

Analysis of central equilibrium configurations for certain multi-locus systems in subdivided populations

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SUMMARY

The multi-locus systems expressing non-epistatic and generalized symmetric selection lend themselves to the study of the stability of certain central polymorphic equilibria. These equilibria persist when any form of migration connects demes which share a common equilibrium. The analysis of the stability of the equilibrium in the global system is tractable, thus supplementing known protection results for two alleles at one locus with stability conditions on an internal equilibrium involving an arbitrary number of loci, each with an arbitrary number of alleles. Two of the principal findings are that stability of central Hardy–Weinberg type equilibria increase with ‘more’ migration and ‘more’ recombination. As a corollary, local stability in each deme implies stability in a system with migration superimposed; but instability in each deme when isolated does not imply instability when migration is superimposed.

1. INTRODUCTION

Two areas of population genetics theory which are currently under active investigation are multi-locus multi-allele phenomena and migration–selection (environment) interaction. This work is part of a continuing series of theoretical studies seeking to integrate the two. A particular goal is to delimit the existence and nature of polymorphisms. Recent reviews pertaining to genetic polymorphism under conditions of variable selection and migration are given by Hedrick, Ginevan & Ewing (1976) and Felsenstein (1976), which include numerous references to experimental, field, and theoretical studies. We shall omit most of the relevant references which are cited in these reviews.

Theoretical analyses pertaining to the nature of selection migration interaction have centred on the model of a diploid trait at a single locus involving two alleles mainly seeking to ascertain conditions for a protected polymorphism (i.e. conditions assuring that neither allele ever goes extinct). Characterizations and classifications of the stable equilibrium configurations with several demes have been dealt with only for special migration patterns (e.g. stepping-stone mode and related clinal regimes (Nagylaki, 1976, 1977; Fleming, 1975; Karlin & Richter-Dyn, 1976)

and the gene frequency patterns in the familiar Levene population structure (Karlin, 1977)). Our objective in this work is to analyse in a *multi-deme* context the equilibrium properties of certain ‘central’ polymorphic frequency states emanating from selection migration balance for a multi-locus multi-allele system.

In the case of a single-habitat model, the feasibility of selection balance maintaining a central polymorphic equilibrium has been investigated for two general classes of selection regimes: the ‘*extended non-epistatic*’ *viability structure* (see (i) below) and the ‘*generalized symmetric*’ *selection pattern* (delimited more precisely in (ii), see also Karlin, 1978).

(i) *Extended non-epistatic selection*

The extended non-epistatic selection construction encompasses combinations of multiplicative, additive and neutral viability effects across loci. No restrictions are placed on the numbers of loci and/or alleles per locus, but it is instructive and of independent interest to set forth first the two-locus two-allele case. The concept of non-epistasis involves intrinsic selection coefficients at the separate loci. Let the intrinsic fitness coefficients for the indicated genotypes at the first locus be

$$AA: w_{11}^{(1)}, \quad Aa: w_{12}^{(1)} = w_{21}^{(1)}, \quad aa: w_{22}^{(1)}, \tag{1a}$$

and at the second locus

$$BB: w_{11}^{(2)}, \quad Bb: w_{12}^{(2)} = w_{21}^{(2)}, \quad bb: w_{22}^{(2)}. \tag{1b}$$

In the two-locus two-allele model, there are four basic selection forms which are used for constructing the *extended non-epistatic selection regimes*. It is appropriate to display these four basic non-epistatic regimes, conforming to the haplotype arrangement *AB, Ab, aB, ab*, associated with the intrinsic fitness parameters of (1):

$$W^{(1,1)} = \begin{pmatrix} w_{11}^{(1)} w_{11}^{(2)} & w_{11}^{(1)} w_{12}^{(2)} & w_{12}^{(1)} w_{11}^{(2)} & w_{12}^{(1)} w_{12}^{(2)} \\ w_{11}^{(1)} w_{12}^{(2)} & w_{11}^{(1)} w_{22}^{(2)} & w_{12}^{(1)} w_{12}^{(2)} & w_{12}^{(1)} w_{22}^{(2)} \\ w_{12}^{(1)} w_{11}^{(2)} & w_{12}^{(1)} w_{12}^{(2)} & w_{22}^{(1)} w_{11}^{(2)} & w_{22}^{(1)} w_{12}^{(2)} \\ w_{12}^{(1)} w_{12}^{(2)} & w_{12}^{(1)} w_{22}^{(2)} & w_{22}^{(1)} w_{12}^{(2)} & w_{22}^{(1)} w_{22}^{(2)} \end{pmatrix},$$

$$W^{(0,0)} = \begin{pmatrix} 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \\ 1 & 1 & 1 & 1 \end{pmatrix},$$

$$W^{(1,0)} = \begin{pmatrix} w_{11}^{(1)} & w_{11}^{(1)} & w_{12}^{(1)} & w_{12}^{(1)} \\ w_{11}^{(1)} & w_{11}^{(1)} & w_{12}^{(1)} & w_{12}^{(1)} \\ w_{12}^{(1)} & w_{12}^{(1)} & w_{22}^{(1)} & w_{22}^{(1)} \\ w_{12}^{(1)} & w_{12}^{(1)} & w_{22}^{(1)} & w_{22}^{(1)} \end{pmatrix} \quad W^{(0,1)} = \begin{pmatrix} w_{11}^{(2)} & w_{12}^{(2)} & w_{11}^{(2)} & w_{12}^{(2)} \\ w_{12}^{(2)} & w_{22}^{(2)} & w_{12}^{(2)} & w_{22}^{(2)} \\ w_{11}^{(2)} & w_{12}^{(2)} & w_{11}^{(2)} & w_{12}^{(2)} \\ w_{12}^{(2)} & w_{22}^{(2)} & w_{12}^{(2)} & w_{22}^{(2)} \end{pmatrix} \tag{2}$$

Thus, the fitness of the genotype *AB/Ab* corresponding to $W^{(1,0)}$ has value $w_{11}^{(1)}$ reflecting selection acting only at the first locus. Similarly, the fitness value of *AB/Ab* corresponding to $W^{(0,1)}$ is $w_{12}^{(2)}$ and that of *AB/Ab* associated with $W^{(1,1)}$ is $w_{11}^{(1)} w_{12}^{(2)}$. Finally, the fitness ascribed to *AB/Ab* (in fact any genotype) by $W^{(0,0)}$ is 1.

In the two-locus context the extended non-epistatic selection structure founded on the intrinsic fitness parameters of (1) consists of the combined fitness expression

$$F = \alpha W^{(1,1)} + \beta W^{(1,0)} + \gamma W^{(0,1)} + \delta W^{(0,0)} \quad (\alpha, \beta, \gamma, \delta \geq 0); \tag{3}$$

that is, a weighted sum of the four basic fitness matrices. Observe that F for the determination $\beta = \gamma = \delta = 0, \alpha = 1$ reduces to the classical multiplicative non-epistatic regime. The specialization $\beta = \gamma = 1, \alpha = \delta = 0$ in (3) leads to the classical additive non-epistatic regime.

It is illuminating and helpful to pass to three loci to better convey the scope and nature attendant to the ‘extended’ non-epistatic selection form. We may assume that there is a general number of alleles, m_k , at the k th locus ($k = 1, 2, 3$). Let the intrinsic fitness matrix for the k th locus be $W^{(k)} = \|w_{ij}^{(k)}\|_{i,j=1}^{m_k}$ specifying the fitnesses associated with the diplotypes $(A_i^{(k)}A_j^{(k)})$. These matrices combine in eight ways (2^n for n loci) to generate the basic selection regimes underlying ‘extended’ non-epistatic selection structures. We highlight these matrices in tabular form indicating the fitness associated with the genotype

Matrix	Entry	Remarks
$W^{(1,1,1)}$	$w_{im}^{(1)} w_{jp}^{(2)} w_{kq}^{(3)}$	Independent multiplicative factors accruing from all three loci
$W^{(1,1,0)}$	$w_{im}^{(1)} w_{jp}^{(2)}$	Loci 1 and 2 interact multiplicatively while locus 3 manifests neutrality
$W^{(1,0,1)}$	$w_{im}^{(1)} w_{kq}^{(3)}$	Loci 1 and 3 interact multiplicatively while locus 2 manifests neutrality
$W^{(0,1,1)}$	$w_{jp}^{(2)} w_{kq}^{(3)}$	Loci 2 and 3 interact multiplicatively while locus 1 manifests neutrality
$W^{(1,0,0)}$	$w_{im}^{(1)}$	Selection only acting at locus 1
$W^{(0,1,0)}$	$w_{jp}^{(2)}$	Selection only acting at locus 2
$W^{(0,0,1)}$	$w_{kq}^{(3)}$	Selection only acting at locus 3
$W^{(0,0,0)}$	1	Neutral

With this notation *extended non-epistasis* induces a fitness matrix of the form

$$F = \alpha_{111} W^{(1,1,1)} + \alpha_{110} W^{(1,1,0)} + \alpha_{101} W^{(1,0,1)} + \alpha_{011} W^{(0,1,1)} + \alpha_{100} W^{(1,0,0)} + \alpha_{010} W^{(0,1,0)} + \alpha_{001} W^{(0,0,1)} + \alpha_{000} W^{(0,0,0)}. \tag{4}$$

As with two loci, the standard multiplicative non-epistatic form ensues from the choice $\alpha_{111} = 1$ with all other α 's equal to zero. Additive non-epistasis results from an equal weighting of certain groupings of the marginal fitness matrices; namely

$$\alpha_{100} = \alpha_{010} = \alpha_{001} = 1, \quad \alpha_{111} = \alpha_{110} = \alpha_{101} = \alpha_{011} = \alpha_{000} = 0.$$

Other interesting specializations of (4) reflect a mixed additive multiplicative interaction among the loci. For example, the choice $\alpha_{110} = \alpha_{001} = 1$ (with the remaining α 's equal to zero) entails multiplicative non-epistasis between the first two loci, but additive non-epistasis between the gene complex consisting of the first two loci and the third locus. The extension of the construction of (4) to more loci follows, *mutatis mutandis*.

Hardy-Weinberg multilocus type polymorphic equilibrium. A notable feature of an extended non-epistatic selection is the existence of multilocus Hardy-Weinberg (H.-W.) type equilibria which we presently delimit. Assume for each k the existence of a polymorphic equilibrium $(\hat{x}_1^{(k)}, \hat{x}_2^{(k)}, \dots, \hat{x}_{m_k}^{(k)}) = \hat{\mathbf{x}}_k$ for the one-locus m_k -allele system induced by the intrinsic fitness matrix $W^{(k)}$. We may construct a haplotype frequency array of the multi-locus system by multiplying the marginal frequencies of the constituent alleles. In this manner, the frequency of the haplotype

$$\{A_i^{(1)}A_j^{(2)}A_k^{(3)}\} \text{ is } \hat{x}_i^{(1)}\hat{x}_j^{(2)}\hat{x}_k^{(3)}.$$

This haplotype frequency array is an equilibrium independent of the recombination distribution of the multi-locus system associated with the fitness matrix F . An equilibrium state composed by multiplying the marginal loci genotype component frequencies is called a Hardy-Weinberg (H.-W.) configuration. In the two-locus case a H.-W. state exhibits linkage equilibrium, and in the multi-locus case it renders zero higher order measures of association in most senses (see Bennett (1954) and also Hill (1976)).

(ii) ‘Generalized symmetric’ selection

Generalized symmetric selection expression is an extension of the notions of symmetric under- and overdominance. In this perspective, fitness depends on which loci are homozygous or heterozygous and otherwise is not influenced by the specific allelic composition at the locus. As before the theory is readily forthcoming without restriction on the number of loci and alleles involved, but to facilitate the exposition we shall initially confine the discussion to the cases of two and three loci carrying two alleles each. The prototype two-locus fitness matrices are

$$W_s = \begin{pmatrix} 1 & \alpha & \alpha & \beta \\ \alpha & 1 & \beta & \alpha \\ \alpha & \beta & 1 & \alpha \\ \beta & \alpha & \alpha & 1 \end{pmatrix}, \quad W_p = \begin{pmatrix} 1 & \alpha' & \alpha & \beta \\ \alpha' & 1 & \beta & \alpha \\ \alpha & \beta & 1 & \alpha' \\ \beta & \alpha & \alpha' & 1 \end{pmatrix}. \tag{5}$$

W_s , which is the Lewontin-Kojima (1960) symmetric viability model, prescribes fitness values invariant under relabelling of alleles. Equivalently, fitness is a function of the number of heterozygous loci. The fitness array W_p incorporates loci position effects signifying that fitness depends on which loci are heterozygous. The population state which assigns equal frequency (in this case $\frac{1}{4}$) to all haplotypes is an equilibrium which we refer to as the *central equilibrium*.

In the three-locus case the corresponding fitness values of a genotype are as follows:

- α where all separate loci are homozygous;
 - β_i where locus number i is heterozygous while the other two loci are homozygous;
 - δ_i where locus i is homozygous while the other two loci are heterozygous;
 - γ where all three loci are heterozygous.
- (6)

Thus the corresponding fitness matrix has the form

$$\begin{matrix}
 & ABC & ABc & AbC & Abc & aBC & aBc & abC & abc \\
 ABC & \alpha & \beta_3 & \beta_2 & \delta_1 & \beta_1 & \delta_2 & \delta_3 & \gamma \\
 ABc & \beta_3 & \alpha & \delta_1 & \beta_2 & \delta_2 & \beta_1 & \gamma & \delta_3 \\
 AbC & \beta_2 & \delta_1 & \alpha & \beta_3 & \delta_3 & \gamma & \beta_1 & \delta_2 \\
 Abc & \delta_1 & \beta_2 & \beta_3 & \alpha & \gamma & \delta_3 & \delta_2 & \delta_1 \\
 aBC & \beta_1 & \delta_2 & \delta_3 & \gamma & \alpha & \beta_3 & \beta_2 & \beta_1 \\
 aBc & \delta_2 & \beta_1 & \gamma & \delta_3 & \beta_3 & \alpha & \delta_1 & \beta_2 \\
 abC & \delta_3 & \gamma & \beta_1 & \delta_2 & \beta_2 & \delta_1 & \alpha & \beta_3 \\
 abc & \gamma & \delta_3 & \delta_2 & \beta_1 & \delta_1 & \beta_2 & \beta_3 & \alpha
 \end{matrix} = \Gamma. \quad (7)$$

The central equilibrium has each haplotype with frequency $\frac{1}{8}$. The fitness values as defined above in (6) are independent of the number of alleles, but the indexing system must be modified for more loci. The general formulation can be found in Karlin (1978).

The multi-deme selection–migration model

We assume the standard model for a population which evolves subject to mating, recombination, and selection forces acting within habitats connected by gene flow among demes comprising the aggregate population. The present formulation assumes N distinct habitats (each with an associated deme). Within each habitat, the genetic composition of the deme is affected by mating and selection. The transformation of haplotype frequencies is incorporated into a vector function \mathbf{f}_k appropriate to the k th habitat. In the framework of multi-locus and multi-allele models investigated here, a vector of haplotype frequencies describes the genetic composition of each deme and each \mathbf{f}_k is vector valued (a collection of functions involving a multivariate argument that determine the changes of the haplotype frequency array over successive generations due to the local selection–mating–recombination interaction). The explicit form of \mathbf{f}_k for the extended non-epistatic and generalized symmetric models are displayed in Karlin (1978, 1979). For our purposes, the explicit transformation formulas are not needed.

The effects of geographical gene flow are summarized by an $N \times N$ backward migration matrix $M = \|m_{ij}\|_1^N$ which prescribes in each generation the proportion of the i th deme originating from the j th habitat. We assume that M is time homogeneous and independent of the genetic composition of the demes. Details on the construction of M and elaborations on the formulation can be found in, e.g., Karlin (1976). It is helpful to display the order of forces in the process:

$$\text{post-migration individuals} \rightarrow \text{recombination and mating} \rightarrow \text{selection (on progeny)} \rightarrow \text{migration} \quad (8)$$

We are interested in delineating the nature of the stable equilibrium configurations for multi-locus multi-allele systems evolving under the influence of various forms of selection–migration interactions. In this vein, we concentrate on the following specific objectives, concepts and problems.

We note in Section 2 that when each habitat experiences an extended non-epistatic selection regime which may vary between habitats such that all these selection forms are based on the same set of marginal overdominant fitness matrices (or each environment (habitat) expresses a case of generalized symmetric selection), then a common Hardy–Weinberg polymorphic equilibrium configuration exists uniformly over the population range, independent of the various local recombination rates and also unaffected by the population-dispersal pattern. We inquire as to the conditions for stability of this equilibrium state expressed in terms of the local selection–recombination regimes and the migration and population structure parameters. Detailed mathematical formulae delimiting the precise stability conditions for these polymorphic equilibria are available (see Result I and also consult the Appendix).

We treat primarily a number of qualitative inquiries as to how changing various parameter specifications affects the character and/or strength of stability of the central H.–W. equilibrium configuration. It is informative and revealing to ascertain some robust properties concerning the dynamics and equilibrium behaviour via suitable comparisons of the ‘degree’ of stability (i.e. the magnitude of the principal eigenvalue of the local linear approximation) for the H.–W. polymorphic equilibrium state. The three strata of the selection–migration model (8), allowing various levels and representations, are migration, recombination, and the selection structures. We investigate the consequences of altering the parameters specifying these structures.

(1) *Migration* is most conveniently described by interdeme dispersal rates coupled to population structure, relative deme sizes, influences of local selection, mating system, etc. There is *no* intrinsic total ordering among migration patterns. That is, generally no single real parameter m can summarize the migration strength and such reductions are mostly inappropriate. Several natural concepts and indices for comparing migration forms have been proposed (Karlin, 1976). We shall discuss the implications of two of these which we spell out in Section 1 pertinent to the following:

What is the effect of ‘more mixing’ or ‘more migration’ on the degree of stability of the H.–W. or central equilibria?

(2) *Recombination*. The interactions of selection and linkage are more subtle and are usually studied in the cases of clusters of tightly linked genes (small recombination rates throughout) or loosely linked blocks of genes (free recombination throughout). However, recombination varies between these extremes. The variation may be temporal or spatial, systematic or random. The following problem is naturally suggested.

What is the effect of varying linkage relationships relative to deme sites on the stability of ‘central’ H.–W. equilibria?

(3) *Selection* generally varies over the population range, i.e. between habitats; this is a foundation of ecological genetics. In the case of extended non-epistasis, there is a natural interpretation for the variation between habitats. The invariance of the intrinsic selection coefficients suggests that the underlying biological and biochemical processes associated with the loci are invariant. The different weightings

reflect the relative importance of those processes in the particular habitat (e.g. water conservation may be important in some habitats whereas efficient use of potassium is more important in others). Cryptic coloration will vary in its importance as components of the total fitness in accordance with the nature of the habitat.

Apart from varying the relative importance of the loci (for fitness), the intensity of selection across all loci may vary. This form of variation is perhaps better suited to the generalized symmetric model; in the extended non-epistatic model it is equivalent to increasing (or decreasing) the weight of the neutral selection term. With the foregoing motivations in mind, we may pose the following problem quite generally as:

What is the effect of contrasting selection intensities relative to habitat sites on the degree of stability of the H.-W. or central equilibria?

(4) Another objective of this work is to investigate conditions under which the multi-deme problem can be reduced to an equivalent (or 'effective') single-deme problem. This is often possible if a Levene population subdivision model is in force and rarely for other population migration structures.

We also compare the results obtained on stability of the H.-W. or central equilibria to known results for protection (i.e. stability of the boundary equilibria).

2. RESULTS

(A) *Methods*

It is useful to commence the treatment by detailing formally the model. The population involving n loci, and m_k alleles $A_1^{(k)}, A_2^{(k)}, \dots, A_{m_k}^{(k)}$ at the k th locus is distributed over N habitats (or demes). We characterize the haplotype frequency array in each deme by the vector \mathbf{x} comprised of $\prod_{k=1}^n m_k$ components. The haplotype frequencies at the i th deme are distinguished by appending the appropriate subscript, $\mathbf{x}_{(i)}$. The consequences of selection and mating are implemented through the set of vector-valued functions, $\mathbf{f}_{(i)}$ acting in the i th habitat; accordingly

$$\tilde{\mathbf{x}}_{(i)} = \mathbf{f}_{(i)}(\mathbf{x}_{(i)}) \tag{9}$$

describes the change due to selection, recombination, and mating in the i th habitat.

The generation cycle is completed by migration exchange converting $\{\tilde{\mathbf{x}}_{(i)}\}$ to $\{\mathbf{x}'_{(i)}\}$ by the formula

$$\mathbf{x}'_{(i)} = \sum_{j=1}^N m_{ij} \tilde{\mathbf{x}}_{(j)} = \sum_{j=1}^N m_{ij} \mathbf{f}_{(j)}(\mathbf{x}_{(j)}) \quad (i = 1, 2, \dots, N), \tag{10}$$

where the prime refers to the next generation. These global transformation equations can be written more compactly in terms of the extended vector

$$\mathbf{z} = \langle \mathbf{x}_{(1)}, \mathbf{x}_{(2)}, \dots, \mathbf{x}_{(N)} \rangle$$

and the vector-valued function $\mathbf{F} = \langle \mathbf{f}_{(1)}, \mathbf{f}_{(2)}, \dots, \mathbf{f}_{(N)} \rangle$ which has \mathbf{z} as its argument such that $\mathbf{f}_{(i)}$ acts on $\mathbf{x}_{(i)}$. In this notation, (10) becomes

$$\mathbf{z}' = \mathbf{MF}(\mathbf{z}) \quad \text{abbreviated to} \quad \mathbf{z}' = T(\mathbf{z}). \tag{11}$$

Henceforth, we stipulate that the environmental selection regime

$$F = (f_1, f_2, \dots, f_N) \tag{12}$$

consists of component extended non-epistatic selection regimes based on the same marginal overdominant fitness matrices (that is, the $f_{(i)}$ are each representations of extended non-epistatic viability effects constructed in terms of the same marginal viability matrices) or all $f_{(i)}$ are cases of generalized symmetric selection forms. Moreover, to ease the exposition we will juxtapose the results for the extended non-epistatic and generalized symmetric models as their analyses paraphrase one another.

For all representations of extended non-epistasis with marginal over-dominance at each locus there exists a Hardy-Weinberg (H.-W.) polymorphic fixed point

$$\hat{x} = f_{(i)}(\hat{x}), \tag{13}$$

which is dependent solely on the marginal fitness matrices (i.e. the extended H.-W. polymorphism \hat{x} is independent of the local selection regime; that is, the choices for α in (4). It follows from substituting (13) into (10), since we assume that each $f_{(i)}$ is based on the same marginal fitnesses, that the common frequency vector \hat{x} in each habitat or the geographical population array $\hat{z} = \langle \hat{x}, \hat{x}, \dots, \hat{x} \rangle$ constitutes an equilibrium state of the transformation equation (11). We underscore this fact:

Where extended non-epistasis is operating in each habitat based on the same over-dominant marginal fitness matrices, there exists an extended Hardy-Weinberg polymorphic equilibrium $\hat{z} = \langle \hat{x}, \hat{x}, \dots, \hat{x} \rangle$ exhibiting the same single-deme H.-W. equilibrium.

In the case of generalized symmetric selection, the central state x^* exhibiting equal frequency for all haplotypes is a fixed point for each $f_{(i)}$. We may introduce $z^* = (x^*, x^*, \dots, x^*)$ analogous to \hat{z} and we have:

When a representation of generalized symmetric selection is in force at each habitat of the population range, there is present an extended central multi-deme equilibrium z^ with the property that all haplotype frequencies have equal value in each deme.*

(B) *Stability conditions for the extended Hardy-Weinberg equilibrium \hat{z} and the central equilibrium z^**

The ascertainment of stability for any interior equilibrium follows a classical methodology of non-linear analysis. In this procedure, we compute the local linear approximation to the transformation (11) applicable in a neighbourhood of the equilibrium point p in question. This procedure produces a matrix mapping written $T'(p)$ (see the Appendix) and p is stable if the dominant eigenvalue of $T'(p)$ (designated $\rho(T')$) is in magnitude less than 1. It is usual to employ $1 - \rho(T')$ as an index of the degree (or strength) of stability. All perturbations must reflect a zero net change in haplotype frequencies since the frequencies sum to one. Hence, the perturbation space has dimension

$$R = \left(\prod_{k=1}^n m_k \right) - 1$$

in each deme and correspondingly the global system is NR dimensional. For a general environmental selection regime the discernment of stability for an interior equilibrium requires computation of NR eigenvalues of a matrix of order $NR \times NR$. This may not be feasible, even for reasonable values of N and R . However, under extended non-epistasis based on the same marginal fitnesses across habitats we have available the fact that

the $\mathbf{f}_{(i)}$ share a common set of eigenvectors (independent of i) for their linear approximation matrices L_i about $\hat{\mathbf{x}}$ (14)

(cf. Karlin & Liberman (1978*b*)). We designate the set of common eigenvectors (restricted to the perturbation space) by $\mathbf{u}_1, \mathbf{u}_2, \dots, \mathbf{u}_R$. Let $\Lambda_{\mathbf{u}_r} (= \Lambda_{(r)})$ be the $N \times N$ diagonal matrix whose i th entry (down the diagonal) is the eigenvalue of L_i corresponding to \mathbf{u}_r . The significance of (14) is that it reduces the verification of stability of $\hat{\mathbf{z}}$ to establishing the R inequalities

$$\rho(M\Lambda_{\mathbf{u}_r}) < 1 \quad (r = 1, 2, \dots, R), \tag{15}$$

where $\rho(C)$ designates the magnitude of the dominant eigenvalue of the matrix C . (For a sketch of the proof attendant to (15) see the Appendix). Observe that the evaluations in (15) involve calculating eigenvalues for R matrices each of order N . This is a much reduced effort compared with calculating the eigenvalues for an $NR \times NR$ matrix. We record the conclusion of (15) as:

Result I

(i). *Under extended non-epistasis based on a common set of marginal over-dominant fitness matrices, the condition for stability of the extended H.-W. equilibrium $\hat{\mathbf{z}}$ is*

$$\rho(M\Lambda_{\mathbf{u}_r}) < 1 \quad (r = 1, 2, \dots, R) \tag{15}$$

(see following (14) for the definition of $\Lambda_{\mathbf{u}_r}$).

A completely parallel result applies for generalized symmetric selection forms (the eigenstructure appears in Karlin & Avni (1979)):

(ii) *Under generalized symmetric selection, the condition for stability of the central equilibrium \mathbf{z}^* is*

$$\rho(M\Lambda_{\mathbf{u}_r}) < 1 \quad (r = 1, 2, \dots, R). \tag{15}$$

In view of certain symmetry attributes a number of the conditions of (15) coincide. Moreover, in the case of extended non-epistasis about half the inequalities of (15) are superfluous provided the intrinsic matrices are overdominant.

Example. In the case of two habitats where the fitness matrices are of the form W_p in (5) (generalized symmetric selection two loci, two alleles each),

$$R = \prod_{k=1}^2 m_k - 1 = 3.$$

The expressions for Λ are

$$\Lambda_{(1)} = \begin{pmatrix} \frac{2(1+\alpha_{(1)})}{1+\alpha_{(1)}+\alpha'_{(1)}+\beta_{(1)}} & 0 \\ 0 & \frac{2(1+\alpha_{(2)})}{1+\alpha_{(2)}+\alpha'_{(2)}+\beta_{(2)}} \end{pmatrix},$$

$$\Lambda_{(2)} = \begin{pmatrix} \frac{2(1+\alpha'_{(1)})}{1+\alpha_{(1)}+\alpha'_{(1)}+\beta_{(1)}} & 0 \\ 0 & \frac{2(1+\alpha'_{(2)})}{1+\alpha_{(2)}+\alpha'_{(2)}+\beta_{(2)}} \end{pmatrix},$$

$$\Lambda_{(3)} = \begin{pmatrix} \frac{2(1+\beta_{(1)}-2r\beta_{(1)})}{1+\alpha_{(1)}+\alpha'_{(1)}+\beta_{(1)}} & 0 \\ 0 & \frac{2(1+\beta_{(2)}-2r\beta_{(2)})}{1+\alpha_{(2)}+\alpha'_{(2)}+\beta_{(2)}} \end{pmatrix}.$$

In this example, the recombination parameter r appears only in $\Lambda_{(3)}$. Further, in the case of symmetry between loci with $\alpha = \alpha'$, the first two matrices coincide. Reductions of this sort hold in higher dimensions, particularly in circumstances of multiple alleles.

(C) *How does 'increased' migration affect the stability of the extended H.-W. or central equilibrium?*

A first approach to this question is to consider the dichotomy of no migration versus migration. It follows on the basis of the stability criterion that, *if the H.-W. (central) equilibrium is stable in each habitat with no migration, it remains stable in the global system where any level or form of migration is introduced.* Of course, where the H.-W. (central) equilibrium is stable in some habitats and unstable in others, the stability in the global system depends on the particular migration pattern.

We highlight an example which shows that the H.-W. (central) equilibrium can be *unstable in each habitat when there is no migration, but stable when migration is introduced.* For this purpose, consider a two-locus, two-allele, two-deme system with selection matrices of the generalized symmetric form W_p as prescribed in (5). The relevant eigenvalues are

$$\frac{2+2\beta-4\beta r}{1+\alpha+\alpha'+\beta}, \quad \frac{2+2\alpha}{1+\alpha+\alpha'+\beta}, \quad \frac{2+2\alpha'}{1+\alpha+\alpha'+\beta}. \tag{16}$$

If we set

(i) $\alpha = 1.4, \quad \alpha' = 1.2, \quad \beta = 1.1$

in the first habitat and

(ii) $\alpha = 1.2, \quad \alpha' = 1.4, \quad \beta = 1.1$

in the second habitat, the second and third eigenvalues guarantee instability in the first and second habitats, respectively, when there is no migration. However, if we introduce uniform migration exchange, that is

$$M = \begin{pmatrix} \frac{1}{2} & \frac{1}{2} \\ \frac{1}{2} & \frac{1}{2} \end{pmatrix}, \tag{17}$$

it is readily checked that the central equilibrium is stable despite local instability.

A number of different approaches and concepts of broader scope than the above dichotomy for comparing migration patterns and classifying levels of migration flow are set forth in Karlin (1976). For our present objectives we consider two of these notions positing a partial ordering corresponding to 'more' migration.

One concept prescribes a backward migration matrix M_3 as *more mixing* than M_1 (or M_2) if

$$M_3 = M_1 M_2 \quad (18)$$

with all matrices non-negative, positive definite, and mutually commuting.

This is an expression of the notion that, if individuals migrate twice per generation rather than once, more migration is innate to M_3 than to M_1 . The restriction to positive definite implicates a small to moderate migration flow per generation precluding excessive and strongly oscillatory inter-deme gene dispersal patterns. In particular, it disallows the case with

$$M_1 = M_2 = \begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}, \quad M_3 = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

in which M_3 is clearly less mixing than M_1 and concomitantly for which result II below does not hold.

Subject to the assumptions (18) it has been established (Karlin, 1979) that

$$\rho(M_1 M_2 \Lambda) \leq \rho(M_1 \Lambda), \quad (19)$$

where Λ is a positive diagonal matrix. If recombination is 'natural', then the diagonal elements in Λ_{α} are positive. ('Natural' recombination, in the case of two loci, reduces to the constraint that $0 \leq r \leq \frac{1}{2}$. A formal definition in the multi-locus context appears in Karlin & Liberman (1978a). It encompasses recombination distributions straddled between zero and free recombination. These include the non-interference phenomena of independent crossover events between loci where each recombination has probability not exceeding $\frac{1}{2}$.) We have

Result II

(i) *Consider a multi-deme population subject to an extended non-epistatic selection regime (i.e. every local selection matrix is a version of extended non-epistasis based on the same marginal fitness matrices). Where migration is more mixing in the sense of (18), then the degree of stability of the extended H.-W. equilibrium \hat{z} is increased.*

(ii) *Where migration is more mixing in the sense of (18), then, under generalized symmetric selection, the conditions for stability of the central equilibrium are less stringent.*

For a Deakin (1966) migration pattern of the form $M = (1 - \alpha)R + \alpha I$, where R is a rank one migration matrix, a reduced homing propensity α provides a *more mixing* (in the sense of (18)) migration structure. Thus, in this example, decreasing the homing rate enhances the opportunities for stability of the H.-W. polymorphic equilibrium. Actually, the fact that with an increased homing rate the degree of stability of the H.-W. polymorphic equilibrium is diminished is a general affirmation applicable to all migration structures. This conclusion rests on the following mathematical fact:

The dominant eigenvalue

$$\rho([(1-\alpha)M + \alpha I]\Lambda) \text{ increases as } \alpha \text{ increases } (0 < \alpha < 1), \quad (20)$$

where M is an arbitrary migration matrix and Λ is any positive diagonal matrix. The proof of (20) is quite recondite (Karlin, 1979). Accepting the assertion of (20), we infer

Result III

(i) *Under extended non-epistatic selection based on the same set of marginal over-dominant fitness matrices in each habitat and a natural recombination-segregation distribution, the stability of the extended H.-W. equilibrium is facilitated by a uniform decrease in homing over deme sites.*

(ii) *Under generalized symmetric selection and natural recombination rates, the stability of the central equilibrium is enhanced with a uniform decrease in homing.*

The migration form $(1-\alpha)M + \alpha I$ can be construed as a mixture of the pattern M and a *uniform* rate of homing with respect to all deme sites. In the situation of *variable* homing rates such that the degree of homing varies with habitat location, the proposition corresponding to (20) is not a valid principle and concomitantly Result III may not hold.

(D) *What is the effect of changing the recombination distribution on the stability of the central or H.-W. equilibrium?*

In the case of two loci, recombination is fully delimited by a single parameter r . We can say unambiguously that r_1 involves more recombination than r_2 if $r_1 > r_2$; restricted to the range of 'natural' recombination, $0 \leq r \leq \frac{1}{2}$. (Many results do not hold for $r > \frac{1}{2}$.) When there are more than two loci, a single parameter is no longer sufficient for the recombination process. In fact, in the presence of three loci the general recombination-segregation distribution is characterized by three parameters, and four loci require seven parameters. The notions of zero and free recombination are well defined, but what represents 'natural' recombination between those two levels is a subtle affair. Also, the notion of 'more recombination' is not automatic. These problems are considered in Karlin & Liberman (1978a). The reader may bear in mind the two-loci case for the subsequent results although they are valid in the context of multiple loci.

It has been established for extended non-epistatic selection and/or generalized symmetric selection that the diagonal values appearing in Λ_n are non-increasing as recombination 'increases'. 'Natural' recombination assures that the eigenvalues are non-negative. Recall that $\Lambda_1 < \Lambda_2$ (this inequality is meant componentwise) entails

$$\rho(M\Lambda_1) < \rho(M\Lambda_2). \quad (21)$$

To sum up:

Result IV

(i) *Under extended non-epistatic selection in each habitat based on the same over-dominant marginal fitness matrices and natural recombination, the degree of stability of the extended H.-W. equilibrium is enhanced by 'more recombination'. Also,*

(ii) *Under generalized symmetric selection, the stability of the central equilibrium is facilitated by 'more recombination'.*

(E) *What is the comparative influence of spatially and/or temporally varying selection regimes on the stability of the H.-W. central equilibrium?*

We are not able to resolve this question in general terms, but discussion of the following case is informative. Consider two representations of a two-locus two-allele viability model which are simultaneously extended non-epistatic and generalized symmetric; to wit, the classical symmetric additive and symmetric multiplicative non-epistatic models (see (3)). The corresponding fitness matrices are

$$W_A = W^{(1,0)} + W^{(0,1)} = \begin{pmatrix} 2 & 1 + \alpha & 1 + \alpha & 2\alpha \\ 1 + \alpha & 2 & 2\alpha & 1 + \alpha \\ 1 + \alpha & 2\alpha & 2 & 1 + \alpha \\ 2\alpha & 1 + \alpha & 1 + \alpha & 2 \end{pmatrix} \tag{22a}$$

and

$$W_M = W^{(1,1)} = \begin{pmatrix} 1 & \alpha & \alpha & \alpha^2 \\ \alpha & 1 & \alpha^2 & \alpha \\ \alpha & \alpha^2 & 1 & \alpha \\ \alpha^2 & \alpha & \alpha & 1 \end{pmatrix} \tag{22b}$$

based on the marginal fitness matrices

$$W^{(1)} = W^{(2)} = \begin{pmatrix} 1 & \alpha \\ \alpha & 1 \end{pmatrix} \quad (\alpha > 1).$$

The presence of the single parameter α suggests its use as a natural index of selection intensity.

We examine first the effect of perturbing α in a single habitat where either W_A or W_M is in force. Because $\alpha > 1$ (which is necessary for marginal overdominance), inspection of (16) reveals that we need consider only one eigenvalue (which depends on r and α) for determining the stability of the H.-W. polymorphic equilibrium.

In the additive case, this eigenvalue is

$$\frac{2 + (1 - 2r)(2\alpha)}{2 + 2\alpha}. \tag{23}$$

It is directly verified that over the range $\alpha > 1$ (synonymous with intrinsic overdominance) the quantity (23) is smaller than 1 and monotonically decreasing in r and α .

The multiplicative case is not as simple. The relevant eigenvalue is

$$\frac{[2 + (1 - 2r) 2\alpha^2]}{(1 + \alpha)^2}. \tag{24}$$

The behaviour of this quantity as a function of r and α is depicted graphically in Fig. 1.

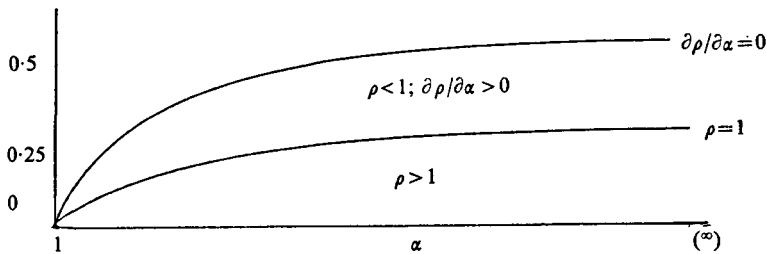


Fig. 1. For the multiplicative model, the behaviour of ρ in (24) is displayed as a function of r and α ; $\partial\rho/\partial\alpha = 0$ is simply the curve $r = (\alpha - 1)/2\alpha$; the condition $\rho = 1$ gives rise to the curve $r = (\alpha - 1)^2/4\alpha^2$.

We infer on the basis of Fig. 1 and the previous discussion that in a single-deme population, where either the selection regime W_A or W_M is in force, that increasing selection intensities can never cause the establishment of stability of the H.-W. (central) equilibrium. This is trivial in the additive case since stability always ensues provided the marginal fitness matrices are overdominant. However, stability can be lost in the multiplicative case where $r < \frac{1}{4}$.) In contrast, however, in the context of a multi-deme population involving only additive or multiplicative non-epistatic selection expression (of the forms (22)) in each habitat, then suitably increasing selection intensities locally can cause either the establishment or the abrogation of stability of the H.-W. (central) equilibrium without any restriction on the local state of the recombination rates.

(F) *Can we specify some meaningful and accessible necessary and/or sufficient conditions for a stable polymorphism?*

An immediate consequence of the stability criterion (15) provides that marginal overdominance and enough positive recombination are necessary in the establishment of a stable extended H.-W. polymorphism in the multi-deme case. This conclusion ensues as an easy extension of the collateral necessary conditions in a single deme model. We state this formally as

Result V

Marginal overdominance and enough positive recombination are essential (in particular, marginal overdominance and free recombination always suffice) for the maintenance of a stable H.-W. polymorphism under an extended non-epistatic selection regime with any migration structure.

Remark

There is no analogue to Result V for generalized symmetric selection. Marginal fitnesses do not exist, and the central equilibrium can be either stable or unstable with either zero or free recombination.

(G) *When can we reduce the multi-deme selection–migration dynamics and/or equilibrium structure to an equivalent single deme?*

We treat this problem in the context of the stability analysis for the Levene (1953) population subdivision model. Result IV describes the relative stability requirements of the central equilibrium when the recombination rate is concordantly either increased or diminished throughout the population range (i.e. over all habitats). However, there are circumstances where recombination could increase over part of the population range and decrease over a different part of the population range.

A case of interest has the same selection regime operating in each deme, but different local recombination rates. In the context of the Levene migration pattern which is of rank 1, the criterion for stability of the central (H.–W.) polymorphism is that for a single deme which has the recombination rate collapsed to a weighted (with respect to deme sizes) arithmetic mean of the local recombination rates. This is because the recombination parameter occurs linearly in the expression of the eigenvalues and for the Levene migration pattern the criterion for stability is a weighted arithmetic mean of the local corresponding eigenvalues.

If the migration pattern is not of the special Levene form the criteria do not reduce to an averaging of the local r 's. Assuming that the migration flow is small to moderate (formally this means that the backward migration matrix is positive definite) there is available an expeditious sufficient condition (cf. Karlin, 1976) for instability. A workable sufficient criterion for *stability* is not available as yet.

Another question of interest concerns a system of demes each carrying a version of the extended non-epistatic selection regime (3) where the parameters α , β , γ and δ may vary with habitat site. We seek to compare and/or reduce the conglomerate (multi-deme) selection structure to a single-deme model involving a case of the extended non-epistatic selection regime.

This question is tractable if the migration pattern is the special Levene subdivision structure and recombination is independent of the local environmental state in the population range. For concreteness, we consider the symmetric additive and multiplicative non-epistatic selection patterns where the underlying marginal fitness matrix is given by

$$W^{(1)} = W^{(2)} = W = \begin{pmatrix} 1 & \alpha \\ \alpha & 1 \end{pmatrix}, \quad \alpha > 1$$

(see (2)).

A particular generalized non-epistatic selection pattern of interest is

$$W = \frac{1}{2} W^{(1,1)} + \frac{1}{2} \left[\frac{1}{2} W^{(1,0)} + \frac{1}{2} W^{(0,1)} \right].$$

The first term on the right conveys multiplicative non-epistasis and the expression in brackets corresponds to additive non-epistasis (cf. (22)). As noted earlier, following (22), we may confine attention to a single perturbation eigenspace. Rearrangement of (16), using (23) and (24), gives

$$\frac{1}{\frac{1}{2}(1+\alpha)^2 + \frac{1}{2}(2+2\alpha)} \left[\frac{1}{2}(1+\alpha)^2 \left(\frac{2+(1-2r)2\alpha^2}{(1+\alpha)^2} \right) + \frac{1}{2}(2+2\alpha) \left(\frac{2+(1-2r)2\alpha}{2+2\alpha} \right) \right] < 1$$

as the condition for stability. This may be written in more suggestive notation in the form

$$\frac{1}{\bar{w}} \sum_{i=1}^N c_i w_i \lambda_i,$$

where $\sum_{i=1}^N c_i = 1$, w 's are fitness terms corresponding to the components of (3),

$$\bar{w} = \sum_{i=1}^N c_i w_i,$$

and $\{\lambda_i\}$ comprise the eigenvalues of the local linear approximations at the central H.-W. equilibrium.

A little reflexion provides that this is the criterion for stability under hard selection with a Levene migration pattern for deme sizes c_i . This conclusion is justified because the net change of a perturbation is the weighted average of the local changes. We used the additive and multiplicative selection schemes solely for illustrative purposes; any generalized non-epistatic selection pattern can be decomposed in this manner. This points up that either hard selection is a more natural concept than soft selection in this context or the generalized non-epistatic selection patterns should be appropriately weighted to engender soft selection.

Remark

We noted previously that all representations of extended non-epistatic selection patterns based on the same marginal fitness matrices share the same Hardy-Weinberg equilibrium. Furthermore, in a system of demes any such common equilibrium persists as an equilibrium independent of the migration structure. This should not be construed to imply that these common H.-W. equilibria are the only polymorphic equilibria. In fact, the example of one-locus symmetric underdominance (e.g. Bazykin, 1972; Karlin & McGregor, 1972, p. 192) shows that a multi-deme population under small migration flow can have other nonsymmetric equilibria. Symmetric underdominance is a generalized symmetric selection pattern and is assuredly generalized non-epistatic when there is only one locus.

3. DISCUSSION

The study of multi-deme population genetic systems has concentrated mostly on the ascertainment of conditions for a protected polymorphism, while classifications and direct analysis pertinent to stable polymorphic configurations are uncommon. Some exceptions occur pertaining to delineations of clinal morphotones (e.g. Slatkin, 1973; Nagylaki, 1976; Karlin & Richter-Dyn, 1976) and with respect to the characterizations of gene frequency patterns in the Levene subdivision model (Karlin, 1977). These latter works are restricted to one-locus two-allele traits.

This paper seeks to shift the focus of multi-deme population genetic dynamics from the study of boundary equilibria relevant to the ascertainment of conditions for a protected polymorphism and the problem of initial increase upon introduction of rare alleles to the analysis of internal equilibrium forms. This work also enlarges the scope to include multiple-locus multiple-allele systems.

In our models the representation of the extended non-epistatic selection structures (based on the same marginal selection coefficients) or generalized symmetric selection regimes can differ with habitat site reflecting spatial and temporal variations in limiting resources, primary predators, climatic conditions, geographical terrain, etc.

Our results are structurally stable, i.e. qualitatively invariant under small perturbations on the parameters of the models. In this perspective we have concentrated on aspects of degree of stability of the central or H.-W. equilibrium rather than stability versus instability as a dichotomy. The impreciseness of parameter estimates from nature and fluctuations due to statistical sampling further dictate that we emphasize the qualitative conclusions of the analyses derived from available analytic formulae.

A number of the findings extend the single-deme results. These include:

(i) *Increases in the recombination frequency in one or several demes strengthens the stability of the H.-W. and central equilibria.*

(ii) *Stability in each deme without migration implies stability in the system with any form of migration superimposed.*

Other of the determinations bear no analogue in the case of a single deme. One key result in this vein affirms:

(iii) *An increased level of migration mixing entails more opportunities for stability of the H.-W. and central equilibria.*

Finally, several of our analyses contrast the single-deme with the multi-deme case. Specifically,

(iv) *Instability of the H.-W. (or central) equilibria in each deme when isolated does not imply instability of this common equilibrium in the system coupled by migration.*

(v) *Under extended non-epistasis some cases of increasing selection intensity can abrogate stability.*

Another facet of this work was the investigation of circumstances under which the analysis of the central polymorphic equilibrium in the multi-deme formulation can be reduced to an 'equivalent' single-deme version. This is rarely possible except for the special Levene subdivision structure. In this case it is possible if the recombination rate is allowed to differ between habitats; and also if recombination is the same in all habitats, but selection expression varies with deme site maintaining throughout representations of either extended non-epistasis or generalized symmetric selection.

A final matter is the comparison of these results concerning stability of internal H.-W. or central equilibrium with known criteria for 'protection'. Protection in each deme implies protection in the system coupled by migration in contrast to (iv) above because instability of fixation states is studied in the context of one dimensional perturbation spaces. We established that although 'more migration diminishes the chances for protection, in striking contrast it increases the degree of stability of the H.-W. and central equilibria. This result may appear offhand internally contradictory. We can merely conclude that the phenomenon of protection and the stability of central equilibria are not synonymous realizations. In

particular, this means that increased migration flow does not cause a shift from circumstances of stable fixation states to stable H.-W. or central equilibria outcomes (or vice versa). Indeed, there exist other categories of polymorphic equilibrium configurations which are stable with low migration and unstable with high migration.

The nature of these other internal equilibria is the subject of a later paper in this series.

APPENDIX

We sketch here the method for studying the stability of an equilibrium in the case where all the linear approximations to the local fitness functions about the equilibrium share the same eigenvectors. In particular, this case includes the H.-W. polymorphic equilibrium of the extended non-epistatic model and the central equilibrium of the generalized symmetric model discussed in the text.

Let the eigenvectors of the linear approximations (restricted to the perturbation space) be designated by

$$\mathbf{u}_1, \mathbf{u}_2, \dots, \mathbf{u}_K.$$

Then the perturbation in the *i*th deme can be written as

$$\sum_{j=1}^K \alpha_{ij} \mathbf{u}_j$$

and, if we designate the *i*th local linear approximation by L_i , selection changes the perturbation to

$$L_i \left(\sum_{j=1}^K \alpha_{ij} \mathbf{u}_j \right) = \sum_{j=1}^K \alpha_{ij} L_i(\mathbf{u}_j) = \sum_{j=1}^K \alpha_{ij} \lambda_{ij} \mathbf{u}_j$$

by the linearity of L_i , where λ_{ij} is the eigenvalue of L_i associated with \mathbf{u}_j . After selection has acted in each habitat, migration changes the gamete frequencies to

$$\sum_{j=1}^m m_{ij} \left(\sum_{k=1}^K \alpha_{jk} \lambda_{jk} \mathbf{u}_k \right) = \sum_{k=1}^K \mathbf{u}_k \sum_{j=1}^m m_{ij} \lambda_{jk} \alpha_{jk}$$

in the *i*th deme. Thus,

$$\alpha'_{ij} = \sum_{k=1}^m m_{ik} \lambda_{kj} \alpha_{kj},$$

which is independent of α_{kl} , $l \neq j$. Thus, the coefficient of the *k*th eigenvector in the *i*th habitat depends solely on the coefficients of that eigenvector in all the demes in the previous generation.

The condition for instability of the equilibrium is that the largest eigenvalue of the linear approximation is greater than one. We have just shown that all eigenvectors of the multi-deme transformation are concatenations of multiples of an eigenvector for the single-deme transformation (i.e. of the form $(\eta_{1j} \mathbf{u}_j, \eta_{2j} \mathbf{u}_j, \dots, \eta_{nj} \mathbf{u}_j)$). Therefore, a necessary and sufficient condition for instability is that $\alpha < M \Lambda_{\mathbf{u}_k} \alpha$ (component-wise) for some non-negative α , where $\Lambda_{\mathbf{u}_k}$ is the diagonal matrix with

entries λ_{jk} which, in the generic case when all recombination frequencies are less than $\frac{1}{2}$, are non-negative. This is the condition which we stated in the text:

$$\rho(M\Lambda_n) > 1 \quad \text{for some eigenvector } \mathbf{u}.$$

The condition for stability is the negation, i.e.

$$\rho(M\Lambda_n) < 1 \quad \text{for all relevant eigenvectors } \mathbf{u}.$$

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