_i - \hat{\bar{w}})^2 .$$

The second term can be rewritten also, since

$$\beta p_i - \alpha s_i + \frac{\gamma_i}{\gamma}(\alpha-\beta) = \frac{1}{\gamma}\alpha\beta(p_i - s_i) .$$

This yields

$$\overset{\circ}{\rho} = \Big(\sum_i \frac{1}{\gamma_i}\hat{v}_i^2 w_i\Big)^{-1} \frac{1}{\gamma^2}\Big[\frac{\alpha-\beta}{\bar{w}}\sum_i \frac{1}{\gamma_i}\hat{v}_i^2(\hat{w}_i - \bar{w})^2 + \alpha\beta\gamma\sum_i \hat{v}_i\hat{w}_i\frac{(p_i-s_i)}{\gamma_i}\Big] .$$

The second term in the brackets can be rewritten as

$$\alpha\beta\gamma\sum_i \hat{v}_i\hat{w}_i\frac{p_i-s_i}{\gamma_i} = \alpha\beta\gamma\Big[\bar{w}\bar{\delta} + \operatorname{cov}\Big(w_i, \frac{p_i-s_i}{\gamma_i}\Big)\Big]$$

where

$$\operatorname{cov}\Big(\hat{w}_i, \frac{p_i-s_i}{\gamma_i}\Big) \triangleq \sum_i \hat{v}_i(\hat{w}_i - \bar{w})\Big(\frac{p_i-s_i}{\gamma_i} - \bar{\delta}\Big) ,$$

and

$$\bar{\delta} \triangleq \sum_i \hat{v}_i\frac{p_i-s_i}{\gamma_i} .$$

Into the expression

$$\bar{\delta} = \sum_i \Big(\hat{v}_i - \frac{\gamma_i}{\gamma}\Big)\frac{p_i-s_i}{\gamma_i}$$

we can substitute the following derivation from the equilibrium identity,

$$\hat{v}_i - \frac{\gamma_i}{\gamma} = \hat{v}_i - \frac{1}{\gamma}\Big(1-(1-\gamma)\frac{w_i}{\bar{w}}\Big)\hat{v}_i = \frac{(1-\gamma)}{\gamma}\frac{\hat{v}_i}{\bar{w}}(\hat{w}_i - \bar{w}) , \qquad (3.22)$$

to yield

$$\alpha\beta\gamma\sum_i \hat{v}_i\hat{w}_i\frac{p_i-s_i}{\gamma_i} = \alpha\beta\Big[(1-\gamma)\sum_i \hat{v}_i(\hat{w}_i-\bar{w})\Big(\frac{p_i-s_i}{\gamma_i}\Big) + \gamma\operatorname{cov}\Big(\hat{w}_i, \frac{p_i-s_i}{\gamma_i}\Big)\Big] .$$

Therefore,

$$\rho(Y_a D) = 1 + (m_a - m^*)\Big(\sum_i \frac{1}{\gamma_i}\hat{v}_i^2 w_i\Big)^{-1}\frac{1}{\gamma^2}$$

$$\cdot\Big[\frac{(\alpha-\beta)}{\bar{w}}\sum_i \frac{1}{\gamma_i}\hat{v}_i^2(\hat{w}_i-\bar{w})^2 + \alpha\beta\Big((1-\gamma)\sum_i \hat{v}_i(\hat{w}_i-\bar{w})\Big(\frac{p_i-s_i}{\gamma_i}\Big) + \gamma\operatorname{cov}\Big(\hat{w}_i, \frac{p_i-s_i}{\gamma_i}\Big)\Big)\Big]$$

This completes the proof.

In Case 1., a new modifier allele can change frequency at a geometric rate when introduced only if it changes the amount of transformation occurring, i.e. only if

$$(m_a - m^*)(\alpha - \beta) \neq 0 ,$$

and it can increase if and only if it reduces the amount of transformation.

In Case 2. the terms in the brackets show two different forces that contribute to the change in the spectral radius. The first term

$$\frac{\alpha - \beta}{\hat{\bar{w}}} \sum_i \frac{1}{\gamma_i} \hat{v}_i^2 \, (\hat{w}_i - \bar{w})^2$$

is the contribution of the marginal fitness variance to decreasing the overall amount of transformation occurring. It is zero if and only if either

1) the marginal fitness variance is zero, so

$$\hat{w}_i = \hat{\bar{w}} \quad \forall \quad i , \text{ or}$$

2) the new modifier paramter m_a does not change the total amount of transformation $(1-m_a)\alpha + m_a\beta$, which requires $\alpha = \beta$.

When the marginal fitness variance is not zero, then the term is positive if increasing m_a decreases the overall amount of transformation, and is negative in the opposite case.

Another interesting feature of this term is seen by substituting from the alternative form of the equilibrium identity (3.22),

$$\frac{\gamma \, \hat{\bar{w}}}{1-\gamma} (\hat{v}_i - \frac{\gamma_i}{\gamma}) = \hat{v}_i (\hat{w}_i - \hat{\bar{w}}) .$$

The first term becomes

$$(\alpha - \beta) \hat{\bar{w}} \frac{\gamma^2}{(1-\gamma)^2} \sum_i \frac{1}{\gamma_i} (\hat{v}_i - \frac{\gamma_i}{\gamma})^2 .$$

If no selection were acting, then under transformation alone the equilibrium haplotype frequencies would all be

$$\hat{v}_i = \frac{\gamma_i}{\gamma} .$$

So the squared term is the deviation of the selected haplotype frequencies from where they would be under pure transformation. The effect of adding selection to a system of pure transformation is to create selection for decreased amounts of transformation.

The second two terms are the contribution from increasing the transformation probabilities toward the fitter types. Increasing m_a shifts the transformation distribution from the s_i values toward the p_i values. When the higher p_i's are sufficiently more associated with the higher marginal fitnesses than the s_i's , then this term is positive.

If the variation is linear, which occurs if and only if

$$\alpha = 0 \text{ , or } \beta = 0 \text{ , or } s_i = p_i \text{ for all } i ,$$

then the second term is zero. It is also zero if the marginal fitness variance is zero.

The basic conclusion from this derivation is that, at least in this case, whether or not a new modifier allele can increase in the population depends on a combination of how much it reduces the overall amount of transformation occurring, and how much it shifts the transformation distribution toward the production of fitter types.

I cannot say whether the results of this derivation would also hold for transformation with other than memoriless distributions, for loosely linked modifiers, or for new marginal modifier parameters far from m^* .

However, in models of recombination modification where there is also migration (Charlesworth and Charlesworth, 1979), or mutation (Feldman et al., 1980), the variation in the transformation is affine because, as was discussed in Section 2., cases 2) and 5) show that when the modifier has only partial control of the transformations occurring, the variation in the transformations can be affine. In these cases where the addition of mutation or migration makes the variation affine, it is possible for a modifier increasing recombination to increase when introduced into the population. This suggests the following principle:

THE PRINCIPLE OF PARTIAL CONTROL:

When a modifier gene has only partial control over the transformations occurring at selected loci, then it is possible for this part of the transformations to evolve an increase.

THE CO-EVOLUTION OF TRANSFORMATIONS

An interesting question is how different parts of a transformation under the control of different modifiers will coevolve. Is it possible, since each modifier will have only partial control over the transformation, for all these parts to evolve an increase? In other words, by fragmenting the control over the transformation among various modifier genes, is it possible for the transformation to "bootstrap" itself away from perfect transmission? For the case of transformations with memoriless distributions, at least, this appears not to be the case.

Suppose that the transformation acting on the selected haploytpes is composed of several processes, each of which is controlled linearly

be a modifier locus, as in case 5) of Section 2.. Consider when there are two such processes and each has a memoriless distribution. The transformation matrix will be of the form

$$Y = \| T_k^{j \to i} \|_{i,j} = \big[(1-a)I + aF\big]\big[(1-b)I + bG\big]$$
$$= (1-a)(1-b)I + aF + (1-a)bG \quad , \qquad (3.23)$$

where F and G are rank one stochastic matrices.

Now let a modifier control either a or b. (3.23) can be translated into the form of (3.14) choosing either a or b to be the modifier parameter, with the substitutions as shown in the following table:

TABLE 12

MODIFIER CONTROL OVER TWO LINEARLY VARYING TRANSFORMATIONS

values for:	α	β	αS	βP	$P - S$
MODIFIER CONTROLS a:	b	1	bG	F	$F - G$
MODIFIER CONTROLS b:	a	1	aF	$(1-a)G + aF$	$(1-a)(G - F)$

In each case, $\gamma_i = af_i + (1-a)bg_i$.

Let us look at how Theorem 3.2b. applies. For modifiers of both a and b, the coefficient on the term

$$\sum_i \frac{1}{\gamma_i} \hat{v}_i^2 (\hat{w}_i - \hat{\bar{w}})^2$$

from Theorem 3.2b, case 2., will be negative, contributing toward decreasing both a and b. The only way for both a and b to evolve an increase is for the second two terms in the brackets from case 2. to be sufficiently positive. But the values $p_i - s_i$ for the modifier of a will be of opposite sign of those values for the modifier of b, as seen from the last column of Table 12. Therefore, if the second two terms in the brackets are positive for one modifier they will be negative for the other. This yields the following:

RESULT 3.15:

For transformations with memoriless distributions, where two modifiers each have linear control over only a part of the transformation, if one modifier evolves to increase the part of the transformation it controls, then the other modifier must evolve to decrease the part of the transformation it controls.

It would be of interest to know whether Result 3.15 extends to other forms of transformation.

1.2. THE INTERIOR STABILITY OF VIABILITY-ANALOGOUS, TENSOR PRODUCT EQUILIBRIA FOR MODIFIERS YIELDING UNIFORM VARIATION

Here I will evaluate the local interior stability of a viability-analogous, tensor product modifier polymorphism for a modifier that yields uniform variation in the transformations.

Using the general form for representing uniform variation, the recursion for system is

$$z'_{ai} = \sum_{bjk} z_{aj} z_{bk} \frac{w_k^j}{w} \left[(1-R)\left(\delta_{ji} + A_k^{j\to i} + m_b^a B_k^{j\to i}\right) + R\left(\delta_{ki} + \tilde{A}_j^{k\to i} + m_b^a \tilde{B}_j^{k\to i}\right)\right] .$$

Letting

$$z_{ai} = \hat{z}_{ai} + \varepsilon_{ai} = \hat{x}_a \hat{v}_i + \varepsilon_{ai} ,$$

where the perturbations $\sum_{ai} \varepsilon_{ai} = 0$, we obtain the following linearized recursion on the perturbations:

$$\begin{aligned}
\hat{w}\,\varepsilon'_{ai} = {} & (\varepsilon_{ai}\hat{w}_i + \hat{x}_a\hat{v}_i \sum_{bj} w_j^i \varepsilon_{bj})(1-R) + (\hat{x}_a\hat{w}_i \sum_b \varepsilon_{bi} + \hat{v}_i \sum_j w_j^i \varepsilon_{aj})\, R \\
& + (\sum_{hj} \hat{v}_h w_j^h A_h^{j\to i} \varepsilon_{aj} + \hat{x}_a \sum_{hjb} \hat{v}_h w_j^h A_j^{h\to i} \varepsilon_{bj})(1-R) \\
& + (\hat{x}_a \sum_{hjb} \hat{v}_h w_j^h \tilde{A}_k^{j\to i} \varepsilon_{bj} + \sum_{hj} \hat{v}_h w_j^h \tilde{A}_j^{h\to i} \varepsilon_{aj})\, R \\
& + (m^* \sum_{hj} \hat{v}_h w_j^h B_h^{j\to i} \varepsilon_{aj} + \hat{x}_a \sum_{hjb} \hat{v}_j w_j^h B_j^{h\to i} m_b^a \varepsilon_{bj})(1-R) \\
& + (\hat{x}_a \sum_{hjb} \hat{v}_h w_j^h \tilde{B}_h^{j\to i} m_b^a \varepsilon_{bj} + m^* \sum_{hj} \hat{v}_j w_j^h \tilde{B}_j^{h\to i} \varepsilon_{aj})\, R \\
& - 2\hat{x}_a\hat{v}_i \sum_{bj} \varepsilon_{bj}\hat{w}_j .
\end{aligned}$$

This can be represented in vector form using tensor products:

$$\underline{\varepsilon}' = \begin{bmatrix} I_1 \otimes [(1-R)(I_2 + A + m^* B) + R(Q + \tilde{A} + m^* \tilde{B})] \\ + \operatorname{diag}(\hat{\underline{x}})U_1 \otimes [R(I_2 + A) + (1-R)(Q + \tilde{A})] \\ + \operatorname{diag}(\hat{\underline{x}})M \otimes [RB + (1-R)\tilde{B}] \\ - 2 \operatorname{diag}(\hat{\underline{x}})U_1 \otimes \operatorname{diag}(\hat{\underline{v}})U_2 \end{bmatrix} (I_1 \otimes D)\underline{\varepsilon}$$

$$\triangleq \Gamma \underline{\varepsilon} ,$$

where

$$A \triangleq \| \sum_k \hat{v}_k \frac{w_k^j}{\hat{\bar{w}}} A_k^{j \to i} \|_{i,j} , \quad \tilde{A} \triangleq \| \sum_k \hat{v}_k \frac{w_k^j}{\hat{\bar{w}}} \tilde{A}_j^{k \to i} \|_{i,j} ,$$

B and $\tilde{B}$ are defined analogously, and Q and D are defined as before. U_1 is an n_1 by n_1 matrix of ones, where n_1 is the number of modifier alleles, and U_2 is that for n_2, the number of selected-loci haplotypes. M is the matrix of modifier parameters, $M = \| m_j^i \|$. I_1 and I_2 are the appropriate identity matrices.

To begin the analysis, first, let us project the vector $\underline{\varepsilon}$ on to the space of perturbations in the selected haplotypes, by adding up, $\sum_a \varepsilon_{ai}$. This is accomplished by premultiplication with

$$\underline{e}_1^T \otimes I_2 .$$

Since

$$\underline{e}_1^T \operatorname{diag}(\hat{\underline{x}})U_1 = \underline{e}_1^T , \qquad \underline{e}_1^T \operatorname{diag}(\hat{\underline{x}})M = m^* \underline{e}_1^T ,$$

we have

$$\begin{aligned} (\underline{e}_1^T \otimes I_2)\,\underline{\varepsilon}' &= (\underline{e}_1^T \otimes I_2)\Gamma\underline{\varepsilon} \\ &= GD[(\underline{e}_1^T \otimes I_2)\,\underline{\varepsilon}] , \end{aligned} \tag{3.24}$$

where

$$G \triangleq I_2 + Q + A + \tilde{A} + m^*(B + \tilde{B}) - 2\,\mathrm{diag}(\hat{\underline{v}})U_2 .$$

This recursion on the perturbations of the selected haplotype frequencies is identical to the recursion when the modifier is fixed,

$$\underline{\nu}' = GD\,\underline{\nu} .$$

Thus we obtain the following:

THEOREM 3.16:

If the selection-transformation equilibrium is unstable when the modifier is fixed, it is also unstable for the viability-analogous, tensor product modifier polymorphism. For the polymorphism to be stable, at least the equilibrium with fixed modifier must be stable, i.e.,

$$\rho(GD) < 1 .$$

Although this was demonstrated here only for uniform variation, it can be seen to hold for any V.A.T.P. equilibrium.

Vectors which project to 0 under $\underline{e}_1^T \otimes I_2$ form a linear subspace of $\{\underline{\varepsilon}\}$, call it N. It will be of dimension $(n_1 - 1)n_2$, where n_1 is the number of modifier alleles, and n_2 the number of selected haplotype. This is seen because we can use as a basis for N

$$\{\underline{\alpha}_i \otimes \underline{\gamma}_j\} ,$$

where $\underline{\alpha}_i$ are n_1 long vectors, $\underline{\gamma}_j$ are n_2 long vectors, and

$$\underline{e}_1^T\underline{\alpha}_i = 0 \quad \forall\, i = 1 \ldots n_1 - 1 , \quad \underline{\gamma}_j = \begin{pmatrix} 0 \\ \vdots \\ 1 \\ \vdots \\ 0 \end{pmatrix} \leftarrow \text{jth component is 1.}$$

There are assumed to be at least two modifier alleles, for otherwise N would consist of the zero vector. To fill out $\{\underline{\varepsilon}\}$, we define the space H, orthogonal to N. H is of dimension $n_2 - 1$. For all $\underline{\beta} \in H$, we know

$$(\underline{e}_1^T \otimes I_2)\,\underline{\beta} \neq 0 \text{ , and } (\underline{e}_1^T \otimes \underline{e}_2^T)\,\underline{\beta} = 0 .$$

For each $\underline{\varepsilon}$ there is always a unique representation

$$\underline{\varepsilon} = \tilde{\underline{\varepsilon}} + \underline{\beta} \quad \text{where } \tilde{\underline{\varepsilon}} \in N,\ \underline{\beta} \in H .$$

Then, from (3.24),

$$(\underline{e}_1^T \otimes I_2)\,\Gamma^n \underline{\varepsilon} = (GD)\,(\underline{e}_1^T \otimes I_2)\,\Gamma^{n-1}\underline{\varepsilon} = (GD)^n(\underline{e}_1^T \otimes I_2)\,\underline{\varepsilon}$$
$$= (GD)^n(\underline{e}_1^T \otimes I_2)(\tilde{\underline{\varepsilon}} + \underline{\beta}) = (GD)^n[(\underline{e}_1^T \otimes I_2)\,\underline{\beta}]$$

Since we have already required that

$$\lim_{n\to\infty}(GD)^n\underline{x} = 0 \quad \forall\, \underline{x}:\ \underline{e}_2^T\,\underline{x} = 0 \text{ , we have}$$

$$\lim_{n\to\infty}(\underline{e}_1 \times I_2)\,\Gamma^n\underline{\varepsilon} = 0, \quad \forall\ \underline{\varepsilon} .$$

Therefore, trajectories converge to points in N, all components from H in $\underline{\varepsilon}$ damping out, so we need only consider perturbations $\tilde{\underline{\varepsilon}} \in N$.

Now, for

$$\tilde{\underline{\varepsilon}} = \sum_{ij} a_i b_j\, \underline{\alpha}_i \otimes \underline{\gamma}_j \quad \in N ,$$

we have

$$(I_1 \otimes D)\tilde{\underline{\varepsilon}} = \sum_{ij} a_i b_j \underline{\alpha}_i \otimes D\,\underline{\gamma}_j \in N \text{ also.}$$

So

$$(U_1 \otimes D)\,\tilde{\underline{\varepsilon}} = 0 \quad \forall\, \tilde{\underline{\varepsilon}} \in N ,$$

which gives

$$\tilde{\underline{\varepsilon}}' = \Big(I_1 \otimes \big[(1-R)(I_2 + A + m^* B) + R(Q + \tilde{A} + m^* \tilde{B})\big]$$
$$+ \operatorname{diag}(\hat{\underline{x}})M \otimes \big[RB + (1-R)\tilde{B}\big] \Big)\ (I_1 \otimes D)\tilde{\underline{\varepsilon}} .$$

In the analogy to viability selection, the modifier parameters m_j^i behave as fitnesses except that, whereas a new selected allele must have $w_i > \bar{w}$ to increase, the modifier must have $m_i < m^*$, from the last section. Therefore, the analog to the fitness matrix would be the matrix $U - M$. Pursuing this analogy, we might expect that modifier overdominance would be required to make a modifier polymorphism stable.

Maximal overdominance is attained when

$$M = \text{diag}(m_i^i) .$$

Here, the phenotype that is overdominant is the extent to which perfect transmission of the haplotypes is occurring, rather than the extent of transformation. The best biological example of maximal overdominance is a chromosomal inversion bordered by two loci under selection. The inversion acts as a tightly linked modifier of recombination, which as a heterozygote eliminates recombination between the two loci.

Since $\hat{m}_a = \sum_b m_b^a \hat{x}_b = m_a^a \hat{x}_a = m^*$, this gives $\text{diag}(\hat{\underline{x}})M = m^* I_1$. Substituting, we obtain

$$\tilde{\underline{\varepsilon}}' = \left(I_1 \otimes \left[(1-R)(I_2 + A) + R(Q + \tilde{A}) + m^*(B + \tilde{B}) \right] D \right) \tilde{\underline{\varepsilon}}$$

$$\triangleq (I_1 \otimes JD)\, \tilde{\underline{\varepsilon}} .$$

For this case, the V.A.T.P. equilibrium is stable if $\rho(JD) < 1$, and unstable if $\rho(JD) > 1$.

It is significant that neither the specific modifier parameters nor the modifier allele frequencies appear directly here, which gives the following result:

THEOREM 3.17:

For a maximally overdominant modifier locus, neither the degree of allelic multiplicity at the modifier locus, nor the specific modifier parameters of the modifier homozygotes, are relevant to the stability of a V.A.T.P. modifier polymorphism with uniform variation in the transformation.

Note that $J = (1-R)Y^* + R\tilde{Y}^* + m^*(RB + (1-R)\tilde{B})$,

$G = 2\left(\frac{1}{2}(Y^* + \tilde{Y}^*) - \mathrm{diag}(\hat{\underline{v}})U\right)$,

where Y^* and $\tilde{Y}^*$ are defined as in the exterior stability analysis (I.1c.). Now,

$\rho([(1-R)Y^* + R\tilde{Y}^*]D) = 1 \quad \forall\, R$ and $\rho(GD) < 1$ by assumption, thus

$$\rho\left(\left[\tfrac{1}{2}(Y^* + \tilde{Y}^*) - \mathrm{diag}(\hat{\underline{v}})U\right]D\right) < \tfrac{1}{2} .$$

We wish to know

$$\rho([(1-R)Y^* + R\tilde{Y}^* + m^*(RB + (1-R)\tilde{B})]D) .$$

I cannot solve this generally, but will consider some special cases.

I.2a. UNLINKED MODIFIERS

Note the following relation:

At $R=1/2$,

$$J = \tfrac{1}{2}(I_2 + A + Q + \tilde{A}) + m^*(B + \tilde{B}) .$$

In comparison, at $R=1/2$, the stability matrix for the initial increase of a new modifier allele whose marginal transformation falls within the same uniform variation is

$$\Omega_a = \frac{1}{2}(I_2 + A + Q + \tilde{A}) + \frac{m_a}{2}(B + \tilde{B}) .$$

Therefore, we have the very interesting result:

THEOREM 3.18:

For an unlinked modifier, a V.A.T.P. equilibrium with uniform variation in transformations and maximal modifier overdominance will be stable internally if and only if it is stable to the introduction of a new modifier allele having marginal parameter

$$m_a = 2m^* .$$

I do not know what is entailed when $2m^*$ is beyond the feasible range of m_a .

Unfortunately, the exterior stability to the introduction of new modifier alleles with $m_a > 0$ has not been tractible for $R > 0$ in the general case. In the cases in Feldman et al. (1980), analysis for loci with two alleles has been done. In the case of a recombination modifier when there is no mutation, so that the variation in the transformation is linear, their results imply that at $R= 1/2$,

$$\rho(JD) < 1 \quad , \text{ since } \rho(\Omega_a D) < 1 \text{ at } m_a = 2m^* .$$

This yields the following:

RESULT 3.19:

For an unlinked modifier of recombination at two loci, subject to no other transformations, when there are two alleles at each of the selected loci, and an arbitrary number of maximally overdominant alleles at the modifier locus, a viability-analogous, tensor product equilibrium is stable given that polymorphism among the selected loci under the equilibrium recombination rate is stable.

This extends the result of Feldman and Balkau (1973) to arbitrary selection regimes and arbitrary numbers of modifier alleles, which, however, are restricted to being maximally overdominant.

If the reduction principle could be shown to hold also for the general case of linear variation in transformations with unlinked modifiers, in other words, if it could be shown that a new allele linearly increasing transformation is always excluded, then Result 3.19 could be extended generally. Given that a polymorphism among the selected loci under a given transformation is stable, then a V.A.T.P. polymorphism with the same equilibrium transformation, with an unlinked, maximally overdominant modifier, and linear variation in the transformation, is always stable.

Now let us consider affine variation in the transformation. At a V.A.T.P. equilibrium, if a new modifier allele increasing transformation by any amount can get into the population, then Theorem 3.18 implies that the V.A.T.P. polymorphism will be unstable for an unlinked modifier. This would hold for the case of recombination modification with mutation present, in Feldman et al. (1980), provided the critical

value of R at which the exterior stability changes is greater than one half. This is to be expected if the viability analogy is reconsidered for the affine case. In this case, the modifier locus would appear to be underdominant, because lower amounts of transformation are being selected against. In analogy with viability selection, polymorphic equilibria with underdominance are unstable.

I will now consider two special cases of transformation: recombination and mutation. In both these cases, the variation in the transformation will be linear, so $A=0$, and $B=P-I$. I will assume there is no interference. Thus

$$J = (1-R-m^*)I + (R-m^*)Q + m^*(P+\tilde{P}),$$

where

$$T^{aj\to ai}_{bk} = (1-m^a_b)\delta_{ji} + m^a_b P^{j\to i}_k ,$$

$$P \triangleq \| \sum_k \hat{v}_k \frac{w^j_k}{\hat{w}_j} P^{j\to i}_k \|_{i,j} \quad \text{and} \quad \tilde{P} \triangleq \| \sum_k \hat{v}_k \frac{w^j_k}{\hat{w}_j} P^{k\to i}_j \|_{i,j} .$$

I.2b. MUTATION MODIFIERS

For the general mutation transformation, $P^{j\to i}_h = P_{j\to i}\ \forall\ h$.

$$\text{Thus } \tilde{P} = \| \sum_H \hat{v}_h \frac{w^h_j}{\hat{w}_j} P_{h\to i} \| = PQ, \quad P = \| P_{j\to i} \| .$$

$$\text{So } J = (1-R)\ I + RQ + m^*(P-I)(I+Q).$$

I will analyze the case with 2 alleles at the selected locus. In the following derivation, m refers to m^* and w_{ij} refers to $w\frac{i}{j}$.

$$D = \begin{Vmatrix} \frac{\hat{w}_1}{\bar{\hat{w}}} & 0 \\ 0 & \frac{\hat{w}_2}{\bar{\hat{w}}} \end{Vmatrix}, \qquad Q = \begin{Vmatrix} \hat{v}_1 \frac{w_{11}}{\hat{w}_1} & \hat{v}_1 \frac{w_{12}}{\hat{w}_2} \\ \hat{v}_2 \frac{w_{21}}{\hat{w}_1} & \hat{v}_2 \frac{w_{22}}{\hat{w}_2} \end{Vmatrix} = \begin{Vmatrix} q_1 & q_3 \\ q_2 & q_4 \end{Vmatrix},$$

$$P = \begin{Vmatrix} p_1 & p_3 \\ p_2 & p_4 \end{Vmatrix}, \text{ and}$$

$$J = (1-m^*-R)\begin{Vmatrix} 1 & 0 \\ 0 & 1 \end{Vmatrix} + m^*\begin{Vmatrix} P_1 & P_3 \\ P_2 & P_4 \end{Vmatrix}\begin{Vmatrix} 1+q_1 & q_3 \\ q_2 & 1+q_4 \end{Vmatrix} + (R-m^*)\begin{Vmatrix} q_1 & q_3 \\ q_2 & q_4 \end{Vmatrix}.$$

I will drop the superscripts where convenient at this point.

Thus $JD =$

$$\frac{1}{\bar{w}}\begin{Vmatrix} w_1[1-m-R+mp_1+(R-m)q_1+m(p_1q_1+p_3q_2)] & w_2[mp_3+(R-m)q_3+m(p_1q_3+p_3q_4)] \\ w_1[mp_2+(R-m)q_2+m(p_2q_1+p_4q_2)] & w_2[1-m-R+mp_4+(R-m)q_4+m(p_2q_3+p_4q_4)] \end{Vmatrix}$$

To evaluate $\rho(JD)$, we examine the characteristic determinant and its derivative at $\lambda=1$. The characteristic determinant is

$$ch(\lambda) = \frac{1}{\bar{\hat{w}}}\begin{vmatrix} C_{11} - \hat{Rv}_2w_{12} & C_{12} + \hat{Rv}_1w_{12} \\ C_{21} + \hat{Rv}_2w_{12} & C_{22} - \hat{Rv}_1w_{12} \end{vmatrix},$$

where

$$C_{11} = \hat{w}_1 - \hat{\bar{w}}\lambda + m(-\hat{w}_1 p_2 - \hat{v}_1 w_{11} + p_1 \hat{v}_1 w_{11} + p_3 \hat{v}_2 w_{12}) ,$$
$$C_{12} = m(p_3 \hat{w}_2 - \hat{v}_1 w_{12} + p_1 \hat{v}_1 w_{12} + p_3 \hat{v}_2 w_{22}) ,$$
$$C_{21} = m(p_2 \hat{w}_1 - \hat{v}_2 w_{12} + p_2 \hat{v}_1 w_{11} + p_4 \hat{v}_2 w_{12}) ,$$
$$C_{22} = \hat{w}_2 - \bar{w}\lambda + m(-p_3 \hat{w}_2 - \hat{v}_2 w_{22} + p_2 \hat{v}_1 w_{12} + p_4 \hat{v}_2 w_{22}) .$$

The R^2 terms all cancel.

The R term is:

$$-Rw_{12}[v_1(C_{11} + C_{21}) + v_2(C_{12} + C_{22})] = -Rw_{12}[v_1(w_1 - \bar{w}\lambda) + v_2(w_2 - \bar{w}\lambda)]$$
$$= -Rw_{12}(1-\lambda)\bar{w} .$$

At $\lambda = 1$, the R term is also zero.

Thus

$$ch(1) = \frac{1}{\hat{\bar{w}}} \begin{vmatrix} C_{11} & C_{12} \\ C_{21} & C_{22} \end{vmatrix} = \frac{1}{\hat{\bar{w}}} \begin{vmatrix} w_1 \hat{-} \bar{w} - m\alpha_1 & m\alpha_2 \\ m\alpha_1 & \hat{w}_2 - \bar{w} - m\alpha_2 \end{vmatrix}$$

$$= (\hat{w}_1 - \hat{\bar{w}})(\hat{w}_2 - \hat{\bar{w}}) - m(\alpha_1(\hat{w}_2 - \hat{\bar{w}}) + \alpha_2(\hat{w}_1 - \hat{\bar{w}}))$$

where $\alpha_1 \triangleq p_2(\hat{v}_1 w_{11} + \hat{w}_1) - p_3 \hat{v}_2 w_{12}$, $\alpha_2 \triangleq p_3(\hat{v}_2 w_{22} + \hat{w}_2) - p_2 \hat{v}_1 w_{12}$.

The identities

$$\hat{w}_1 - \hat{\bar{w}} = \hat{v}_2(\hat{w}_1 - \hat{w}_2), \text{ and } w_2 - \bar{w} = -\hat{v}_1(\hat{w}_1 - \hat{w}_2),$$

give

$$ch(1) = -(\hat{w}_1 - \hat{w}_2)^2 \hat{v}_1 \hat{v}_2 - m(\hat{w}_1 - \hat{w}_2)(\hat{v}_2 \alpha_2 - \hat{v}_1 \alpha_1) .$$
$$= -(w_1 - w_2)^2 \hat{v}_1 \hat{v}_2 - 2m(\hat{w}_1 - \hat{w}_2)(p_3 \hat{v}_2 \hat{w}_2 - p_2 \hat{v}_1 \hat{w}_1) .$$

Using one of the equilibrium identities,

$$\bar{w} \hat{v}_2 = v_2 w_2 (1 - m) + m(p_2 w_1 v_1 + p_4 w_2 v_2),$$

which gives

$$(\bar{w} - w_2)v_2 = (w_1 - w_2)v_1 v_2 = m(p_2 v_1 w_1 - p_3 v_2 w_2) ,$$

we obtain

$$ch(1) = v_1v_2(w_1 - w_2)^2 = (w_1 - \bar{w})(\bar{w} - w_2) .$$

In the general case where there is an equilibrium fitness load, meaning the equilibrium $\hat{\underline{v}}$ is mutation dependent, then $w_1 \neq w_2$, thus $ch(1) > 0$.

The derivative of the characteristic polynomial is:

$$\frac{\partial ch(\lambda)}{\partial \lambda} = \frac{1}{\bar{w}}\left(c_{11}\frac{\partial c_{22}}{\partial \lambda} + \frac{\partial c_{11}}{\partial \lambda}c_{22}\right) - R\frac{w_{12}}{\bar{w}}\left(\hat{v}_2\frac{\partial c_{22}}{\partial \lambda} + v_1\frac{\partial c_{11}}{\partial \lambda}\right)$$

$$= Rw_{12} - c_{11} - c_{22} .$$

Therefore

$$\frac{\partial ch(\lambda)}{\partial \lambda}\bigg|_{\lambda=1} > 0 \quad \forall R \quad \text{iff} \quad c_{11} + c_{22} < 0 \quad \text{at } \lambda = 1 .$$

Now,

$$c_{11}+c_{22} = \hat{w}_1-\bar{w} + \hat{w}_2-\bar{w} + m\left(p_2(\hat{v}_1w_{12}-\hat{v}_1w_{11}-\hat{w}_1) + p_3(\hat{v}_2w_{12}-\hat{v}_2w_{22}-\hat{w}_2)\right)$$

The equilibrium identities

$$\hat{\bar{w}} - \hat{w}_2 = \frac{m}{\hat{v}_2}(p_2\hat{v}_1\hat{w}_1 - p_3\hat{v}_2\hat{w}_2), \text{ and } \hat{\bar{w}} - \hat{w}_1 = \frac{m}{\hat{v}_1}(p_3\hat{w}_2\hat{v}_2 - p_2\hat{w}_1\hat{v}_1),$$

give

$$c_{11}+c_{22} = \frac{m}{\hat{v}_1\hat{v}_2}\left[p_2\hat{v}_1\left(\hat{v}_1(v_2w_{12}-w_1) - \hat{v}_1\hat{v}_2w_{11}\right) + p_3\hat{v}_2\left(\hat{v}_2(\hat{v}_1w_{12}-\hat{w}_2) - \hat{v}_1\hat{v}_2w_{22}\right)\right]$$

$$= -(p_2\hat{v}_1^2w_{11} + p_3\hat{v}_2^2w_{22}) < 0 .$$

Therefore, since

$$ch(1) > 0, \quad \frac{\partial ch(\lambda)}{\partial \lambda}\bigg|_{\lambda=1} > 0 ,$$

no eigenvalues are greater than or equal to 1. Since JD is non-

negative, by the Perron-Frobenius theorem we know that $\rho(JD) < 1 \; \forall \; R$. Thus we have:

RESULT 3.20:

The viability-analogous, tensor-product modifier polymorphism has local interior stability for a mutation modifier having maximal overdominance, with two alleles at the selected locus.

I.2c. RECOMBINATION MODIFIERS.

Here, there will be 2 loci under selection, each with 2 alleles, whose recombination rate is controlled by a third, modifier locus, not between the 2 selected loci. The existence and stability of a viability analogous-random association equilibria for this model was worked out by Feldman and Balkau (1973) for the Lewontin-Kojima and Wright symmetric viability regimes, and for 2 modifier alleles with symmetric parameters. Here I analyze the stability for general viability selection, and maximal overdominance at an arbitrary number of modifier alleles.

The four haplotypes at the selected loci,

$$A_1B_1 \; , \; A_1B_2 \; , \; A_2B_1 \; , \; A_2B_2 \; ,$$

will be indexed 1, 2, 3, 4, respectively. The matrix P represents the probabilities, given that a crossover occurs, that each haplotype is produced. The modifier locus, M, will be positioned with A between it and B. Therefore, with no recombination between M and A, a haplotype $M_aA_iB_j$ will always come out M_aA_i with possible change

at B . It will be assumed that there is no interference in recombination among the three loci.

Using the form w_{ij} for the fitnesses of selected genotypes $\frac{(AB)_i}{(AB)_j}$, i,j = 1,2,3,4 , matrices PD and $\tilde{P}D$ have the form:

$$\hat{\bar{w}}\,PD = \begin{Vmatrix} \hat{v}_1w_{11} + \hat{v}_3w_{13} & v_1w_{12} + \hat{v}_3w_{32} & 0 & 0 \\ \hat{v}_2w_{21} + \hat{v}_4w_{14} & \hat{v}_2w_{22} + \hat{v}_4w_{24} & 0 & 0 \\ 0 & 0 & \hat{v}_1w_{13} + \hat{v}_3w_{33} & \hat{v}_1w_{14} + \hat{v}_3w_{34} \\ 0 & 0 & \hat{v}_2w_{23} + \hat{v}_4w_{43} & \hat{v}_2w_{24} + \hat{v}_4w_{44} \end{Vmatrix},$$

$$\hat{\bar{w}}\,\tilde{P}D = \begin{Vmatrix} \hat{v}_1w_{11} + \hat{v}_2w_{12} & 0 & \hat{v}_1w_{13} + \hat{v}_2w_{23} & 0 \\ 0 & \hat{v}_1w_{12} + \hat{v}_2w_{22} & 0 & \hat{v}_1w_{14} + \hat{v}_2w_{24} \\ \hat{v}_3w_{13} + \hat{v}_4w_{14} & 0 & \hat{v}_3w_{33} + \hat{v}_4w_{43} & 0 \\ 0 & \hat{v}_3w_{23} + \hat{v}_4w_{24} & 0 & \hat{v}_3w_{34} + \hat{v}_4w_{44} \end{Vmatrix}.$$

This yields

$$(P - I + \tilde{P} - Q)D = \begin{pmatrix} -1 \\ 1 \\ 1 \\ -1 \end{pmatrix} (\hat{v}_4w_{14} - \hat{v}_3w_{23} - \hat{v}_2w_{23}\,\hat{v}_1w_{14}) \frac{1}{\hat{\bar{w}}}.$$

Since $JD = \left((1 - R)I + RQ + m^*(P - I + \tilde{P} - Q) \right)$, we have

$$ch(\lambda) = \det (JD - \lambda I) \triangleq \det(k) =$$

$$\begin{vmatrix}
\hat{Rv}_1 w_{11} - \hat{mv}_4 w_{14} + \hat{w}_1(1 - R) - \lambda\hat{\bar{w}} & \hat{Rv}_1 w_{12} + \hat{mv}_3 w_{23} & \hat{Rv}_1 w_{13} + \hat{mv}_2 w_{23} & \hat{Rv}_1 w_{14} - \hat{mv}_1 w_{14} \\
\hat{Rv}_2 w_{12} + \hat{mv}_4 w_{14} & \hat{Rv}_2 w_{22} - \hat{mv}_3 w_{23} + \hat{w}_2(1 - R) - \lambda\hat{\bar{w}} & \hat{Rv}_2 w_{23} - \hat{mv}_2 w_{23} & \hat{Rv}_2 w_{24} + \hat{mv}_1 w_{14} \\
\hat{Rv}_3 w_{13} + \hat{mv}_4 w_{14} & \hat{Rv}_3 w_{23} - \hat{mv}_3 w_{23} & \hat{Rv}_3 w_{33} - \hat{mv}_2 w_{23} + \hat{w}_3(1 - R) - \lambda\hat{\bar{w}} & \hat{Rv}_3 w_{34} + \hat{mv}_1 w_{14} \\
\hat{Rv}_4 w_{14} - \hat{mv}_4 w_{14} & \hat{Rv}_4 w_{24} + \hat{mv}_3 w_{23} & \hat{Rv}_4 w_{44} + \hat{mv}_2 w_{23} & \hat{Rv}_4 w_{44} + \hat{mv}_1 w_{14} + \hat{w}_4(1 - R) - \lambda\hat{\bar{w}}
\end{vmatrix}$$

The determinant operations used by Feldman et al. (1980) for the initial increase analysis of recombination modifiers are again appropriate for the interior stability analysis.

The following elementary determinant operations were performed on det(k):

1) $k'_{ij} = \frac{1}{\hat{v}_j} k_{ij} \quad \forall\ i,j$.

2) $k'_{1j} = \sum_{i=1}^{4} k_{ij} \quad \forall\ i$.

3) $k'_{i4} = \sum_{j=1}^{4} k_{ij} \quad \forall\ i$.

4) $k'_{2j} = k_{2j} + k_{4j}$, $k'_{3j} = k_{3j} + k_{4j} \quad \forall\ j$.

Define $\hat{d} \triangleq \hat{v}_1\hat{v}_4w_{14} - \hat{v}_2\hat{v}_3w_{23}$, and $\Pi = \prod_{i=1}^{4}\hat{v}_i$.

This yields

$\hat{\bar{w}}\,\Pi\ ch(\lambda) =$

$$\begin{vmatrix}
(\hat{w}_1 - \lambda\ \bar{w})v_1 & (\hat{w}_2 - \lambda\ \hat{\bar{w}})\hat{v}_2 & (\hat{w}_3 - \lambda\ \hat{\bar{w}})\hat{v}_3 & (1-\lambda)\hat{\bar{w}} \\
R\hat{v}_1(\hat{v}_2w_{12}+\hat{v}_4w_{14}) & R\hat{v}_2(\hat{v}_2w_{22}+\hat{v}_3w_{23}) + \hat{v}_2(\hat{w}_2(1-R) - \lambda\hat{\bar{w}}) & R\hat{v}_3(\hat{v}_2w_{23}+\hat{v}_4w_{34}) & \hat{v}_2w_2+\hat{v}_4w_4 - \lambda\hat{\bar{w}}(\hat{v}_2+\hat{v}_4) \\
R\hat{v}_1(\hat{v}_3w_{13}+\hat{v}_4w_{14}) & R\hat{v}_2(\hat{v}_3w_{23}+\hat{v}_4w_{24}) & R\hat{v}_3(\hat{v}_3w_{33}+\hat{v}_4w_{34}) + \hat{v}_3(\hat{w}_3(1-R) - \lambda\hat{\bar{w}}) & \hat{v}_3\hat{w}_3+\hat{v}_4\hat{w}_4 - \lambda\hat{\bar{w}}(v_3+v_4) \\
(R-m)\hat{v}_1\hat{v}_4w_{14} & R\hat{v}_2\hat{v}_4w_{24}+m\hat{v}_2\hat{v}_3w_{23} & R\hat{v}_3\hat{v}_4w_{34}+m\hat{v}_2\hat{v}_3w_{23} & \hat{v}_4\hat{w}_4 - 2m\hat{d} - \lambda\hat{\bar{w}}\hat{v}_4
\end{vmatrix}$$

The equilibrium identity,

$$\hat{v}_i = \frac{1}{\bar{w}}\left(\hat{v}_i\hat{w}_i(1-m^*) + m^*\sum_{hj}{}' \hat{v}_h\hat{v}_j w_{hj}\ p_{\frac{j}{h}\to i}\right),$$

yields

$$(\bar{w}_1 - \hat{\bar{w}})v_1 = -(\hat{w}_2 - \hat{\bar{w}})\hat{v}_2 = -(\hat{w}_3 - \hat{\bar{w}})\hat{v}_3 = (\hat{w}_4 - \hat{\bar{w}})\hat{v}_4 = m^*\hat{d}.$$

Substituting in the above identities, and defining $\beta = (1-\lambda)\bar{w}$, this gives

$\Pi\bar{w}\ ch(\lambda) =$

$$\begin{vmatrix} md + \beta & -md + \beta & -md + \beta & \beta \\ Rv_1(v_2w_{12} + v_4w_{14}) & Rv_2(v_2w_{22} + v_3w_{23}) & Rv_3(v_2w_{23} + v_4w_{34}) & (v_2 + v_4)\beta \\ & - md + \beta - Rv_2w_2 & & \\ Rv_1(v_3w_{13} + v_4w_{14}) & Rv_2(v_3w_{23} + v_4w_{24}) & Rv_3(v_3w_{33} + v_4w_{34}) & (v_3 + v_4)\beta \\ & & - md + \beta - Rv_3w_3 & \\ (R - m)v_1v_4w_{14} & Rv_2v_4w_{24} + mv_2v_3w_{23} & Rv_3v_4w_{34} + mv_2v_3w_{23} & - md + \beta \end{vmatrix}$$

(superscripts dropped).

At $R = 0$, $\lambda = 1$, we obtain

$$ch(1) = \frac{1}{\hat{v}_1\hat{v}_2\hat{v}_3\hat{v}_4\bar{w}} \begin{vmatrix} m^*d & - m^*d & - m^*d & 0 \\ 0 & - m^*d & 0 & 0 \\ 0 & 0 & - m^*d & 0 \\ - m^*\hat{v}_1\hat{v}_4w_{14} & 0 & m^*\hat{v}_2\hat{v}_3w_{23} & - m^*d \end{vmatrix}$$

$$= \frac{- (m^*d)^4}{\hat{v}_1\hat{v}_2\hat{v}_3\hat{v}_4\bar{w}} \leq 0 .$$

When $\hat{\underline{v}}$ is m^* dependent, that is, when there is an equilibrium marginal fitness load for the four selected haplotypes, then there is linkage disequilibrium, so $d \neq 0$. Therefore $\rho(JD) > 0$, giving this result:

RESULT 3.21:

The V.A.T.P. equilibrium for a recombination modifier is internally unstable, for two selected loci with two alleles, with one of the selected loci tightly linked to a maximally overdominant modifier locus.

This is the same result as for the cases in Feldman and Balkau (1973), extended to multiple modifier alleles and arbitrary selection regime, but restricted to a maximally overdominant modifier locus.

I do not have results for in the general case for what happens to the population after it diverges away from an unstable V.A.T.P. equilibrium. However, we know that each modifier allele is protected by virtue of its maximal overdominance, as long as there is a marginal fitness load in the population. Therefore, I would guess that the population settles on some high complementarity equilibrium comparable to those found in Feldman and Balkau (1973).

From the result of these two stability analyses, it is apparent that the interior stability of a viability-analogous, tensor product equilibrium depends upon the nature of the transformation occurring. This is the first result derived here in which the form of the transformation plays a role.

I.3. AN EXAMPLE OF TRANSFORMATION ACTING ON THE TRANSFORMATION TYPE: MODIFIERS OF SEGREGATION DISTORTION

Previous treatments of modifiers of segregation distortion have considered them to be modifiers of selection parameters (Karlin and McGregor, 1974), therefore coming under direct selection (Feldman and Krakauer, 1976). However, it is clear from the dichotomization of selection and transformation employed here that segregation distortion is actually a form of transformation. It may be due to selection at the gamete level, but as long as it does not affect an individual's fitness, that is, the number of offspring in the next generation to whose genotype that individual contributes, it will be purely a form of transformation, affecting only the content of an individual's reproductive output. It can be seen that there is no intrinsic selection acting on a modifier of segregation distortion since, when it is in linkage equilibrium with the selected distorting locus, the frequencies of its alleles will not change. It can evolve only through hitchhiking. What is unique about segregation distortion is that when a modifier is linked to a distorting locus, it too will be distorted, a form of transformation, which is a situation I have excluded from the analysis up till now.

Here I consider a model where segration distortion is the only transformation acting on the selected and modifier loci, and the modifier locus controls this segregation distortion. It is an extension to multiple alleles of the model of Prout et al. (1973), treated also by Hartl (1975), Thomson and Feldman (1976), and Liberman (1976).

The transformation matrix for segregation distortion takes the form

$$T_{\overline{bk}}^{\overline{aj}\to ai} = \begin{cases} T_{\overline{bk}}^{\overline{ai}\to ai} & \text{for } j=i \\ 0 & \text{for } j\neq i \end{cases}$$

where $T_{\overline{bk}}^{\overline{ai}\to ai}$ is twice the fraction of gametes from genotype $\frac{M_aA_i}{M_bA_k}$ that are of haplotype M_aA_i. Let us use a simpler notation for this,

$$T_{\overline{bj}}^{\overline{ai}} \triangleq T_{\overline{bj}}^{\overline{ai}\to ai} .$$

Again I assume no position effect of the modifier, so

$$T_{\overline{bj}}^{\overline{ai}} = T_{\overline{aj}}^{\overline{bi}} .$$

Moreover,

$$0 \leq T_{\overline{bj}}^{\overline{ai}} \leq 2 \quad \text{and} \quad T_{\overline{bj}}^{\overline{ai}} + T_{\overline{bi}}^{\overline{aj}} = 2 \quad \forall\ a,b,i,j .$$

Segregation distortion is occurring when $T_{\overline{bj}}^{\overline{ai}} \neq 1$.

If there is interference between the segregation distortion and recombination between the modifier and selected loci, then a second segregation distortion matrix, $\tilde{T}$ must be specified.

The recursion is

$$z'_{ai} = \sum_{bk} \left((1-R)z_{ai}z_{bk}T_{\overline{bk}}^{\overline{ai}} + Rz_{ak}z_{bi}\tilde{T}_{\overline{bk}}^{\overline{ai}} \right) \frac{w_{\overline{k}}^{\overline{i}}}{\bar{w}} .$$

VIABILITY-ANALOGOUS, TENSOR PRODUCT EQUILIBRIA

The viability-analogous, tensor-product equilibrium can be described for this case as before, with an interesting result. Suppose that the population is fixed on a modifier yielding T^* and $\tilde{T}^*$ for segregation distortion matrices, and that the population has reached an equilibrium under selection and segregation distortion. Then

$$\hat{v}_i = \hat{v}_i \sum_j \hat{v}_j \frac{w_{\overline{j}}^{\overline{i}}}{\hat{\bar{w}}} \left((1-R)T^{*\overline{i}}_{\overline{j}} + R\tilde{T}^{*\overline{i}}_{\overline{j}} \right) .$$

In the absence of interference, this yields

$$\sum_j \hat{v}_j w_j^i T_j^{*i} = \hat{\bar{w}} \quad \forall\, i \,.$$

Define the values $\Psi_i = \sum_j v_j w_j^i T_j^{*i}$ to be the "marginal transmission values" for the selected alleles. They form a new set of marginal values for each of the alleles which, for those alleles present, must all be equal to the mean fitness at any equilibrium.

The equilibrium marginal fitnesses of the selected alleles are given by

$$\hat{w}_i = \hat{\bar{w}} + \sum_j \hat{v}_j w_j^i \left(1 - T_j^{*i}\right) \,.$$

The marginal fitnesses of the selected alleles will have a variance at equilibrium unless the marginal amount of segregation distortion acting on each of them is zero:

$$\sum_j \hat{v}_j w_j^i \left(T_j^{*i} - 1\right) = 0 \quad \forall\, i \,.$$

We see that at any polymorphism, alleles with a segregation advantage have a fitness disadvantage, and alleles with a fitness advantage have a segregation disadvantage. Any allele have both advantages would be fixed.

Consider now where the modifier is polymorphic, and in linkage equilibrium with the selected loci, so that

$$z_{ai} = x_a \hat{v}_i \,.$$

The recursion is now

$$z'_{ai} = x_a \hat{v}_i \sum_j \hat{v}_j \frac{w_j^i}{\hat{\bar{w}}} \left((1-R)\hat{T}a_j^i + R\hat{\tilde{T}}a_j^i \right) \,,$$

where

$$\hat{T}a\frac{i}{j} = \sum_b x_b T\frac{ai}{bj} \quad \text{and} \quad \tilde{\hat{T}}a\frac{i}{j} = \sum_b x_b \tilde{T}\frac{ai}{bj}$$

are the marginal transformations for each modifier allele M_a. If the marginal transformations are all equal to T^* and $\tilde{T}^*$,

$$\hat{T}a\frac{i}{j} = T^*\frac{i}{j} \quad \text{and} \quad \tilde{\hat{T}}a\frac{i}{j} = \tilde{T}^*\frac{i}{j} \quad \forall\ a,i,j\ ,$$

then the population is at an equilibrium,

$$\hat{z}'_{ai} = \hat{x}_a \hat{v}_i = \hat{z}_{ai}\ .$$

INITIAL INCREASE OF A NEW MODIFIER ALLELE

The recursion on the frequency of a new modifier allele introduced at a polymorphic equilibrium is

$$\underline{\varepsilon}' = \Omega_a D \underline{\varepsilon} = \left((1-R)Y_a + R\tilde{Y}_a \right) D \underline{\varepsilon}\ ,$$

where

$$Y_a \triangleq \text{diag}\left(\sum_{bk} \hat{z}_{bk} \frac{w\frac{i}{k}}{\hat{w}_j} T\frac{ai}{bk} \right) \quad \text{and} \quad \tilde{Y}_a \triangleq \left\| \sum_b \hat{z}_{bi} \frac{w\frac{i}{j}}{\hat{w}_j} \tilde{T}\frac{ai}{bj} \right\| \quad i,j\ ,$$

and D is defined as before.

a. A MODIFIER ALLELE ELIMINATING SEGREGATION DISTORTION

If the new modifier allele eliminates segregation distortion at the selected locus, then the initial increase recursion is identical to that for the Theorem 3.5 :

$$\underline{\varepsilon}' = \left((1-R)I + RQ \right) D\underline{\varepsilon}\ ,$$

where Q is defined as before. The previous result then holds:

RESULT 3.22:

When there is a variance in the equilibrium marginal fitnesses, an allele eliminating segregation distortion will always increase when introduced into the population, whether linked or not to the selected locus.

b. A TIGHTLY LINKED MODIFIER LOCUS

For the case where the new modifier allele has a less extreme effect on the segregation distortion, I will assume that the modifier is tightly linked to the selected locus, for tractability, and will assume that the modifier is monomorphic, because for tight linkage, the viability-analogous, tensor-product equilibrium may not generally be stable, as shown in Thomson and Feldman (1976), and I do not have results for the introduction at other polymorphic equilibria. The recursion on a new modifier is now

$$\underline{\varepsilon}' = \mathrm{diag}\Big(\sum_j \hat{v}_j \frac{\underline{w}^{j}}{\bar{w}} \hat{T}_{a\underline{j}}^{\,i}\Big)\underline{\varepsilon} = \frac{1}{\bar{w}}\,\mathrm{diag}\big(\hat{\Psi}_{ai}\big)\underline{\varepsilon} ,$$

where $\hat{T}_{a\underline{j}}^{\,i}$ are the marginal transformation values for the new modifier allele M_a, and $\hat{\Psi}_{ai}$ are the marginal transmission values for the selected alleles in coupling with the new modifier allele. Notice now that

$$\sum_i \hat{v}_i \hat{\Psi}_{ai} = \sum_{ij} \hat{v}_i \hat{v}_j \underline{w}_j^{\,i} \hat{T}_{a\underline{j}}^{\,i} = \sum_{ij} \hat{v}_i \hat{v}_j \underline{w}_j^{\,i}\Big(\frac{1}{2}\hat{T}_{a\underline{j}}^{\,i} + \frac{1}{2}(2-\hat{T}_{a\underline{i}}^{\,j})\Big) = \bar{\underline{w}} + 0 .$$

Therefore, if

$$\underset{i}{\text{var}}(\hat{\Psi}_{ai}) > 0 \ ,$$

then for some i ,

$$\frac{1}{\bar{w}} \hat{\Psi}_{ai} > 1 \ ,$$

so haplotype $M_a A_i$ increases when introduced. Therefore:

RESULT 3.23:

Unless $\hat{\Psi}_{ai} = \bar{w}$ for all i, the new modifier allele will be able to increase in the population when introduced.

This means that a new modifier making any change in the marginal transmission values of the selected alleles (which at equilibrium all equal the mean fitness) will allow the modifier to increase. The new modifier cannot be exluded, at least at a geometric rate. This result is that obtained by Liberman (1976).

What produces this result is that the new modifier allele always becomes associated with the selected allele whose segregation ratio it improves on the average. Therefore, a new modifier that reduces the overall amounts of segregation distortion increases by associating with fitter alleles, which have a segregation disadvantage. A modifier allele that raises the overall rates of segregation distortion increases by associating with alleles having a segregation advantage, which are less fit.

Because segregation distortion acts on the modifier locus itself, which constitutes a form of transformation acting on the transformation type, the evolutionary behavior of the modifier is completely changed. In the absence of segregation distortion, the previous results showed

that the induced selection on a new modifier allele is at most algebraic when it is introduced at an equilibrium with no variance in the marginal fitnesses of the selected haplotypes. For a modifier of segregation distortion, however, the equilibrium variance in the marginal fitnesses of the selected alleles is irrelevant. All that is relevant is the change in the marginal transmission values of the selected alleles.

Recent work by Eshel (personal communication) has shown that for unlinked modifiers of segregation distortion, when modifier alleles causing segregation distortion are introduced to a population at equilibrium without segregation distortion, they cannot increase. Though I obtain no analytical results here for the general case of unlinked modifiers, it is interesting to note that, when there is no interference between recombination with the modifier and the amount of segregation distortion of the selected locus, then at $R = \frac{1}{2}$

$$\Omega_a = \frac{1}{2}(Y_a + \tilde{Y}_a)$$

is stochastic, since

$$\underline{e}^T\Omega_a = \sum_{ibj} \hat{z}_{bj} \frac{w_j^i}{\hat{w}_j} \frac{1}{2}(T_{bj}^{ai} + T_{bi}^{aj}) = \frac{\hat{w}_j}{\hat{w}_j} = 1 ,$$

because

$$\frac{1}{2}(T_{bj}^{ai} + T_{bi}^{aj}) = 1 \qquad \forall\ a,b,i,j .$$

It may be when the matrix is stochastic that decreased segregation distortion evolves. However, if there is interference, then Ω_a will not be stochastic, and it is unknown what outcome will result in this case.

Holsinger (personal communication) has obtained results for modifiers of selfing rates in a model for plants that are suggestively reminiscent of the results for modifiers of segregation distortion. In the model with mixed selfing and random mating, selfed plants still

contribute to the pollen pool. Holsinger has pointed out that the situation where selfing plants still contribute to the pollen pool constitutes a form of "transmission distortion". There are some ranges on selection values, recombination values, and selfing rates where a new modifier making any change in the selfing rate will increase when introduced, a result just like that for segregation distortion modifiers.

Further analogy between the behavior of this model and that of segregation distortion models is seen in cases tested numerically where the fitnesses of the two selected homozygotes are different. When a selfing-rate reducing modifier allele is introduced, it increases in association with the allele having the less fit homozygote. When a selfing-rate increasing modifier allele is introduced, it increases in association with the allele having the fitter homozygote. In the former case, outcrossing appears with the allele having most to gain by being heterozygous; in the latter case, selfing appears with the allele having the least to lose by being homozygous. Thus, the new modifier allele has a "choice" like the modifier of segregation distortion associating with the fitter alleles or the alleles with segregation advantage. The behavior of this system may therefore be fundamentally analogous to that of systems with segregation distortion.

Models of modifiers of other transformation processes such as mutation or recombination should also be explored when there is segregation distortion occurring. Thomson and Feldman (1974) have examined one such model, a modifier of recombination between a selected locus undergoing segregation distortion and another locus modifying that distortion. In some cases, it is found that a new recombination

modifier allele causing any change in the amount of recombination will increase when introduced.

These few example suggest the following conjecture:

CONJECTURE 3.24: A PRINCIPLE FOR MODIFIERS UNDER TRANSMISSION DISTORTION:

Whenever the exterior stability of a selection-transformation equilibrium is unstable to the introduction of any new modifier allele that causes any change in transformation, then some form of transmission distortion must be occurring for the modifier locus.

II. MIGRATION MODIFIERS

In this section I analyze the evolution of a modifier gene in a diploid organism that controls a transformation outside of the genotype: the probabilities of individuals migrating between different demes. In the following models, a locus that is under selection will also be included and the selection regime may differ between different demes. These models differs from the previous ones in that in addition to the selected genotype, location is now part of the selected type, and mating is not panmictic over the whole population, but restricted to being within demes. The only transformation that will be occurring is

change in location; the selected locus will be transmitted faithfully. In the models dealt with here, mating will always be within a deme. The life cycle consists of several stages: migration, selection, mating and reproduction. These model will generalize to multiple demes and multiple alleles the models of Balkau and Feldman (1973), Karlin and McGregor (1974), Teague (1977), and Asmussen (1983). In addition, they include mixtures of haploid and diploid determination of both migration and selection.

II.1. DERIVATION OF THE MODELS

In developing the models we must define the following:

n_f is the initial size of deme f.

n_f^s is the size of deme f after selection.

n_f^m is the size of deme f after migration.

n_f^r is the size of deme f after recruitment.

$g_{e\frac{ai}{bj}}$ is the frequency of diploid genotype $\frac{M_aA_i}{M_bA_j}$ in deme e.
(If $ai \neq bj$, then actual frequency is $2g_{e\frac{ai}{bj}}$).
Note that $\sum_{aibj} g_{e\frac{ai}{bj}} = 1 \quad \forall\, e$.

$g_{e\frac{ai}{bj}}$ superscripted by s , m , or x is the frequency of the genotype after selection, migration, or mating, respectively.

w_{ej}^{i} is the fitness of genotype $\frac{A_i}{A_j}$ in deme e .

How each process in the life cycle -- selection, migration, and mating -- will change the values of n_e and $g_{e\frac{ai}{bj}}$ are derived as follows:

1. SELECTION:

$$g^{s}{}_{e\frac{ai}{bj}} = g_{e\frac{ai}{bj}} \frac{w_{ej}^{i}}{\bar{w}_e} ,$$

where the average fitness of the individuals in deme e is

$$\bar{w}_e = \sum_{aibj} g_{e\frac{ai}{bj}} w_{ej}^{i} .$$

The only role of n_e is this model is to determine the relative contribution of each deme to the migrant pool. If selection does not affect the size of a deme but acts only to determine <u>which</u> genotypes survive, this is <u>soft selection</u> and can be modeled by assuming n_e after selection is a fixed property of each deme. If selection acts on each individual independently of the others in its deme, this is <u>hard selection</u>, and the contribution of the deme to the migrant pool will be scaled by the mean fitness of the individuals in the deme. Thus:

$$n_e^{s} = \begin{cases} n_e \bar{w}_e & \text{hard selection} \\ n_e & \text{soft selection} \end{cases} .$$

The models of Balkau and Feldman (1973), Karlin and McGregor (1974) and Asmussen (1983) have hard selection, while the model of Teague (1977) has soft selection.

For organisms with an independent haploid phase in the life cycle, the haploids can come under selection. This situation will be described in detail later, in the model of haploid migration.

2. MIGRATION:

Two cases of migration will be distinguished, diploid migration, and a "sea urchin model" of haploid migration.

1) DIPLOID MIGRATION

When the diploid individuals move from one deme to another, after migration,

$$g^{m}_{e\frac{ai}{bj}} = \frac{1}{n^{m}_{e}} \sum_{f} g_{f\frac{ai}{bj}} n_f \; T^{a}_{b}f \to e \ ,$$

where $T^{a}_{b}f \to e$ is the probability that an individual of modifier genotype $\frac{M_a}{M_b}$ will end up in deme e given it is in deme f, and

$$n^{m}_{e} = \sum_{aibjf} g_{f\frac{ai}{bj}} n_f \; T^{a}_{b}f \to e \ ,$$

the size of the migrant pool plus remaining residents in deme e after migration.

2) HAPLOID MIGRATION

In a "sea urchin" model of haploid migration, it is the gametes

that disperse and form pools in each new deme which will unite to form the new diploids.

Define

$$z_{eai}$$

to be the frequency of haplotype M_aA_i in deme e.

Then after dispersal,

$$z^{m}_{eai} = \frac{1}{n^{m}_{e}} \sum_{bjf} \left(g_{f\frac{ai}{bj}} (1 - R) + g_{f\frac{ai}{bi}} R \right) n_f \, T^{a}_{\frac{}{b}} f \to e \quad .$$

If the dispersal depends only on the haplotype's own modifier allele, then

$$T^{a}_{\frac{}{b}} f \to e = T^{a}_{\frac{}{c}} f \to e \quad \forall \quad b,c \; ; \quad \text{possibly}$$

$$T^{a}_{\frac{}{b}} f \to e \neq T^{b}_{\frac{}{a}} f \to e \; .$$

If the dispersal depends on some combination of haplotype and parental modifier genotypes, then possibly

$$T^{a}_{\frac{}{b}} f \to e \neq T^{b}_{\frac{}{a}} f \to e \quad \text{and} \quad T^{a}_{\frac{}{b}} f \to e \neq T^{a}_{\frac{}{c}} f \to e \; .$$

RECRUITMENT

After migration, "recruitment" will occur, where the migrants and residents become established in the deme. As described in Chapter 2, if the deme size after recruitment is proportional to the number of individuals arriving through migration and those remaining, this will be called "hard recruitment", and if the size of the population after recruitment is a constant property of the deme, this will be called "soft recruitment". Thus

$$n^{r}_{e} = \begin{cases} n^{m}_{e} & \text{hard recruitment} \\ n_e & \text{soft recruitment} \end{cases} .$$

Soft recruitment would be expected for organisms such as intertidal barnacles, where high larval densities saturate bare sections of rock with new recruits.

In the case of hard recruitment and hard selection, the deme size itself can evolve as well as the gene frequencies in the population.

Some models of migration, for example those of Motro (1982), consider selective forces acting during the process of migration itself. Within the formal framework developed here, where selection is a function only of type and not its history of transformation, the fact of being a migrant must be included as a part of ones type. Motro's models involve the extra steps of selection on migrants, then erasure of the migrant's history once it is established in its new deme. The models here will not include these extra steps.

3. REPRODUCTION:

In the diploid migration model, diploids will mate randomly and produce offspring through segregation and syngamy. For the haploid migration model, the haplotypes in the pools in each deme will undergo syngamy randomly with the respect to the modifier alleles, but allowing non-random union with respect to selected haplotype. The only reproductive transformation allowed will be recombination between the modifier and selected loci.

After syngamy, for the sexual diploid model we have

$$g^{x}_{e\frac{ai}{bj}} = \left((1 - R)\sum_{ck} g_{e\frac{ai}{ck}} + R\sum_{ck} g_{e\frac{ak}{ci}}\right)\left((1 - R)\sum_{ck} g_{e\frac{bj}{ck}} + R\sum_{ck} g_{e\frac{bk}{cj}}\right)$$

Define the haplotype frequencies $z_{eai} \triangleq \Sigma_{bj}\, g_{e\frac{ai}{bj}}$. Then

$$z^{x}_{eai} = (1 - R)\sum_{ck} g_{e\frac{ai}{ck}} + R\sum_{ck} g_{e\frac{ak}{ci}}, \quad \text{so}$$

$$g^{x}_{e\frac{ai}{bj}} = z^{x}_{eai}\, z^{x}_{ebj} .$$

Thus Hardy-Weinberg proportions obtain.

Define the values $f_{e\frac{i}{j}}$ to incorporate any non-random union of gametes, yielding for the haploid migration model:

$$g^{x}_{e\frac{ai}{bj}} = z_{eai}\, z_{ebj}\frac{f_{e\frac{i}{j}}}{\bar{f}_{e}} ,$$

$$\text{where } \bar{f}_{e} = \sum_{aibj} z_{eai}\, z_{ebj}\, f_{e\frac{i}{j}} .$$

LIFE CYCLES COMPOSED OF THESE PROCESSES:

These phases of the life cycle can be composed in two different orders: selection, migration, reproduction, or migration, selection, reproduction. These two sequences have very different analytical

properties, The second is generally intractable within the methods I have used thus far, and will not be presented here. Previous models of migration modifiers (Balkau and Feldman, 1973; Karlin and McGregor, 1974; Teague, 1976; Asmussen, 1983) all analyze the first sequence order.

I will consider the following life cycles:

1) "Adult Dispersal": diploid selection, diploid migration, random mating, Mendelian reproduction.
2) "Gamete Dispersal": diploid selection, gamete production, gamete migration, syngamy.

In each case, the censusing occurs right after recruitment.

1) Adult Dispersal:

Random mating and the absence of fertility selection allows the recursions to be written in terms of the haplotype frequencies:

$$z'_{eai} = \frac{1}{n_e^m} \sum_{bjf} n_f^s \frac{w_{fj}^{i}}{\bar{w}_f} T_{bf}^{a} + e\left((1-R)z_{fai}z_{fbj} + Rz_{faj}z_{fbi}\right), \quad (3.25)$$

$$n'_e = \begin{cases} n_e^m & \text{hard recruitment} \\ n_e & \text{soft recruitment,} \end{cases}$$

$$\text{where } n_e^m = \sum_{chdkf} z_{fch}\, z_{fdk} \frac{w_{fk}^{h}}{\bar{w}_f} n_f^s T_{df}^{c} + e,$$

$$\bar{w}_f = \sum_{abjk} z_{vaj} z_{fbk} w_{fj}^{i},$$

and

$$n_f^s = \begin{cases} n_f \bar{w}_f & \text{hard selection} \\ \text{constant} & \text{soft selection.} \end{cases}$$

2) Gamete Dispersal, Sea Urchin Model:

The recursion is the same as for the Adult Dispersal Model, except that $T^{a}_{b}{}_{f \to e}$ is allowed the asymmetries discussed earlier. Moreover, gamete selection or non-random union may enter without altering the form of the recursion.

Consider a life cycle consisting of:

1) gamete selection phase 1,
2) syngamy, possibly non-random with respect to the selected loci,
3) diploid selection,
4) recombination and Mendelian segregation,
5) gamete selection phase 2, and
6) migration.

The fitnesses for each selection phase are as follows:

$s^{(1)}_{fi}$ = fitness of gamete haplotype A_i in deme f at phase 1.

$\Phi_{f\frac{i}{j}}$ = the scalar biasing the frequency of new zygotes according to selection-type in deme f, due to non-random syngamy.

$s_{f\frac{i}{j}}$ = fitness of diploid selected genotype $\frac{A_i}{A_j}$ in deme f.

$s^{(2)}_{fi}$ = fitness of gamete haplotype M_i in deme f at phase 2, after meiosis.

The recursion is:

$$z'_{eai} = \frac{1}{n^{m}_{e}} \sum_{bjf} n^{s}_{f} \frac{s^{(2)}_{fi} s^{(1)}_{fi} s^{(1)}_{fj} \Phi_{f\frac{i}{j}} s_{f\frac{i}{j}}}{\bar{s}_{f}} \left(z_{fai} z_{fbj}(1-R) + z_{faj} z_{fbi} R \right) T^{a}_{b}{}_{f \to e}$$

where $\bar{s}_f$ is the appropriate normalizer.

Define the lumped fitness values

$$w_{f\underline{j}}^{\underline{i}} \triangleq s_{fi}^{(2)} s_{fi}^{(1)} s_{fj}^{(1)} \Phi_{f\underline{j}}^{\underline{i}} s_{f\underline{j}}^{\underline{i}} .$$

These need not be symmetric, allowing $w_{f\underline{j}}^{\underline{i}} \neq w_{f\underline{i}}^{\underline{j}}$.

The recursion becomes

$$z'_{eai} = \frac{1}{n_e^m} \sum_{fbj} \left(z_{fai} z_{fbj} (1-R) + z_{faj} z_{fbi} R \right) \frac{w_{f\underline{j}}^{\underline{i}}}{\bar{w}_f} n_f^s \, T_{\underline{b}}^{\underline{a}} f \to e ,$$

where $\bar{w}_f = \bar{s}_f$, which again is of the same form as (3.25), with the possible asymmetries

$$w_{f\underline{j}}^{\underline{i}} \neq w_{f\underline{j}}^{\underline{i}} \quad \text{and} \quad T_{\underline{b}}^{\underline{a}} f \to e \neq T_{\underline{a}}^{\underline{b}} f \to e .$$

The haploid model of Balkau and Feldman (1973) is a special case of this where

$$s_{fi}^{(1)} = \Phi_{f\underline{j}}^{\underline{i}} = s_{f\underline{j}}^{\underline{i}} = 1 \quad \forall \quad f,i,j \text{ and}$$

$$T_{\underline{b}}^{\underline{a}} f \to e \triangleq T_a f \to e \quad \forall \quad a,b,f,e .$$

In each of these cases, the recursions can be defined in terms of haplotypes because there is no fertility selection or non-random mating occuring at the level of diploid pairs, so the segregation-syngamy transformation decomposes.

The results for these models parallel the results for modifiers of intragenomic transformation. Viability-analogous, tensor product modifier polymorphisms can exist (Feldman and Krakauer, 1976), because

migration still enters as a linear transformation. "Tensor product" in this case means that the modifier allele frequencies are the same among the selected haplotypes, and also among the demes, because the deme is also a part of an individual's type.

The initial increase behavior of a new migration modifying allele also parallels the results for modifiers of intra-genomic transformation.

II.2. VIABILITY-ANALOGOUS, TENSOR PRODUCT EQUILIBRIA

It will be shown here how tensor product frequencies can be equilibria for the two life cycles.

Define x_a to be the frequency of modifier allele M_a, and v_{ei} to be the frequency of selected haplotype A_i in deme e. At a tensor product value of frequencies, the frequency of haplotype M_aA_i in deme e will be

$$z_{eai} = x_a v_{ei} ,$$

or in vector form

$$\underline{z} = \underline{x} \otimes \underline{v} ,$$

where $\underline{x}$ is the vector of modifier allele frequencies, and $\underline{v}$ is the vector of the selected haplotype frequencies in the demes. The frequencies of the selected haplotypes may differ between different demes.

Substitution in recursion (3.25) yields

$$z'_{eai} = \frac{1}{n_e m} x_a \sum_f n_f s v_{fi} \frac{w_{fi}}{\bar{w}_f} T_{af \to e} ,$$

where

$$n_e^m = \sum_{fa} n_f^s x_a T_{af \to e} ,$$

$$T_{af \to e} \overset{\Delta}{=} \sum_b x_b T^a_{bf \to e}$$

are the marginal migration probabilities for modifier alleles M_a, and

$$w_{fi} \overset{\Delta}{=} \sum_j v_{fj} w_{f\frac{i}{j}}$$

are the marginal fitnesses of selected haplotypes A_i in deme e.

Suppose that the population would be at an equilibrium, $\hat{\underline{v}}$, when fixed on a modifier allele yielding migration matrix T^*. Thus

$$\hat{v}_{ei} = \frac{1}{\hat{n}_e^m} \sum_f \hat{n}_f^s \hat{v}_{fi} \frac{\hat{w}_{fi}}{\hat{\bar{w}}_f} T^*_{f \to e} .$$

Then a modifier polymorphism $\underline{z} = \hat{\underline{x}} \otimes \hat{\underline{v}}$ will be an equilibrium if the modifier allele frequencies $\hat{\underline{x}}$ are such that

$$\hat{T}_{af \to e} = T^*_{f \to e}$$

for each modifier allele M_a.

II.3. BALANCED MIXTURE MODIFIER POLYMORPHISMS

In diploids, the only situation in which general conditions for "balanced mixture" modifier polymorphisms can be obtained are where the genotypic fitnesses are equal, in addition to there being no fitness load at equilbrium. In this case, (3.25) at equilibrium yields

$$\hat{\underline{z}}_a = T_a \hat{\underline{z}}_a ,$$

where

$$\underline{z}_a = \begin{pmatrix} z_{i_1 a i_2} \\ \vdots \end{pmatrix} ,$$

$$T_a = \| \sum_b \hat{x}_b \, T^a_{bj \to i} \|_{i,j} \text{ , and } x_b = \sum_{fj} z_{fbj} \text{ .}$$

The situation of interest is where frequency dependent selection would yield a globally stable equilibrium $\hat{\underline{v}}$ of selected haplotype frequencies among the demes in the absence of a modifier polymorphism. The result, discussed in Section 3.(2) is that the normalized forms of the eigenvectors $\hat{\underline{z}}_a$ of the marginal migration matrices of each modifier allele must comprise a convex hull containing $\hat{\underline{v}}$ for the equilibrium to exist. However, there are added constraints. Both T_a and $\hat{\underline{v}}$ depend on the frequency of the modifier alleles, so whether the hull of T_a will be sufficient to include the equilibrium is not readily known.

II.4. EVOLUTION OF THE MODIFIER LOCUS

In this section, the initial increase behavior of a new modifier allele under recursion (3.25), which applies to both the "Adult Dispersal" and "Haploid Dispersal" models. Each of the results derived for modifiers of intragenomic transformation will be shown to hold for modifiers of migration.

THE FITNESS LOAD

The concept of a fitness load in the case of subdivided populations we must consider not only the maximally fit genotype but also the maximally "fit" deme, that is, the deme with the largest bias in contributing to the next generation. Consider a population at equilibrium in the absence of migration. We obtain

$$\hat{v}_{ei} = \frac{1}{n_e^m} \sum_j \hat{v}_{ei} \hat{v}_{ej} \frac{w_{ej}}{\bar{\hat{w}}_e} \hat{n}_e^s ,$$

and

$$\hat{\hat{n}}_e = \hat{n}_e .$$

This gives

$$\frac{\hat{n}_e^s \hat{w}_{ei}}{\hat{n}_e^m \bar{\hat{w}}_e} = 1 \text{ for all } e , i .$$

The fitness load will be defined as

$$L \triangleq \max_{ei} \left(\frac{n_e^s w_{ei}}{n_e^m \bar{w}_e} \right) - 1 .$$

In the absence of migration, then, $L = 0$. If migration is occurring, then at an equilibrium where the maximum probability of migration for each individual in each deme is α , the fitness load will be bounded above by

$$L \leq \frac{\alpha}{1-\alpha} .$$

THEOREM 3.25:

If there is any variance at equilibrium in $\frac{n_e^s \hat{w}_{ei}}{n_e^m \bar{\hat{w}}_e}$ (over e and i), which requires migration be occurring, then the equilibrium fitness load will be greater than zero, that is, there will exist e , and i such that

$$\frac{n_e^s \hat{w}_{ei}}{n_e^m \bar{\hat{w}}_e} > 1.$$

Proof.

Suppose to the contrary that

$$\frac{n_e^s w_{ei}}{n_e^m \bar{w}_e} < 1 \quad \forall\, e,i \quad (\text{ ^ 's dropped}).$$

Since

$$\hat{\bar{w}}_e = \sum_i \hat{v}_{ei}\hat{w}_{ei} \quad \text{and} \quad \sum_i \hat{v}_{ei} = 1,$$

we know for each e, there exists an i such that $\hat{w}_{ei} \geq \hat{\bar{w}}_e$.

Therefore,

$$n_e^s \leq n_e^m \quad \forall e.$$

But

$$\sum_e n_e^m = \sum_{\substack{cdhk \\ fe}} z_{fch} z_{fdk} \frac{w_{f\bar{k}}^{h}}{\bar{w}_f} n_f^s T_{\bar{d}}^{c} \; f \to e = \sum_f n_f^s .$$

So this would yield $n_e^s = n_e^m \;\forall e$. But this requires $\frac{\hat{w}_{ei}}{\hat{\bar{w}}_e} \leq 1 \;\forall e,i$,

thus

$$\hat{w}_{ei} = \hat{\bar{w}}_e \quad \forall e,i,$$

giving finally,

$$\frac{n_e^s w_{ei}}{n_e^m \hat{\bar{w}}_e} = 1 \quad \forall e,i,$$

contrary to there being some variance in $\frac{n_e^s \hat{w}_{ei}}{n_e^m \hat{\bar{w}}_e}$.

We see here that there are two possible sources for the equilibrium fitness load, one due to variance in $(\frac{n_e^s}{n_e^m})$, and the other due to variance in $(\frac{\hat{w}_{ei}}{\hat{\bar{w}}_e})$.

In the case of hard selection and hard recruitment,

$$\hat{n}_e^s = n_e \bar{\hat{w}}_e \quad \text{and} \quad \hat{n}_e = \hat{n}_e^m ,$$

hence

$$L = \max_{e,i}(\hat{w}_{ei}) .$$

So the marginal fitnesses of the selected haplotypes must vary between haplotypes or between demes.

When there is soft selection or soft recruitment, then even when the selective regimes on the selected locus are identical in each deme, it is possible that the migration flux alone can induce a fitness load. In this case,

$$L = \max_e \left(\frac{n_e^s}{n_e^m}\right) ,$$

and

$$\hat{n}_e^m = \sum_f \bar{T}_{f \to e} n_f^s ,$$

where

$$\bar{T}_{f \to e} = \sum_{bc} \hat{x}_b \hat{x}_c T^b_{cf \to e} .$$

In vector form this is

$$\underline{\hat{n}}^m = \bar{T} \underline{\hat{n}}^s .$$

For the fitness load to be zero, $\underline{n}^m = \underline{n}^s$ must be a leading eigenvector of $\bar{T}$. Yet under soft selection or soft recruitment, $\underline{n}^s$ or $\underline{n}^m$ will be fixed properties independent of the migration distribution, and so they will not in general be eigenvectors of the migration matrix, and the fitness load will be positive.

THE INITIAL INCREASE BEHAVIOR OF A NEWLY INTRODUCED MODIFIER ALLELE

Suppose the population is at an equilibrium $\hat{\underline{z}}$ and a new modifier allele M_a is introduced.

The recursion on the frequency of haplotypes bearing M_a is

$$\varepsilon'_{ei} = \frac{1}{n_e^m} \sum_{bjf} \left[\varepsilon_{fi}\hat{z}_{fbj}(1-R) + \varepsilon_{fj}\hat{z}_{fbi}R\right] \frac{w_{fj}^{i}}{\bar{w}_f} n_f^s T_{bf}^a + e \qquad (3.26)$$

RESULT 3.26:

A VALUE CAN BE DERIVED FOR AN UPPER BOUND ON THE AMOUNT OF MIGRATION A NEWLY INTRODUCED MODIFIER ALLELE ALLOWS THAT GUARANTEES IT WILL INCREASE WHEN INTRODUCED INTO A POPULATION WITH A FITNESS LOAD AT EQUILIBRIUM.

DERIVATION:

Define

$$\tilde{m}_e = 1 - \min_b T_{be}^a + e \ .$$

This is the maximum probability of migrating among any of the individuals in deme e bearing M_a .

Then

$$\varepsilon'_{ei} \geq (1-\tilde{m}_e)(1-R) \frac{n_e^s \hat{w}_{ei}}{n_e^m \bar{w}_e} \varepsilon_{ei} \ .$$

Thus, if there exists e and i such that

$$\tilde{m}_e < 1 - \left((1-R)\frac{n_e^s \hat{w}_{ei}}{n_e^m \bar{w}_e}\right)^{-1} ,$$

the haplotype M_aS_i will increase in deme e .

We know that if there is any variance in either $\frac{n_e^s}{n_e^m}$ or $\frac{w_{ei}}{\bar{w}_e}$ then there will be some e and i such that

$$\frac{n_e^s w_{ei}}{n_e^m \bar{w}_e} > 1 .$$

Define

$$\hat{m} \triangleq 1 - \left(\max_{ei} \frac{n_e^s \hat{w}_{ei}}{n_e^m \hat{\bar{w}}_e} \right)^{-1} = 1 - \frac{1}{1+L} .$$

Therefore

$$\frac{\varepsilon'_{ei}}{\varepsilon_{ei}} \geq (1-\tilde{m}_e) \frac{(1-R)}{1-\hat{m}} .$$

If $R < \hat{m}$, and if $0 \leq \tilde{m}_e < \frac{\hat{m}-R}{1-R}$ for some e, then

$$\frac{\varepsilon'_{ei}}{\varepsilon_{ei}} > 1 ,$$

so it is guaranteed that M_a increases.

RESULT 3.27:

A MODIFIER ALLELE WHICH STOPS ALL MIGRATION WILL ALWAYS INCREASE WHEN INTRODUCED TO A POPULATION WITH AN EQUILIBRIUM FITNESS LOAD, FOR ANY LINKAGE TO THE SELECTED LOCUS.

The recursion on a newly introduced modifier allele M_a which stops all migration in its bearers is

$$\varepsilon'_{ei} = \frac{1}{n_e^m} \sum_{bj} \left((1-R)\, \varepsilon_{ei} \hat{z}_{ebj} + R\, \varepsilon_{ej} \hat{z}_{ebi} \right) \frac{w_{ej}^i n_e^s}{\hat{\bar{w}}_e}$$

$$= (1-R) \frac{n_e^s \hat{w}_{ei}}{n_e^m \hat{\bar{w}}_e} \varepsilon_{ei} + R \frac{n_e^s \hat{v}_{ei}}{n_e^m \hat{\bar{w}}_e} \sum_j w_{ej}^i \varepsilon_{ej} ,$$

or in vector form

$$\underline{\varepsilon}'_e = \left[(1-R)I + RQ_e \right] D_e \underline{\varepsilon}_e \quad , \quad \text{where} \tag{3.27}$$

$$Q_e \triangleq \text{diag}(\hat{\underline{v}}_e)\, W_e\, \text{diag}\left(\frac{1}{\hat{w}_{ei}}\right) ,$$

$$D_e \triangleq \text{diag}\left(\frac{n_e^s \hat{w}_{ei}}{n_e^m \bar{\hat{w}}_e}\right) \quad , \text{ and } W_e \triangleq \| w_{ej}^{i} \|_{i,j} .$$

This recursion has the same form as that for a modifiers stopping intragenomic transformation in Theorem 3.5. When applying the proof of Theorem 3.5 , the appropriate normalized eigenvector of Q is

$$\mu_e D_e \hat{\underline{v}}_e \quad , \text{ where } \mu_e = \frac{n_e^m}{n_e^s} .$$

This is seen since

$$\underline{e}^T \mu_e D_e \underline{v}_e = 1 ,$$

and

$$\mu_e (Q_e D_e \hat{\underline{v}}_e)_i = \mu_e \sum_j \frac{\hat{v}_{ei} w_{ej}^{i} n_e^s \hat{v}_{ej}}{\bar{\hat{w}}_e n_e^m} = \mu_e \hat{v}_{ei} \frac{\hat{w}_{ei} n_e^s}{\bar{\hat{w}}_e n_e^m} = \mu_e (D_e \hat{\underline{v}}_e)_i .$$

Thus

$$\rho\left(\left[(1-R)I + RQ_e \right] D_e \right) \geq \mu_e \sum_i \hat{v}_{ei} \left(\frac{n_e^s \hat{w}_{ei}}{n_e^m \bar{\hat{w}}_e} \right)^2 = \frac{n_e^s}{n_e^m} \left(1 + \text{var}\left(\frac{\hat{w}_{ei}}{\bar{\hat{w}}_e} \right) \right) .$$

The inequality depends on the value $\dfrac{n_e^s}{n_e^m}$.

As was shown before, if migration has induced an overall variance in

$$\frac{n_e^s \hat{w}_{ei}}{n_e^m \bar{\hat{w}}_e} ,$$

then either

1) there is some deme e where $n_e^s > n_e^m$, or

2) $n_e^s = n_e^m$ $\forall e$, and then in some deme e, $\mathrm{var}(\frac{\hat{w}_{ei}}{\bar{w}_e}) > 0$.

There is always some deme, therefore, in which the migration stopping allele can increase.

When there is variance in the marginal fitnesses of the selected alleles within in deme, then the selection on the modifier is always non-increasing with looser linkage, as in the case of modifiers of intragenomic transformation, since Karlin (1982) Theorem 5.2 can again be applied to (3.27). If Q is irreducible, then the selection on the modifier strictly decreases with looser linkage to the selected locus.

THE EXTERIOR STABILITY OF VIABILITY-ANALOGOUS, TENSOR PRODUCT EQUILIBRIA

Let the population be at a viability-analogous, tensor product equilibrium

$$\hat{\underline{z}} = \hat{\underline{x}} \otimes \hat{\underline{v}} ,$$

with marginal migration probabilities

$$T^*_{f \to e} = \sum_c \hat{x}_c T^b_{\underline{c}f \to e} \text{ for all modifier alleles } M_b .$$

From (3.25), the recursion on a new modifier allele M_a introduced to the population is

$$\varepsilon'_{ei} = \frac{1}{\hat{n}_e^m} \sum_{fj} \hat{n}_f^s \frac{w^i_{\underline{fj}}}{\hat{\bar{w}}_f} \left((1-R)\varepsilon_{fi} \hat{v}_{fj} + R\varepsilon_{fj} \hat{v}_{fi} \right) T_{af \to e} , \qquad (3.28)$$

where

$$T_{af \to e} \triangleq \sum_b \hat{x}_b T^a_{\underline{b}f \to e}$$

are the marginal migration probabilities determined by the new modifier allele.

Again I can analyze only the case of tight linkage. With $R = 0$, (3.28) is

$$\varepsilon'_{ei} = \frac{1}{\hat{n}^m_e} \sum_f \hat{n}^s_f \frac{\hat{w}_{fi}}{\hat{\bar{w}}_f} T_{af \to e} \varepsilon_{fi} ,$$

or in vector form, letting i and j index the demes now, and h index the selected haplotypes,

$$\underline{\varepsilon}'_h = D_1 T_a D_2 \underline{\varepsilon}_h ,$$

where

$$D_1 \triangleq \text{diag}\left(\frac{1}{\hat{n}^m_i}\right) , \quad T_a \triangleq \| T_{aj \to i} \|_{i,j} , \text{ and } \quad D_2 \triangleq \text{diag}\left(\frac{\hat{n}^s_i \hat{w}_{ih}}{\hat{\bar{w}}_i}\right) .$$

This is a slightly different form from the previous cases for the matrix on the initial increase of the new modifier, but using the general eigenvalue property that

$$\rho(D_1 T_a D_2) = \rho(T_a D_1 D_2) ,$$

we see that we need to know

$$\rho\left(T_a \text{diag}\left(\frac{\hat{n}^s_i \hat{w}_{ih}}{\hat{n}^m_i \hat{\bar{w}}_i}\right)\right) .$$

From the equilibrium identity on the V.A.T.P. equilibrium,

$$\underline{\hat{v}}_h = \text{diag}\left(\frac{1}{\hat{n}^m_i}\right) T^* \text{diag}\left(\frac{\hat{n}^s_i \hat{w}_{ih}}{\hat{\bar{w}}_i}\right) \underline{\hat{v}}_h ,$$

where

$$T^* \triangleq \| T^*_{j \to i} \|_{i,j} .$$

Therefore, we know

$$\rho\left(T^* D_1 D_2\right) = 1 .$$

This yields the following:

RESULT 3.28:

1) The new modifier allele can change frequency at a geometric rate, that is, $\rho(T_a D_1 D_2) \neq 1$, only if there is an equilibrium fitness load in the population, so that $D_1 D_2 \neq I$.
2) The spectral radius for the new modifier allele depends only on how its marginal migration matrix T_a is related to the equilibrium marginal migration matrix T^* . The results of Theorem 3.13 for linear variation, and of Theorem 3.2b for affine variation among memoriless distributions therefore apply directly.

(2) A MODEL FOR SELECTION ON SEXUAL REPRODUCTION

The evolution of sexual reproduction is a long standing topic of evolutionary investigation. Although the effect of sex on genetic variation has been the major reason forwarded for the evolution of sex, no modifier models have been analyzed to my knowledge that include genetic variation both for selected traits and for the sexual reproduction itself. In the following model, sexual reproduction will be treated as a form of transformation process under genetic control. The organsisms modeled here will have a life cycle like Chlamydomonas, which reproduce clonally as haploids or can fuse to make diploids, which undergo meiosis, recreating the haploid phase. In this model, mitotic replications between times of diploidy will be lumped together,

requiring the assumptions that the population changes phase synchronously, and that the number of mitotic divisions has no effect.

Let z_{ai} represent the frequency of haploids with selected haplotype A_i and modfier allele M_a , M_aA_i. The life cycle will consist of the following:

1) Individual selection biases the frequencies of the haploids by the scalar s_i.
2) With probability $1-m_a$ the haploid will reproduce clonally, without transformation, and with probability m_a it will enter a pair-mating pool.
3) In this pool, it pairs randomly with another haploid, M_bS_k.
4) The fitness of the diploid genotype $\frac{A_i}{A_j}$ is f_{ik} .
5) The diploid then yields haploid progeny through a reproductive transformation T , not affected by the modifier. This reproductive transformation would include processes affecting the selected haplotypes during the diploid phase, such as recombination and gene conversion. Moreover, if recombination occurs between the modifier locus and the selected haplotype, then another transformation $\tilde{T}$ is specified to account for any interfence of this with the reproductive transformation.

This yields the following recursion for the population:

$$z'_{ai} = \frac{1}{\bar{w}}\left[(1-m_a)z_{ai}s_i + \frac{1}{\Theta}\sum_{bjk} (z_{aj}s_jm_a)(z_{bk}s_km_b)f_{jk}\, T^{R}_{\substack{j\\k}} \to i \right] ,$$

or in vector form

$$\underline{z}'_a = \left[(1-m_a)I + m_aC(\underline{z}) \right] D(\underline{z})\, \underline{z}_a ,$$

where

$$\underline{z}_a \triangleq \begin{pmatrix} z_{a1} \\ z_{a2} \\ \vdots \end{pmatrix} ,$$

with

$$C(\underline{z}) \triangleq \| \frac{1}{\Theta} \sum_{bk} z_{bk} s_k m_b f_{jk} T^{R}_{\substack{j \\ k}} \to i \| \quad i,j ,$$

and

$$D(\underline{z}) \triangleq \frac{1}{\bar{w}} \operatorname{diag}(s_i) ;$$

the mean fitness is

$$\bar{w} = \sum_{ai} (1-m_a) z_{ai} s_i + \frac{1}{\Theta} \sum_{abjk} (z_{aj} s_j m_a)(z_{bk} s_k m_b) f_{jk} ,$$

the size of the mating pool is

$$\Theta = \sum_{ai} z_{ai} s_i m_a ,$$

and the transformation probabilities are

$$T^{R}_{\substack{j \\ k}} \to i \triangleq (1 - R) T^{j \to i}_{k} + R T^{k \to i}_{j} ,$$

where R is the rate of recombination between modifier and selected loci.

Unless the diploid fitnesses satisfy

$$\sum_{ai} z_{ai} s_i m_a f_{ij} = \sum_{ai} z_{ai} s_i m_a \text{ for all } j ,$$

then the matrix $C(\underline{z})$ will not be stochastic, and varying m_a will change the column sums of $\Omega_a D$.

Clearly, though, if the diploid fitness values f_{jk} are large enough,

$$\rho(\Omega_a D) \text{ will increase with larger } m_a ,$$

and if they are small enough,

$$\rho(\Omega_a D) \text{ will increase with smaller } m_a ,$$

showing that a new modifier allele increasing sexual reproduction gets in if there is a strong fitness advantage of the diploid phase, and is excluded if going through the diploid phase has a strong fitness cost. Therefore:

RESULT 3.29:

Strong selection for or against the diploid organism can dominate the evolution of the probability of sexual reproduction in this model.

Suppose now that there is no selection on the diploid, so $f_{jk} = 1$, for all j and k. Then $C(\underline{z})$ is a stochastic matrix. From Karlin (1982) Theorem 5.2, we see that as long as the fitnesses, s_i, of each selected type i are not all equal, the matrix on the frequencies of the individuals with the modifier allele yielding the smallest value m_a will have the largest spectral radius. This of course will change as the frequencies z_{ai} change, but in the limit, the evolutionary outcome will be:

RESULT 3.30:

The population fixes on the modifier causing the highest rate of asexual reproduction (the lowest m_a). The best that modifiers increasing sexual reproduction can do under any condition is be neutral.

This force of induced selection against sexual reproduction is distinct from Williams's (1975) "cost of meoisis". It is more along the lines of "recombinational load" that Williams (1975) discusses.

In this model, when an organism reproduces asexually, transmission is perfect, so that the variation produced by the modifier is linear. However, in real organisms transformation occurs in the asexual organisms also, due to mutation. Incorporation of mutation into the model would change the variation in transformations that the modifier controls to be affine instead of linear. In this case, it may be possible that sexual reproduction would evolve to increase, and the question of what sorts of additional transformation processes could produce an increase in sexual reproduction poses an interesting question.

(3) A MODEL FOR MODIFIERS IN CULTURAL TRANSMISSION

Because cultural transmission is mediated by complex cognitive processes, the idea of transformation can have some interesting applications in this area. Cultural transmission usually goes on within a context of human relationships. The choice of who will be the transmitters of cultural information may depend on these relationships. More importantly, cultural transmission need not be simply the replication of transmitter traits in the receiver; in cases of personality, religious preference, and politics for example, the traits adopted in the receiver can be as much a reaction to these traits in the transmitters as a replication of them because of the nature of the relationship between them. The theories of "family systems" that have been developed are good example of the transformation of behavior. In these theories, the behavior that offspring adopt is

causally related to the behavior of their parents, but does not necessarily resemble it.

The model I pose here considers how culture itself might evolve to affect the degree to which offspring copy the cultural traits of their parents as opposed to adopting traits that are transformed results of their parents traits.

The model has the following components:

1) Individuals bear two kinds of culturally transmitted trait. One affects the individual fitness of its bearer and the fertility of a mated pair. The other, which I refer to as "traditionalism", affects the transmission of the first.
2) Offspring are produced from two parents. Offspring randomly choose one of their parents with whom they will "identify".
3) The offspring acquire from the parent with whom they identify their degree of traditionalism.
4) This degree of traditionalism determines the probability that they also acquire the same selected cultural trait as the parent with whom they identify. Otherwise, they acquire a selected trait which is some function of the selected traits in both their parents.

To represent this, the following are defined:

z_{ai} is the frequency of individuals with traditionalism type a and selected type i before selection.

w_{ij} is the lumped individual fitness and fertility of parental pairs with selected types i and j.

$1-m_a$ is the probability that an offspring adopts the selected trait of the parent with whom it identifies.

$P_{j,k\to i}$ is the probability that an offspring of parental selected types j and k is of selected type i given that it does not simply copy the parent with whom it identifies. These probabilities do not depend on the traditionalism type.

A most important assumption is that the traditionalism itself is transmitted faithfully, in a particulate fashion. It is transmitted without bias, so it can evolve only through hitchhiking with the selected cultural trait.

For a life cycle consisting of selection, random mating with fertility selection, and cultural transmission, the recursion on the frequencies of types is

$$z'_{ai} = \sum_{bjk} z_{aj} z_{bk} \frac{w_{jk}}{\bar{w}} \left((1-m_a)\delta_{ji} + m_a P_{j,k\to i} \right)$$

$$= (1-m_a)\, z_{ai} \frac{w_i}{\bar{w}} + m_a \sum_{jk} z_{aj} v_k \frac{w_{jk}}{\bar{w}} P_{j,k\to i} ,$$

or in vector form

$$\underline{z}'_a = \left[(1-m_a) I + m_a C(\underline{z}) \right] D(\underline{z})\, \underline{z}_a ,$$

where

$$v_k = \sum_a z_{ak}, \qquad w_j = \sum_k v_k w_{jk},$$

$$C(\underline{z}) \triangleq \| \sum_k v_k \frac{w_{jk}}{w_j} P_{j,k\to i} \|_{i,j} , \qquad \bar{w} \triangleq \sum_{jk} v_j v_k w_{jk}, \text{ and}$$

$$D(\underline{z}) \triangleq \frac{1}{\bar{w}} \operatorname{diag}(w_j) .$$

The variation in cultural transformation determined by the tranditionalism type is linear, so from Karlin (1982) Theorem 5.2, we see that as long as the marginal fitnesses, w_i, of each selected type i are not all equal, the matrix on the frequencies of the individuals with the traditionalism type yielding the smallest value m_a will have the largest spectral radius. This of course will change as the frequencies z_{ai} change, but in the limit, given that the selected cultural traits still maintain marginal fitness differences the evolutionary outcome will be:

RESULT 3.31:

The population fixes on the highest degree of traditionalism in the population (the lowest m_a). The best that the traditionalism types with larger m_a can do is be neutral, and this can occur only for some cases where C at the limit is a reducible matrix.

This simple model suggests that in populations that are allowed to go to equilibrium, forms of culturally transmitted "traditionalism", or faithfulness in cultural transmission of traits that affect fitness will increase. It shows how the trend toward perfect transmission can be found in other contexts, and how the mathematics of these models follow a similar pattern.

5. THE STRENGTH OF SELECTION ON MODIFIERS AND THE EFFECT OF PLEIOTROPY

In the initial increase analyses throughout this chapter, we obtained results on the spectral radius of the exterior stability matrix. Recall that this spectral radius is actually the induced asymptotic relative marginal fitness of the modifier allele (or transformation type in general). Several of the results yield values on the magnitude of this induced marginal fitness.

In the case of tightly linked modifier alleles stopping all transformation, their induced marginal selective advantage was equal to the equilibrium fitness load. This value decreased with looser linkage but was always greater than the equilibrium fitness variance.

For modifiers with lesser effect on the transformations, the result on affine variation with memoriless distributions gives us an estimate of the amount of selection on the modifier as its marginal transformation deviates from the equilibrium marginal transformation of the population. From Theorem 3.2b we obtain

$$\frac{w_a}{\tilde{w}} = 1 + (m_a - m^*)\Big(\sum_i \frac{1}{\gamma_i}\hat{v}_i^2 w_i\Big)^{-1} \frac{1}{\gamma_2}$$
$$\cdot \Big[\frac{\alpha-\beta}{\tilde{w}} \sum_i \frac{1}{\gamma_i}\hat{v}_i^2(\hat{w}_i - \tilde{w})^2 + \alpha\beta\Big((1-\gamma)\sum_i \hat{v}_i(\hat{w}_i - \tilde{w})\Big(\frac{p_i - s_i}{\gamma_i}\Big) + \gamma \operatorname{cov}\Big(\hat{w}_i, \frac{p_i - s_i}{\gamma_i}\Big)\Big)\Big]$$

The selection for or against the modifier will be on the order of the equilibrium fitness variance in the population times the deviation of its marginal transformation matrix from the equilibrium transformation matrix.

What sort of estimates can be obtained for these values in nature? The upper bound on the equilibrium fitness load,

$$\frac{1}{1-\alpha},$$

increases without limit for populations with larger and larger amounts, α, of transformation occurring. The typical values of α in nature depend on the particular transformation process. In the case of the segregation-syngamy transformation, α equals one. Selection on modifiers that lead to ameiotic parthenogenesis or forms of apomixis with the same result can therefore be quite strong. In the case of mutation, although per-locus mutation rates are quite small, per chromosome or per genome rates can range up to order one. Similarly, per-chromosome recombination rates can be on this order. The amount of selection on modifier genes can therefore be quite strong in typical populations. An interesting example is the following:

RESULT 3.32:

The amount of induced selection on a chromosomal inversion can range up to the map length of the inversion, in units of crossover frequency.

What occurs when there is direct selection on the modifier due to pleiotropic effects it may have beyond its effect on transformation? If the pleiotropic selection interacts multiplicatively with the fitnesses of the selected loci, then this pleiotropic selection on the modifier allele is simply multiplied by the induced selection on the modifier due to its effects on transformation. In the case of modifiers completely stopping transformation, the amount of pleiotropic selection against

it, s_p, that it can withstand and still increase when introduced to the population can be as large as α, where its intrinsic fitness relative to the modifier alleles at equilibrium is $1 - s_p$.

The amount of selection on the modifier will actually be a complex function of the transformation probabilities and the selective values of the types in the population; the very course estimates on the possible strength of selection on modifier alleles shown above were made merely to illustrate that the induced selection on modifiers due to their effects on transformation can be on the order of selection acting directly on selected genes.

If the transformations in the population were to continue evolving to reduce the equilibrium fitness load, then the source of induced selection on the modifier will be gradually eliminated. So when the modifier genes that have various degrees of pleiotropic selective effects, the final stages of evolution of the transformations will come to be dominated by these effects.

CONCLUSIONS

In this chapter, the general framework of selection and transformation has been adopted to study the evolution of transformations. Variation for fitness and for transformations has been partitioned into independent dimensions of an individual's type. Perhaps the most basic statement to be derived from the results of this chapter is that the evolution of transformations is driven by an effect of transformation-- the equilibrium variance in the marginal fitnesses

of the selected types. The general result of evolution in the transformations appears to be the elimination of this variance in fitnesses. The state where all marginal fitnesses are equal may be an evolutionarily attractive state for populations at equilibrium when transformation does not act on the transformation types.

The direction in which the transformations evolve depends, however, on the nature of the variation in transformations in the population. Several kinds of variation in transformation have been described: uniform, consisting of linear and affine variation, and non-uniform variation. Three forces have been identified in the evolution of transformations:

1. Selection due to reduction in the amount of transformation.
2. Selection due to increase in the production of the fitter types.
3. Transformation acting on the transformation types.

Only 1. is available when there is linear variation and no transformation of transformation types. With affine variation, or non-uniform variation, 2. becomes available. With segregation distortion or other transmission distortion, 3. becomes available.

A number of properties of the population do <u>not</u> seem to affect the direction in which transformations evolve, including

the nature of the equilibrium at which the new transformation type is introduced,

the nature of the type being transformed, be it genetic, geographic, or cultural,

the nature of the transformations,

the selection regime,

frequency dependent selection or transformation,

allelic multiplicity, or

topology of descent.

It is unknown whether the linkage of the modifier affects the direction of evolution of the transformations, but other work in the literature suggests that it does not unless transformation is acting on the modifier genotype.

Modifiers were found to be potentially able to resist the effects of direct selection, due to pleiotropy, ranging up to the order of the variance in fitness in the population. But if the population is evolving to minimize this fitness variance, at some point pleiotropic effects can come to dominate.

Modifier genes, like selected genes, can maintain polymorphisms. Three kinds of polymorphism have been identified: viability-analogous, tensor product polymorphisms, high complementarity polymorphisms, and "balanced mixture" polymorphisms. I have explored mainly the behavior of viability-analogous, tensor product polymorphisms. They are a general feature of modifiers giving uniform variation in the transformations in randomly mating populations. The addition of tensor product modifier polymorphisms cannot stabilize an unstable selected-locus polymorphic equilibrium. The stability of these polymorphisms <u>does</u> depend on

the stability of the selected haplotype polymorphism,

the nature of the transformation,

the linkage of the modifier,

frequency and density dependent selection and transformation,

the topology of descent,

and most likely, the overdominance of the modifier locus.

But, except as they affect the features above, the stability does not appear to depend on

the kind of selected haplotype polymorphism,

the selection regime, or

allelic multiplicity.

CHAPTER 4

DISCUSSION

In this chapter I discuss the diverse issues relating to the results of the previous chapters.

SPECULATIONS IN THE LITERATURE

Work by Feldman et al. addressed speculations by other authors on the evolution of modifier genes. Maynard Smith (1978) guessed that whenever there is linkage disequilibrium in a population at a stable equilibrium in a uniform environment then there will always be selection for reduced recombination. Feldman et al. (1980) showed this to be true when no other transformation processes were occurring, but not to be true in the presence of mutation. Karlin and McGregor (1974) speculated to the contrary that it might be possible with an asymmetrical selection regime for two loosely linked loci that even looser linkage could evolve. Feldman et al. (1980) showed that the reduction of recombination is independent of the selection regime or the existing degree of linkage between the two selected loci. The results of Theorem 3.9 confirm the results of Feldman et al. (1980) for multiple alleles at the selected loci.

Turner (1967) has speculated that when more than two loci are undergoing recombination, that increased recombination may evolve. Charlesworth (1976) showed for multiple loci that modifiers increasing recombination cannot successfully invade a population at an equilibrium with no recombination. When there is complete interference in the recombination between the selected loci, then the variation in the transformation caused by uniformly altering the linkage between the loci will be linear, so from Theorem 3.9, reduction in the rate of recombination is the only possible outcome, at least for a tightly linked modifier, for arbitrary selection regime and number of alleles. Even in the absence of complete interference, which makes the variation non-uniform for a modifier controlling recombination between more than two loci, Theorems 3.5 and 3.8 show that reduction in recombination will still always be able to evolve if the reduction is sufficiently large, regardless of the linkage of the modifier locus, or polymorphism at the modifier locus. Therefore, in cases where the modifier controls recombination generally, there are no indications that Turner's conjecture will hold. The one way that Turner's conjecture might hold is when the modifier controls recombination between only some of the loci, in which the Principle of Partial Control could come into play.

In the mutation rate modification model that Karlin and McGregor (1974) examined, mutation occurred unidirectionally toward the deleterious allele. They speculated that if there were also mutation toward the fitter allele, an increase in mutation might be able to evolve. Holsinger and Feldman (1983b) showed, however, that for symmetrical mutation between the alleles in a random mating population, selection for reduced mutation was the only outcome, regardless of the

selection regime or polymorphism at the selected locus. Theorems 3.9 and 3.14 show this to be a property of the variation in the transformation being linear. So, the speculation of Karlin and McGregor can be definitely ruled out, at least for a tightly linked modifier, since only reduced mutation will be selected for when the variation is linear in randomly mating populations, regardless of any mutation occurring toward fitter types, or other features of the mutation distribution, the number of selected alleles, or the selection regime.

LIMITATIONS OF THE ANALYSIS

In spite of the generalizations of modifier theory that have been possible in this treatment, there remain a number of limitations in the analysis. The analysis of affine variation in transformations was possible only for the special case of memoriless transformations, and only for small variations in the transformations. The present lack of results comparable to Karlin (1982) Theorem 5.2 for affine variation also limits the analysis of linear variation to modifiers that are tightly linked to the selected haplotype.

The cases requiring second order analysis have gone untreated here. These include cases where the marginal fitnesses are equal at equilibrium, where the marginal transformation of a new modifier allele is the same as the equilibrium marginal transformation, and where there is perfect transmission at equilibrium. Fortunately, these situations are not as likely to be biologically significant, since they are eigenvalue one problems where the selective force on the transformation

types is very small, and easily overwhelmed by any pleitropic selection acting directly on the transformation types.

In addition, I have not attempted analysis of diploid modifier models with partial selfing, assortative mating, sexual selection, other non-random mating, or fertility selection. It may be that some of these cases fit those that are analyzed here, but in general they will involve transformation of the transformation types and affine or non-uniform variation in the transformations. Of course, in cases with eigenvalues distinct from one, continuity (Karlin and McGregor, 1972) guarantees that the results obtained for random mating and multiplicative fertility selection will extend to some regions for the above variations, meaning that the results have "structural stability". However, as has been shown in Holsinger and Feldman (1983a), these regions can in some cases be so small as to be biologically insignificant.

It was not possible to obtain full results on the interior stability of viability-analogous, tensor product equilibria, and no attempt was made to obtain results for the interior stability of the other known kinds of equilibria.

ON THE USES OF THE TERM "MODIFIER"

Karlin and McGregor (1974) have said that the it can be argued that the concept of modifier genes cannot be unambiguously defined. In this thesis, "modifier" has been used to mean a source of heritable variation for transformation processes. This partitioning of the forces acting on a population into a dichotomy of selection and transformation makes the

classification of modifier effects unambiguous. "Modifier" has been used more generally to refer to any gene which interacts with variation in other genes. It has been used in the context of post-translational modification of proteins, genes with small effects on phenotypes when genes with large effect exist, genes affecting the probability that an organism with a given genotype at another locus has a given phenotype, and genes posited to affect dominance. These are each cases where the modifier will have an intrinsic effect on selection.

However, it should be mentioned that soft selection at one level of population may result in transformation at a higher level of population. For example, segregation distortion may result from a form of selection between the different haploid genotypes within the population of sperm of a diploid individual. When there is saturation of the ovum by sperm during fertilization, this selection would not affect the quantity of reproductive output of the diploid individual, making it a form of "soft selection". Its effect, rather, would be to change only the content of the male's reproductive output, making it a form of transformation. Scudo (1967) has examined models with selection on both haplo and diplophase, and considered both the "hard" and "soft" haploid selection, the "soft" selection case being segregation distortion. When one considers group selection, in a model where groups are surviving or founding other groups at rates dependent on their genetic composition, selection within the group results in a transformation of the composition of the group, and will not alter directly the reproductive output of the group if it is soft selection. Therefore, it is not necessarily an intrinsic property of particular genetic variation that it affects selection versus transformation, but

rather it may depend on the greater biological context of the organism.

In all of these uses, the essence of the concept does not require the presence of other genes; in the case of migration modifiers, selection for reduced migration can occur in the absence of any genetic variation in fitness; only variation in habitat fitness is required. So what is required is rather the presence of some sort of transmissible variation in fitness, be it variation in location, habitat, or cultural traits.

UNDERLYING HOMOLOGY BETWEEN PHENOTYPE DISTRIBUTION MODELS AND MODIFIER MODELS

An important class of models in the literature are those which are concerned with the evolution of phenotypes. In these models, selection is determined by the phenotype, while the genotype, rather than directly specifying fitnesses, specifies probabilities that individuals have different phenotypes. These models have been posed to investigate situations where the fitnesses of the phenotypes are dependent on their frequencies. They include models of sex ratio, altruism, behavioral contests, habitat selection, and general frequency dependent selection. What is quite significant is that in each of these models there are two kinds of polymorphic equilibria that bear strong resemblance with two of the kinds of polymorphisms that occur with modifiers: viability-analogous, tensor product polymorphisms and balanced mixture modifier polymorphisms. The table below lists these examples and the nomenclature that has been used in the different papers for these two kinds of polymorphism.

TABLE 13

HOMOLOGY BETWEEN MODIFIER AND PHENOTYPE DISTRIBUTION MODELS

Topic	Phenotypes	Type of Polymorphism		References
		V.A.T.P.	Balanced Mixture	
		term used for polymorphism:		
Sex Ratio	male, female	"symmetric"	"asymmetric"	Eshel & Feldman (1982)
			"even sex ratio"	Karlin & Lessard (1983)
Kin Selection	selfish, altruist	"viability-analogous"	"structural"	Uyenoyama et al (1981)
Behavioral Contests	hawk, dove	"not ESS"	"ESS"	Maynard Smith (1981)
Habitat Preference	habitat choice	"symmetric"	"asymmetric"	Rausher (1984)
Frequency Dependent Selection	phenotype	"genotype"	"phenotypic"	Lessard (1984)
			"equilibriated fitnesses"	Slatkin (1979)

V.A.T.P = Viability Analogous, Tensor Product

In correspondence between modifier and phenotype distribution models is as follows:

MODIFIER MODEL	PHENOTYPE DISTRIBUTION MODEL
selected type	phenotype
transformation type	genotype
transformation probabilities	phenotype distribution

In these models, the two kinds of polymorphism can be characterized this way:

1) Viability-analogous, tensor product equilibria. The gene frequencies are the same in each phenotypic class, and therefore the phenotype distribution is the same for each gene. Thus the tensor product and viability-analogous properties refer to the same thing.
2) Balanced mixture equilibria. The fitnesses of each phenotype are equal. But different genes may have different phenotype distributions, and different phenotypic classes may have different gene frequencies.

In the different cases in the literature, each model has different means by which the phenotypic fitnesses become equal for the balanced mixture equilibria:

In the case of behavioral contests, the population is at an equilibrium of classic game theory, where the payoffs for each behavior are the same.

In the habitat selection case, soft selection in each habitat results in culling in those habitats that are over their carrying capacity, and filling-out in habitats that are under their carrying capacity. At a balanced mixture equilibrium, each habitat is filled to the same extent with respect to its carrying capacity, and this is achieved by a balance mixture of different genotypes that prefer different habitats.

In the sex ratio case, it may be possible to define a value for the "fitness" of each sex, and at equilibrium the fitnesses for the two sexes are equal. This fitness is defined in diploid models by allowing random mating between all combinations of the two sexes and assigning fertility values of zero to matings of the same sex. Sex ratios of one-to-one give equal fitnesses for each sex. A different method must be employed for the haplodiploid model of Eshel and Feldman (1982). The gene frequencies among each sex can be different.

In the kin selection case, the fitness of a phenotype is not so readily defined. At the analog of the balanced mixture equilibria in these cases, the cost of being altruistic equals the benefit conferred to the recipients discounted by their relatedness, which is the situation where altruism is expected to be neutral.

In the general frequency dependent case, the frequencies of the phenotypes have reached a point where, because of frequency dependence, their fitnesses are all the same, but the gene frequencies within each phenotypic class need not be equal. In Slatkin's model (1979), the generic requirement to obtain a balanced mixture equilibrium is that there be as many alleles as

phenotypes, which is analogous to the requirement for the modifier model, in Section 3.(2), that there be as many transformation types as selected types.

The reason that phenotype distribution models and modifier models should share these two kinds of polymorphic equilibria can be understood at least heurisically. In both modifier and phenotype distribution models, selection is not an intrinsic property of the gene, but is induced on it by its association with types that are selected. V.A.T.P. polymorphisms are equilibria because the marginal distribution of selected types associated with each gene are the same. Balanced mixture polymorphisms are equilibria because there are no longer selective differences between the selected types.

But the connection between modifier models and phenotype distribution models can be shown to be even more basic. These two kinds of models actally form a continuum.

In the case of memoriless transformation, when there is no component of perfect transmission in the transformation matrix, a modifier model actually becomes a phenotype distribution model. At this extremum for the transformation matrix, an individual's type becomes irrelevant to the selected types of its offspring, so their selected type need no longer be considered a genotype and can be thought of as a phenotype. The frequency of this phenotype among the offspring will be simply the transformation distribution, which is determined by the modifier locus. So this modifier model is equivalent to a phenotype distribution model where the distribution is controlled by the parents, which have been studied for models where the sex ratio, habitat, or behavior are determined the genotype of the parent.

It has been pointed out to me (Uyenoyama, personal communication) that under non-random mating, the viability-analogous equilibria of phenotype distribution models usually no longer exist. That this occurs would be expected, since non-random mating reveals the action of the segregation-syngamy transformation on the diploid genotypes. This is analogous to modifier models with non-random mating which I have not investigated here.

Although there is both a qualitative homology and a similarity of results between modifier models and the different phenotype distribution models, these models are mathematically distinct, so I am claiming only that in some cases they result in the same behavior.

THE FITNESS LOAD PRINCIPLE

The Mean Fitness Principle of Karlin and McGregor must hold in the case of frequency independent selection in asexual populations, and for transformation near perfect transmission in pair mating populations. But it has been found to fail in several cases.

Although I have not investigated the general scope of validity of the Fitness Load Principle, I present one case in which the Mean Fitness Principle of Karlin and McGregor (1974) fails where the Fitness Load Principle nevertheless appears to hold.

Feldman et al. (1980) showed that reduction in recombination rates was the only evolutionary outcome for a two-locus, two-allele system with random mating and arbitrary viability selection regime, in the absence of other transformations on the loci. Yet, Karlin and Carmelli

(1975) found fitness regimes for which a decrease in the rate of recombination would cause a decrease in the equilibrium mean fitness of the population. What is the result of decreased recombination on the fitness loads for these selection regimes however?

I have calculated these values for one case they consider, shown below in Table 14.

TABLE 14

Comparison of mean fitness, marginal fitness variance, and marginal fitness load:

R_{AB}	$\hat{\bar{w}}$	$\mathrm{var}\left(\frac{\hat{w}_i}{\hat{\bar{w}}}\right)$	$L=\max_i\left(\frac{\hat{w}_i}{\hat{\bar{w}}}\right)-1$	Upper Bound on L $= \frac{R_{AB}}{1-R_{AB}}$
.025	.461854	.00161	.0253	.0256
.027	.461845	.00150	.0274	.0277
.030	.461866	.00131	.0306	.0309

Derived from 2 locus model, Table 1, in Karlin and Carmelli (1975)

Shown are the mean fitness, the variance in the relative marginal fitnesses of the four two-locus haplotypes, the fitness load, and the upper bound on the fitness load determined by the recombination rate. We see that as recombination decreases, the mean fitness decreases then

increases, the marginal fitness variance increases, and the fitness load decreases. The Fitness Load Principle therefore fits in this case.

It is interesting to note that the actual fitness load in these cases is around 98% of the maximum possible amount. The fitnesses on the two-locus genotype are not extreme, ranging by a factor of 3 . It is an interesting question as to how close fitness loads stay to their maximum over the range of possible selection regimes and transformation matrices.

Clearly, the Fitness Load Principle does not hold generally in cases where the transformation type is itself being transformed, as in the case of modifiers of segregation distortion. Yet, it is clear that as long as there is a positive fitness load at equilibrium, there is the opportunity for new modifiers to invade the population. In this sense, the importance of the fitness load is that unless it is reduced, a population can always be potentially invaded by new variants having the appropriate changes in the transformations operating on them.

IMPLICATIONS OF THE PRINCIPLE OF PARTIAL CONTROL

One of the more significant implications from the Principle of Partial Control is that transformation processes of widely different origin may have a strong impact on each others' evolution. An example where this idea has been employed, though not in the framework of co-evolving transformation processes, is in theories of dispersal. One of the forces postulated to select for dispersal is the avoidence of inbreeding (Maynard Smith, 1978; Shields, 1983). Inbreeding can be

harmful because it exposes recessive deleterious mutations and because it produces more homozygotes than outbreeding, which are expected to be less fit when the polymorphism is being maintained by overdominance. We can immediately recognize that two transformations are responsible for these effects-- mutation, and segregation and syngamy. Therefore, the presence of these transformations has implicitly been posited as a cause for the evolution of another transformation, dispersal.

Other causes have been proposed for the evolution of transformations:

1. Pleiotropic selection for transformation processes or against the reduction of transformation processes.
2. Lack of variation for further reduction in transformation.
3. Transient phases for the population recur due to drift, selection changes, or the introduction of novel types, making transient dynamics more important than equilibrium dynamics.

Therefore, a transformation process such as mutation could be maintained for any of the above reasons, and then generate selection for other transformation processes such as segregation and syngamy, recombination, and dispersal. There is the further possibility that synergistic interactions between these transformations, once they are established, may alter their evolution-- for example, migration selecting for recombination (Charlesworth and Charlesworth, 1979 b).

Recombination could also act as a source of selection for increased mutation. When a population has stable linkage disequilibrium between two loci at a recombination-selection balance, the haplotypes with positive disequilibrium will have above average marginal fitnesses.

Therefore, if the mutation distribution controlled by a particular mutator locus happens to favor overall mutation from the haplotypes with negative disequilibrium to those with positive disequilibrium, it is conceivable that increased mutation will be selected for.

If a modifier controls the transformation acting at only one or a few loci, then the transformations acting at other loci will render the variation at this modifier non-linear. It is conceivable, therefore, that a modifier affecting recombination at only a few loci could evolve to increase that recombination when recombination is occurring elsewhere. These are speculations for further investigation.

MODIFIERS IN POPULATIONS WITH SELFING

The Principle of Partial Control gives a rationale as to why selfing can completely alter the behavior of modifier models. In Section 3.(3) of Chapter 2, on diploidy and the segregation-syngamy transformation, it was shown that with random mating and multiplicative fertility selection, the transformation of segregation and syngamy disappears from the dynamics of the population, and the haploid can be considered the "individual" and the diploid the "mated pair". In this case the transformation of haplotypes will be the only transformation relevant to the population dynamics. However, when there is partial or complete selfing, the diploid must be considered the "individual". And because the segregation-syngamy transformation reappears in the dynamics of the population, the transformation of haplotypes will not be the only transformation relevant to the population dynamics. Therefore, linear variation in the haplotype transformations will not be linear with respect to the total transformation acting on the genotype. Unless the modifier acts only in one sex, the variation also will be non-uniform.

Because segregation and syngamy are acting to transform also the modifier genotype, the case of selfing involves transformation of the transformation type, in addition to variation that is not linear. In the one case where transformation of the transformation type was explored, the case of modifiers of segregation distortion, it was found that even with linear variation in the transformations increased transformation could evolve.

Therefore, when there is selfing, both phenomena that have been found to allow an increase in transformation to evolve are present--non-linear variation in the transformation and transformation of the transformation type. It is not unexpected, then, that increases in recombination (Holsinger and Feldman, 1983 a) and mutation (Holsinger and Feldman, 1983 b) have been found to be able to evolve when there is selfing.

But selfing is not the only condition that will cause the segregation-syngamy transformation to reappear in the dynamics of the population. Non-multiplicative fertility selection and assortative or other forms of non-random mating will have this effect. No modifier models in the literature have been analyzed in the presence of fertility selection. Investigation of such models may turn up new cases where recombination or other transformations can evolve an increase.

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