Population Subdivision and Selection Migration Interaction*

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INTRODUCTION

Environmental and/or geographical variation in selection patterns and its coupling with gene flow are considered vital ingredients in speciation and differentiation. Recent literature has witnessed increasing emphasis on the formulation and analysis of a hierarchy of models with aim to understand in more precise terms the interaction between spatial and temporal selection variation and population structure.

In the case of finite populations, numerous authors investigated the effects of some forms of population subdivision and migration patterns <u>without selection</u>, with respect to rates of allelic substitution, rates of approach to homozygosity and correlations in gene frequency maintained by linear external pressures. Notable contributors in this vein include Wright (1943); Malécot (1948), (1951), (1959), (1967); Moran (1962); Kimura and Weiss (1964); Karlin (1968, Chap.2); Bodmer and Cavalli-Sforza (1968); Maruyama (1970), (1972); and others. A number of special deterministic migration models coupled with local differential viability forces were set forth by Levene (1953), Prout (1968), J. Maynard Smith (1970), Strobeck (1974), Christiansen (1974), Deakin (1966), (1968) among others. We have cited theoretical analysis, but needless to say, there is

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voluminous descriptive and taxonometric studies relevant to the above theme.

Several concepts and measures concerning environmental heterogeneity and the degree of migration mixing in relation to the existence of "protected polymorphisms" will be examined in this work. We will report a number of general findings pertaining to a geographical population genetics structure involving almost no restrictions on the parameters of the model.

1. A MULTI DEME POPULATION MODEL SUBJECT TO MIGRATION AND SELECTION FORCES

A population is distributed over a finite region generally composed of separate breeding demes (e.g., geographical or ecological habitats or niches) P_1 , P_2 ,..., P_n . Successive generations in the population are discrete and non-overlapping. It is assumed throughout this work that each subpopulation P_i is of large size so that the effects of genetic drift are inconsequential. We focus principally on a trait with two possible alleles labelled <u>A</u> and <u>a</u>. The action of selection, migration and mating can be coupled in a variety of forms. A number of the concepts and structures pertinent here are now highlighted and refined.

(i) Spatial selection gradients

We assume that viability selection operates independently in each deme. The transformation of gene frequency under local selection in deme $\boldsymbol{\rho}_i$ is determined by the relation $\tilde{\xi} = f_i(\xi)$ (1.1)^{*} such that if ξ is the A-frequency in $\boldsymbol{\rho}_i$ then after the

For a multi allele system the transformation would be described by a vector function $\underline{f}_i(\underline{\xi})$ where $\underline{\xi}$ is the vector allelic frequency state in locality $\boldsymbol{\varrho}_i$.

action of natural selection, the resulting A-frequency is ξ . Generally, $f_i(\xi)$ is continuous and monotone increasing. Also, we stipulate throughout this work that $f_i(0) = 0$ and $f_i(1) = 1$ signifying that selection forces maintain a pure population composition. Thus, in this formulation mutation events are ignored, i.e., new mutant forms arising in the time frame under consideration cannot be established.

An important choice for $f_i(x)$ arising from the classical diploid one-locus two-allele viability model has the form

$$f_{i}(x) = \frac{(1+\sigma_{i})x^{2} + x(1-x)}{1+\sigma_{i}x^{2}+s_{i}(1-x)^{2}}$$
(1.2)

where the viability parameters of the genotypes are as listed

In the corresponding haploid situation, we would take $f_i(x) = \frac{\sigma_i x}{\sigma_i x + s_i (1-x)}$. It is generally unnecessary to spell out explicitly the mating system operating in each deme (locality) as the consequences of mating and selection are implicitly cou-

pled and summarized by the local selection die implicitly out pled and summarized by the local selection functions $f_i(x)$. The choice (1.2) for $f_i(x)$ would, of course, come about from local random mating with standard viability selection in a diploid setting. Other determinations for $f_i(x)$ can be generated by superimposing forms of frequency dependent selection, or selection induced on a single locus when part of a multi locus system or other combined mating and selection forms.

The environmental or geographical selection gradient \mathcal{E} is characterized by the array $\mathcal{E} \approx \{f_1(x), \dots, f_n(x)\}$.

The extent of environmental heterogeneity is reflected by

the differences existing among the components of \mathcal{E} . Where all $f_i(x)$ are identical then unambiguously we speak of a homogeneous environmental selection background. It is still largely unknown how to relate spatial and temporal ecological parameters and selection gradients. Our investigation is mainly in terms of fitness values and we concentrate on achieving qualitative conclusions for different forms of fitness arrays. Specifically, our discussion focuses on concepts involving comparisons of degrees and quality of environmental fitness heterogeneity interrelated with the migration structure.

A general tenet commonly stated is that environmental variability or heterogeneity in the selection gradient is substantially correlated with the proliferation of polymorphism and this is claimed to be the case largely independent of the rate of migration. There are some who contest this as a universal dictum. The above theme is too general and several terms need clarification. By what criteria is a prescribed environmental selection gradient considered more "heterogeneous" or "variable" than another environmental selection form? What are meaningful means for measuring degrees of variability in both ecological and genetic (fitness) terms? The appropriate concepts must take proper account of the migration structure coupled to the spatial selection gradient. We address these questions in Section 2.

(ii) Local relative population sizes

We assume that the individual demes have a characteristic population size at an appropriate stage. Various possibilities have been proposed of which we indicate two : (a) The relative numbers of offspring contributed from deme

i to the total population is c_i , $(c_i > 0, \sum_{i=1}^n c_i = 1)$ constant over successive generations.

(b) The relative size c_i reflects the proportion among the whole adult population located in deme P_i after migration.

The c_i can be construed as a constant expression of "interdeme selection" not altered by the specific genetic composition or local selection forces.

(iii) Hard and soft selection

In a multi deme population there are two principal opposite models relating the interaction between selection and local population size, those of <u>hard</u> and <u>soft</u> selection; this distinction was introduced by Wallace (1968). See also Dempster (1955).

Soft selection stipulates that local viability selection does not change the relative proportions of the deme populations in passing from the offspring to the adult stage. This is the most commonly applied model where each subpopulation carries a constant characteristic fraction of adult individuals in every generation. On the other extreme, hard selection stipulates that each local population after mating includes a characteristic fraction, independent of the generation time, of the total population. With the operation of selection at deme P_i we postulate the existence of $W_i(x_i)$, a function of the A-gene frequency, x_i , such that $c_i W_i(x_i)$ measures the relative population size resulting from the effects of local differential selection. This conversion can be viewed as a local density regulating factor in the process.

For the choice of (1.2) a common determination has $W_{i}(x) =$

the mean fitness function in P_i , viz., $W_i(x) = 1 + \sigma_i x^2 + s_i (1-x)^2$ where x is the A-gene frequency.

(iv) Migration structure

A basic ingredient in the migration pattern is the prescription of the forward migration matrix

$$\Gamma = \left| \left| \mu_{ij} \right| \right|_{i,j=1}^{n}$$
(1.3)

where μ_{ij} is the a-priori probability per generation that an individual of deme i will migrate to deme j . Of course

$$\mu_{ij} > 0 \text{ and } \sum_{j=1}^{n} \mu_{ij} = 1 , i = 1, 2, ..., n$$

It is worthwhile to highlight a number of old and new examples of relevant migration patterns.

(a) Levene Population Sub-Division Model. In the early literature, two main dispersal and migration patterns were considered. The Island Model introduced by S. Wright divides the population into panmictic units each receiving an equal proportion of the total population. The Levene population subdivision model (1953) slightly generalizes the Wright model: a population after mating at random distributes itself into n separate patches, a fraction c; going into the i-th patch. Then selection occurs according to the state of the environment in each patch. Notice after migration the subpopulations involve the same mixture of the whole population for each generation. (It has been suggested that this formulation may be appropriate for a species whose numbers are regulated within each of the separate patches but not on the whole population.) For this case

$$\mu_{ij} = c_{j} \quad \text{independent of } i \quad (1.4)$$

(b) <u>Stepping Stone Mode.</u> A second class of classical migration patterns are based on the principle of <u>isolation by</u> <u>distance</u> where the degree of migration diminishes with the "distance" from a given deme. An extreme, widely applied case is the <u>stepping stone mode</u>. Here the demes occur in an ordered (linear) series. In each generation, a fraction m $(m \leq \frac{1}{2})$ of each deme is exchanged with each contiguous deme as depicted.

The stepping stone mode of migration including two and higher dimensional versions has been widely used in the study of geographical genetic models <u>without selection</u> by Malécot [1948], [1951], [1959]; Kimura and Weiss [1964]; Fleming and Su [1974]; Maruyama [1972], and others.

(c) <u>Non-homogeneous Stepping Stone Mode.</u> Implicit in the stepping stone mode of migration with a constant rate m is the assumption that the demes have essentially equal sizes. Where the relative sizes of the demes differ then the rates of gene flow between neighboring demes are generally not equal or they may have intrinsic unequal rates of migration in reciprocal directions. In this setting the appropriate analog of (1.5) involves general non-constant local migration parameters μ_i , $\mu_i^{'}$ such that

$$\mu_{i,i-1} = \mu'_{i}, \quad \mu_{i,i+1} = \mu_{i} \quad \text{and} \quad \mu_{ii} = 1 - \mu_{i} - \mu'_{i}, \quad (1.6)$$
$$i = 2, 3, \dots, n-1$$
$$\mu_{1,1} = 1 - \mu_{1}, \quad \mu_{1,2} = \mu_{1}; \quad \mu_{n,n-1} = \mu'_{n}, \quad \mu_{nn} = 1 - \mu'_{n}.$$

We will refer to the migration pattern (1.6) as a "Nonhomogeneous stepping stone migration mode".

Other specifications of migration rates depending on distance were considered by Malécot [1959], for models with no differential selection and in practical contexts by Jain and Bradshaw [1966].

As noted by Wright himself [1943], the island model is rather unlikely to be realized in nature whereas the isolation by distance model is more realistic and likely to be interesting.

(d) <u>Circulant Model.</u> If the demes occur in a circular pattern rather than linear (like around the base of a central mountain or along the shores of a lake), then the homogeneous stepping stone migration mode has the pictorial form



A general circulant isolation by distance migration matrix has the form $\mu_{ij} = a_{|i-j|}$.

(e) <u>A Homogeneous Homing Model.</u> An appealing extension of the island model was put forth by Deakin [1966], [1968], [1972] and studied further by Christiansen [1974]. The migration matrix is

$$\mu_{ij} = \alpha c_{j} \qquad ; i \neq j$$

$$\mu_{ii} = 1 - \alpha + \alpha c_{i} \qquad ; i, j = 1, \dots, n . \qquad (1.7)$$

The components in (c_1, c_2, \ldots, c_n) constitute the usual relative deme sizes while the parameter α can be regarded as a measure of the dispersal rate of organisms in a local deme; Maynard Smith [1970]. Other meaningful interpretations of α are possible.

(f) <u>Non-homogeneous Homing Model.</u> We will develop in Karlin [1976] a number of results for a migration pattern generalizing (1.7) to the form

$$\mu_{ij} = \alpha_{i}c_{j} \qquad ; i \neq j$$

$$\mu_{ii} = 1 - \alpha_{i} + \alpha_{i}c_{i} \qquad (1.8)$$

where the rate of homing differs over the respective demes. Already certain results inferred by Christiansen [1974] on the basis of the model (1.7) do not apply for (1.8) indicating that the interactions of migration and selection are more recondite in the presence of a non-uniform homing rate.

(g) <u>A Hybrid Island and Isolation by Distance Model.</u> Another migration pattern in the spirit of (1.8) amenable to analysis has the form

$$\mu_{ii} = 1 - \alpha_{i}$$
 , $i = 1, 2, ..., n$

$$\mu_{ij} = \begin{cases} \alpha_{i}c_{j}, \ 1 \le i \le K, \ K+1 \le j \le n & \sum_{j=K+1}^{n} c_{j}=1, \ c_{j}>0 \\ \alpha_{i}d_{j}, \ K+1 \le i \le n, \ 1 \le j \le K, \ \sum_{j=1}^{K} d_{j}=1, \ d_{j}>0 \end{cases}$$
(1.9)

$$\begin{split} & \mu_{\texttt{ij}} = 0 \quad \texttt{otherwise.} \\ & \texttt{Thus, the demes divide into two groupings, } \boldsymbol{\mathscr{G}}_1 = \{\boldsymbol{\mathscr{P}}_1, \boldsymbol{\mathscr{P}}_2, \dots, \boldsymbol{\mathscr{P}}_K \} \\ & \texttt{and } \boldsymbol{\mathscr{G}}_2 = \{\boldsymbol{\mathscr{P}}_{K+1}, \dots, \boldsymbol{\mathscr{P}}_n \} \quad \texttt{such that an organism either does} \end{split}$$

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not move or when migrating it passes from its group to the other group with a fixed probability of relocation in a specified deme independent of its birthplace. This model and its extensions to r groupings is developed in Karlin [1976]. These can be regarded as hybrid patterns of island and isolation by distance models.

(h) <u>Atoll Migration Pattern</u>. Another migration scheme of some interest has the form

$$\Gamma = \begin{pmatrix} 1 - \mu_{1} & , \mu_{1} & 0 \dots 0 \\ 1 - \mu_{2} & , 0 & \mu_{2} \\ \vdots & & \\ 1 - \mu_{n-1} & , 0 \dots 0 & \mu_{n-1} \\ 1 & , 0 \dots 0 & 0 \end{pmatrix}$$
(1.10)

(v) <u>Backward Migration Matrices.</u> In order to write the appropriate transformation relations connecting gene frequencies in successive generations and to take proper account of a conglomeration of factors including variable deme sizes, the effect of differential viability selection on deme size and gene flow, the concept of the backward migration matrix is indispensable. The elements of the backward migration

matrix $M = ||m_{ij}||$ after selection and migration specify m_{ij} = the fraction in the i-th deme originating (1.11)

from the j-th deme in a given generation. We indicate the calculation of (1.11) for the model where selection precedes migration and following Christiansen [1974], we do this separately in the circumstances of <u>soft</u> and <u>hard</u> selection. As pointed out in paragraph (iii) selection converts the relative population sizes into

$$c_{i} \rightarrow c_{i}^{*} = c_{i} \qquad (\text{soft selection})$$

$$c_{i} \rightarrow c_{i}^{*} = \frac{c_{i}W_{i}(x_{i})}{\sum\limits_{k=1}^{n} c_{k}W_{k}(x_{k})} \qquad (1.12)$$

$$i = 1, 2, \dots, n,$$

where $\{W_i(x)\}$ usually stand for the local fitness functions. An elementary calculation involving conditional probabilities gives

$$m_{ij} = \frac{c_{j}^{*} \mu_{ji}}{\sum_{k=1}^{n} c_{k}^{*} \mu_{ki}} , \quad i,j = 1,...,n . \quad (1.13)$$

It is important to emphasize that with hard selection the backward migration matrix depends on the specific genic population composition at hand while in the situation of soft selection $M = ||m_{ij}||$ is independent of the gene frequency configuration. Equivalently, in hard selection differential viability directly influences the migration structure but not with soft selection.

Where all demes are of equal size and $\Gamma = ||\mu_{ij}||$ is symmetric (as in the homogeneous stepping stone model) then for soft selection $M = \Gamma$ showing in this case that the backward and forward matrices coincide. In this case μ_{ij}

reflects the proportion of population exchange between demes i and j.

(vi) <u>The Influence of the Timing of Migration and Selec-</u> <u>tion Forces.</u> The discussion of paragraph (v) was predicated on the operational order of the genetic forces in each generation being

(followed by) mating and selection — migration. (1.14) Effectively, migration occurs at the adult stage but prior to mating in the next generation.

Another formulation also relevant in the workings of certain natural populations would have the order of application of selection and migration reversed; viz.,

migration — selection and mating. (1.15) For the model of (1.15) the offspring (infant) rather than the the adult population migrates (e.g., as in seed and pollen dispersal) and subsequently differential viability is in force.

Selection generally has two major components reflecting fertility and viability effects so that for some natural populations, either model (1.14) or (1.15), or a mixed model involving possibly two stages of migration, may be appropriate.

The inherent differences to the timing of migration and selection effects are well contrasted by writing out the transformation equations relating gene frequencies in two successive generations.

(vii) Transformation Equations of the Frequency States. Let x_i denote the frequency of type A in deme P_i at the start of a generation and x'_i the frequency for the next generation. Consider first the model of (1.14). The stan-

dard global transformation equations connecting $\underline{x} = (x_1, \dots, x_n)$ to $\underline{x}' = (x_1', \dots, x_n')$ over two successive generations is given by

$$x'_{i} = \sum_{j=1}^{n} m_{ij}f_{j}(x_{j})$$
, $i = 1, 2, ..., n$ (1.16)

where $||m_{ij}||$ is the backward migration matrix computed as in (1.13). Recall that in the hard selection model m_{ij} also depends on the frequency state \underline{x} .

Where the timing of migration and selection operate in reverse order as in (1.15), the transformation equations read as

$$x'_{i} = f_{i} \left(\sum_{j=1}^{n} m_{ij} x_{j} \right) , \quad i = 1, 2, ..., n .$$
 (1.17)

For the problem concerning the existence of a protected polymorphism the models (1.16) and (1.17) are equivalent, see Bulmer [1972]. Pertaining to the characterization of the actual established equilibria, the timing has a significant influence, e.g., see Karlin and Richter-Dyn [1976].

2. OBJECTIVES, COMPARISONS AND SOME RESULTS FOR SELECTION MIGRATION INTERACTIONS

In the previous section a number of the key concepts and structures underlying a broad class of multi deme population models of n demes subject to local selection forces and migration flow were delineated. The main factors are the following:

(I) The environmental selection gradient described by the collection of local selection functions

$$\{f_1(x), \dots, f_n(x)\}$$
 (2.1)

obeying the conditions of paragraph (i), Section 1.

(II) The migration pattern characterized by the parameters of the forward and backward migration matrices, respectively $\Gamma = ||\mu_{ij}||$, $M = ||m_{ij}||$ (see (1.3) and (1.11)). (2.2)

(III) The relative deme sizes given by the vector $\underline{c} = (c_1, c_2, \dots, c_n)$, $c_i > 0$, $\Sigma c_i = 1$. (2.3)

In general terms, the desired objective is to evaluate qualitatively and quantitatively the influence of the factors (I), (II) and (III) separately and in combination on the evolutionary dynamics and equilibrium behavior of a multi deme population obeying the transformation law (1.16). We will consider two categories of problems bearing on the existence of polymorphisms and variability in populations: (a) In Section 3 quite precise conditions in terms of the

parameters (2.1), (2.2) and (2.3) are set forth guaranteeing the persistence of the alleles <u>A</u> and/or <u>a</u>. The property of persistence of allele A (not going ultimately extinct) even when initially rare is now commonly called <u>protection of the A-allele or A-protection</u>. This is intimately connected to the ascertainment of the <u>initial increase</u> of a new allele. These approaches helping in the study of certain population genetics models is now quite classical and widely used.

The maintenance of a protected polymorphism is more than the existence of a "stable polymorphic equilibrium" since fixation of any allele is precluded as a realizable event from any starting frequency state, assuming of course all types are initially present (i.e., protection holds under all initial conditions). With a protected polymorphism there may be several stable equilibria states (this is already the case even for the Levene population subdivision model) or conceivably oscillatory behavior between several polymorphic

states is induced.

In order to make quantitative comparisons we have introduced (in Section 3) a number of <u>measures of environmental</u> <u>heterogeneity</u> for relating alternative spatial selection gradients. We will also propose two modes for classifying <u>intensity of migration mixing</u> (and/or degrees of relative isolation) among the breeding units. The implications for "A-protection" of the interactive effects between selection and migration forces are discussed in a variety of contexts throughout this paper.

(b) A more difficult problem is the determination and

characterization of the possible stable polymorphic states in the multi-deme framework. A description of the qualitative dependence of all the stable equilibria on the environmental components embodied in (2.1)-(2.3) would be of relevance in the explication of variability in natural populations.

We have achieved such characterization in a number of cline models with the results reported in a series of papers by Karlin and Richter-Dyn [1976a,b,c]. Several of these findings are discussed in the following paper (this volume). We will also present in Karlin [1976] various characterizations of the possible polymorphic states in the Levene subdivision model and for some of its extensions.

A. <u>Conditions for protected polymorphisms with general</u> environmental parameters

Consider a multi deme population system involving a general migration structure, selection gradient and distribution of deme sizes as prescribed in (2.1)-(2.3). Let $M = ||m_{ij}||$ be the backward migration matrix constructed as in (1.13) focusing on the soft selection model (an analysis of the hard

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selection formulation is contained in Karlin [1976]). The familiar analytic criterion assuring protection of the Aallele (e.g., see Bulmer [1972]) is the validity of the inequality

the spectral radius of MD = $\rho(MD) > 1$ (2.4) where D is a diagonal matrix involving the values $d_i = f'_i(0)$, (d_1, d_2, \dots, d_n) such that, $d_i = \frac{1}{1+s_i}$ for the example (1.2). Where $\rho(MD) < 1$ then <u>A</u> goes extinct when its initial frequency is small. Therefore, apart from the nongeneric possibility $\rho(MD) = 1$, the condition (2.4) is necessary and sufficient for protection of the A-allele. The inequality $\rho(MD) > 1$ assures protection of the A-allele but information concerning the nature of the ultimate equilibrium state is undetermined. However, it is suggestive that with increasing $\rho(MD)$ the more repellent the state <u>0</u> becomes, concomitantly the established A-frequency is expected to be more substantial in at least one deme.

We will now highlight two categories of sufficient conditions of wide scope bearing on the existence of a protected polymorphism. Actually we present the results in terms of protection of the A-allele. An analogous condition pertains to protection of allele <u>a</u> and these together imply the existence of a protected polymorphism.

Let $\underline{v} = (v_1, v_2, \dots, v_n)$ be the unique left eigenvector corresponding to eigenvalue 1 for the backward migration matrix M obeying the normalization

$$\sum_{i=1}^{n} v_{i} = 1 , v_{i} = \sum_{k=1}^{n} v_{k} m_{ki} , i = 1, 2, \dots, n .$$
 (2.5)

The following result applies to any migration structure and entails no limitations relating to the vicissitudes of any special examples.

A sufficient condition guaranteeing protection of the Aallele is the validity of the inequality

$$\prod_{i=1}^{n} \left(\frac{1}{1+s_{i}}\right)^{v_{i}} > 1 .$$
 (2.6)

Here, the influence of the migration pattern and distribution of deme sizes is reflected by the components of the left eigenvector $\underline{v} = (v_1, v_2, \dots, v_n)$ of M.

Where the relative deme sizes are equal and population exchanges among demes are such that M is symmetric (as in the homogeneous stepping stone migration mode with equal deme sizes) then $v_i = \frac{1}{n}$, i = 1, 2, ..., n, and the condition (2.6) reduces to

$$\begin{pmatrix} n \\ \Pi \\ i=1 \end{pmatrix}^{1/n} > 1$$
 (2.7)

which is always satisfied if the aggregate selection coefficient of the aa-genotype

$$S = \sum_{i=1}^{n} s_i$$
 is non-positive.

The condition (2.6) applies to any migration structure. It is a sharp inequality since for the particular circulant permutation migration pattern, example (d) of Section 1, the equality

$$\rho(MD) = \left(\begin{array}{c} n \\ \Pi \\ i=1 \end{array} \right)^{1/n}$$

holds.

For $\sum_{i=1}^{n} |s_i|$ small the inequality (2.7) is essentially equivalent to

$$\frac{\sigma^2}{2} + \frac{s^2}{2} \left(\frac{1}{n} + \frac{1}{n^2}\right) > \frac{s}{n} \text{ where } \sigma^2 = \frac{1}{n} \sum_{i=1}^n \left(s_i - \frac{s}{n}\right)^2 \quad (2.8)$$

or $\frac{\sigma^2}{2} > \frac{s}{n}$ when s is small.

By restricting slightly the class of migration matrices, we can achieve a substantial refinement of the result of (2.6). More specifically, suppose M is positive definite (such is the case for the homogeneous stepping stone migration pattern with equal deme sizes, provided the migration rate $m \leq \frac{1}{4}$), then protection of the A-allele is assured provided

$$\frac{1}{n} \sum_{i=1}^{n} \frac{1}{1+s_{i}} \ge 1 \quad .$$
 (2.9)

For $\sum_{i=1}^{n} |s_i|$ sufficiently small, such that the cumulative selection effects is of small magnitude, then the condition (2.9) is essentially equivalent to

$$\sigma^2 > \frac{S}{n} \tag{2.10}$$

Thus a sufficient variance of the spatial selection coefficients can override even a slight cumulative aa-selection advantage and protect the A-allele even when it is initially rare.

Notice that (2.10) does not have the factor $\frac{1}{2}$ entering into (2.8).

Suppose the backward migration matrix M admits the representation

$$M = E_1 K E_2$$
(2.11)

where E_1 and E_2 are positive diagonal matrices and K is positive definite, then the analog of (2.9) is as follows:

<u>A sufficient condition for A-protection provided</u> M <u>has</u> the form (2.11) <u>is</u>

$$\sum_{i=1}^{n} \frac{v_i}{1+s_i} \ge 1 \quad , \quad (\underline{v} = (v_1, \dots, v_n) \text{ defined in } (2.5)) . \quad (2.12)$$

Examples where (2.11) holds include among others:

$$M = \left| \left| e_i c_j \right| \right|^n , \underline{e} = (1,1,\ldots,1) , \underline{c} = (c_1,\ldots,c_n)$$

(b) Most cases of the non-homogeneous stepping stone model.

(c) The non-homogeneous homing model of (1.7).

The circulant migration pattern (example (d), Section 1), does not admit the representation (2.11).

Elaborations and proofs of (2.6) and (2.12) are found in Karlin [1976] and Friedland and Karlin [1975].

We proceed to a concrete application of (2.12) for the homogeneous stepping stone migration mode (1.5) with deme sizes described by the array $\underline{c} = (c_1, \dots, c_n)$. The calculation (1.13) produces



with

$$\gamma_{i} = mc_{i-1} + (1-2m)c_{i} + mc_{i+1}$$
, $i = 2, ..., n-1$

and

$$\gamma_1 = (1-m)c_1 + mc_2$$
, $\gamma_n = mc_{n-1} + (1-m)c_n$

A standard determination of the left eigenvector \underline{v} for M in (2.13) leads to

$$v_{i} = \frac{c_{i}\gamma_{i}}{\sum_{k=1}^{n} c_{k}\gamma_{k}}$$
, $i = 1, 2, ..., n$.

Now for $m \leq \frac{1}{4}$ so that the rate of population exchange between neighboring demes does not exceed 50% of their inhabitants (a condition undoubtedly always satisfied in practice), the matrix M possesses the representation (2.11). The criterion of (2.12) then asserts protection of the A-allele subject to the inequality

$$\frac{1}{\sum\limits_{i=1}^{n} c_{i}\gamma_{i}} \sum\limits_{i=1}^{n} \frac{c_{i}\gamma_{i}}{1+s_{i}} \ge 1 \quad .$$

For extensions of this last example allowing unequal local rates of gene flow, consult Karlin and Richter-Dyn [1975a].

B. <u>A method of comparing environmental heterogeneity for</u> classes of selection gradients.

There is a tendency to measure diversity (or heterogeneity) of an environment usually by a single index. Common choices include the variance of selection values (or of an associated ecological parameter), cumulative deviations of selection values (absolute or relative), the inter quartile range of selection values, information index (entropy) for a selection gradient or other indices correlated with those above. A

real valued index for measuring heterogeneity compels essentially a single scaling over all environments. Intrinsically, an environment is complex and should not and cannot be summarized in a single value. It should also be evident that not all environments are comparable. We now propose two concepts for ascertaining that an environment \mathcal{E} is regarded more heterogeneous than a second environment \mathcal{E}' .

Consider an environmental selection regime \mathcal{E} characterized by the local selection functions $\{f_1(x), f_2(x), \dots, f_n(x)\}$ and suppose, for definiteness

$$f_{i}(x) = \frac{x + \sigma_{i} x^{2}}{1 + \sigma_{1} x^{2} + s_{i} (1 - x)^{2}}$$

associated with the viability parameters

AA Aa aa $1+\sigma_i$ l $1+s_i$, i = 1, 2, ..., n.

In this model the environment is determined by the array of selection coefficients

$$\underline{\mathbf{s}} = \{\mathbf{s}_1, \mathbf{s}_2, \dots, \mathbf{s}_n\} \text{ and } \underline{\boldsymbol{\sigma}} = \{\boldsymbol{\sigma}_1, \boldsymbol{\sigma}_2, \dots, \boldsymbol{\sigma}_n\} . \tag{2.14}$$

Definition 1. We say that the selection regime (s,σ) is more heterogeneous than the selection regime induced by the parameters

 $\underline{s'} = (s'_1, s'_2, \dots, s'_n) \text{ and } \underline{\sigma'} = (\sigma'_1, \sigma'_2, \dots, \sigma'_n)$ (2.15) $\underline{if} \underline{s'} \underline{is \text{ "an average" of } \underline{s} \underline{and} \underline{\sigma'} \underline{is \text{ also "an average"}}$

 $\underline{of} \sigma$.

We make precise now the notion of "averaging" applied to vectors. A matrix $A = ||a_{ij}||_{1}^{n}$ is said to be <u>doubly sto-</u><u>chastic</u> if

$$a_{ij} \ge 0$$
, $\sum_{j=1}^{n} a_{ij} = \sum_{i=1}^{n} a_{ij} = 1$, $i, j = 1, 2, ..., n$. (2.16)

(all the row and column sums are 1).

The collection of all doubly stochastic matrices is denoted by $\boldsymbol{\mathcal{A}}$.

Now we stipulate

s' is an average of s provided there exists
a matrix A in
$$\mathcal{Q}$$
 such that
s' = As that is $s'_{i} = \sum_{j=1}^{n} a_{ij}s_{j}$, $i = 1, 2, ..., n$. (2.17)

. . . .

The averaging operation preserves the aggregate selection effects, viz.,

$$\sum_{i=1}^{n} s'_{i} = \sum_{i=1}^{n} s_{i} = S.$$
 (2.18)

Moreover, the relationship (2.17) tends to reduce the variation of the s_i values. In particular, the variance of the <u>s</u>' vector is diminished:

$$\sum_{i=1}^{n} (s'_{i})^{2} \leq \sum_{i=1}^{n} (s_{i})^{2}$$

More generally, for any convex function, $\phi(\xi)$, we have

$$\sum_{i=1}^{n} \phi(s'_{i}) \leq \sum_{i=1}^{n} \phi(s_{i}) . \qquad (2.19)$$

The relation (2.17) also entails the inequality

The specific averaging matrix having $a_{ij} = \frac{1}{n}$ for

all i,j converts <u>s</u> into the constant (homogeneous) environmental selection pattern (2.20) with $s'_{i} = \frac{s}{n}$, i = 1, 2, ..., n.

To reiterate, we say, the environmental selection gradient $(\underline{s}', \underline{\sigma}') = \mathcal{E}'$ is more homogeneous than the environmental selection gradient $(\underline{s}, \sigma) = \mathcal{E}$ if

s' is an average of s and
$$\sigma$$
' is an average

of σ in the sense of (2.17). (2.21)

Formally, (2.21) is equivalent to the existence of A and B in $\boldsymbol{\alpha}$ (not necessarily the same), such that

$$\underline{s}' = A\underline{s}$$
 and $\underline{\sigma}' = B\underline{\sigma}$. (2.22)

We can introduce greater flexibility in the concept (2.21) by allowing the possibility that \mathcal{E} is more heterogeneous than \mathcal{E}' with respect to selection on the AA-genotype while \mathcal{E}' is more heterogeneous than \mathcal{E} with reference to selection expressed at the aa-genotype. We will not pursue these ramifications in this work.

With the specification (2.20) we find that for a prescribed aggregate level of selection coefficients S and Σ for the aa and AA-genotypes, respectively, then the constant selection gradient characterized by the constant selection coefficients

$$s_i = \frac{S}{n}$$
 and $\sigma_i = \frac{\Sigma}{n}$, $i = 1, 2, ..., n$

is more homogeneous than any other environmental gradient with a selection array having the same cumulative selection effects S and Σ .

The following question is natural.

How does increased heterogeneity of the environmental selection gradient correlate with the realization of \underline{A} and a protection and the maintenance of polymorphism?

Definition 1 provides a framework for dealing with this problem. The averaging concept is appealing but appears to be unnatural. It is not a correct fact that the existence of a protected polymorphism is more likely in a more heterogeneous environment (taken in the sense of Definition 1). The weakness is that Definition 1 refers only to selection gradients and does not take account of the nature and interaction of selection with gene flow.

We now extend the idea for comparing selection gradients in a manner to mesh it better with the underlying migration structure. Let M be a fixed backward migration matrix having eigenvectors

$$\underline{\mathbf{v}}^{\mathbf{M}} = \underline{\mathbf{v}} , \ \underline{\mathbf{M}} = \underline{\mathbf{e}} , \ \underline{\mathbf{e}} = (1, 1, \dots, 1) , \ \underline{\mathbf{v}} = (\mathbf{v}_1, \dots, \mathbf{v}_n)$$
(2.23)

and \underline{v} normalized to satisfy $\sum_{i=1}^{n} v_i = 1$.

Let $\mathbf{Q}(\underline{v},\underline{e})$ consist of the collection of all non-negative matrices A with the properties (2.23). $\mathbf{Q}(\underline{v},\underline{e})$ constitutes a convex closed set of matrices containing M and with each A all its powers. The rank one matrix $J = ||e_iv_j||$, $(e_i \equiv 1)$ is also a member of $\mathbf{Q}(\underline{v},\underline{e})$. When $\underline{v} = \underline{e}$, plainly $\mathbf{Q}(\underline{e},\underline{e})$ coincides with the collection of all doubly stochastic matrices.

Definition 2. Consider two arrays of selection coefficients $\underline{s} = (s_1, s_2, \dots, s_n)$ and $\underline{s'} = (s_1', \dots, s_n')$ reflecting two different environmental selection gradients \mathcal{E} and $\mathcal{E'}$ #,

[#]To ease the exposition we have focused on comparing sets of aa-genotype selection coefficients. The extension to selection functions is obvious.

respectively. We say that
$$\mathcal{E}'$$
 is less heterogeneous than
 \mathcal{E} with respect to the migration structure M if the
relation

s' = As holds for some $A \in \mathcal{A}(v,e)$. (2.24)

The least heterogeneous environment in the hierarchy implicit to the above definition is the constant vector

$$\underline{\tilde{s}} = (\tilde{s}_1, \tilde{s}_2, \dots, \tilde{s}_n)$$
 with $\tilde{s}_i = \sum_{i=1}^n s_i v_i = S_i$ for all i .

For s' determined as in (2.24) the analog of (2.18) is

$$\sum_{i=1}^{n} \mathbf{s}'_{i} \mathbf{v}_{i} = \sum_{i=1}^{n} \mathbf{s}_{i} \mathbf{v}_{i} .$$
(2.25)

It also follows that

$$\sum_{i=1}^{n} \mathbf{v}_{i} (\mathbf{s}_{i}^{'} - \mathbf{s}_{\underline{v}})^{2} \leq \sum_{i=1}^{n} \mathbf{v}_{i} (\mathbf{s}_{i} - \mathbf{s}_{\underline{v}})^{2}$$

showing that the environmental selection variance (weighting subpopulation i by the factor v;) is smaller for environment \mathcal{E}' than for environment \mathcal{E}

The following general result holds in many circumstances: Principle I. Let M be a backward migration matrix of the structure (2.11). Let \mathcal{E} and \mathcal{E}' be two environmental selection gradients such that \mathcal{E}' is less heterogeneous than with respect to the migration structure M in the sense E of Definition 2. Symbolically, we write $\mathcal{E}' \prec \mathcal{E}$. Define to be diagonal selection matrix engendered by \mathcal{E}' i.e., D' $D' = \text{diag} \left(\frac{1}{1+s_1'}, \frac{1}{1+s_2'}, \dots, \frac{1}{1+s_2'}\right) \xrightarrow{\text{and}} D \xrightarrow{\text{analogously}}$ determined from the selection coefficients (s_1, s_2, \dots, s_n) . Then

$$\rho(MD) \ge \rho(MD')$$
 . (2.26)
Accordingly, protection of the A-allele is more likely in the
more heterogeneous environment \mathcal{E} over that of \mathcal{E}' .

 $\rho(MD) \ge \rho(MD')$.

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For the extreme case $\underline{s}' = (s_v, s_v, \dots, s_v)$, $s_v = \sum_{i=1}^n s_i v_i$ then $\mathcal{E}' \prec \mathcal{E} = \{s_1, s_2, \dots, s_n\}$ and indeed (2.26) holds by virtue of the analysis leading to (2.12).

Comparison of the models of hard and soft selection with reference to the existence of protected polymorphism reduces to an important case of Principle I. It can be proved that the environments of soft selection $\mathcal{E}^{(S)}$ is more heterogeneous than the environment of hard selection (\mathcal{E}^{H}) in the guise of Definition 2.

We would expect from Principle I that the phenomenon of a protected polymorphism is more fascile with soft selection over that of hard selection: Where local fitnesses also influence the migration flow, the resulting environmental structure amalgamates to a more homogeneous population behavior entailing increased possibilities for total fixation.

The validity of Principle I is established in a number of examples including the stepping stone migration pattern for a monotone cline model, see Karlin and Richter-Dyn [1976a], and in the Deakin migration form and other cases, see Karlin [1976]. This fact for the Deakin case was discovered first by Christiansen [1975]. Principle I appears not to be correct in complete generality without imposing some restrictions on the migration structure.

C. <u>Protection for different degrees of isolation and mixing</u> in migration structures

When does one migration pattern entail more mixing than a second migration pattern? We will introduce two criteria to deal with this question and discuss their implications with reference to the manifestation of protected polymorphisms.

(i) Two stage versus one stage migration flow

We start with the following definition.

Definition 3. A backward migration matrix M_1 is said to be more mixing than the backward matrix M_2 provided M_1 has the form

$$M_1 = M_3 M_2$$
 with M_2 and M_3 commuting
(i.e., $M_2 M_3 = M_3 M_2$)
(i.e., $M_2 M_3 = M_3 M_2$)

and where M₃ is also a migration matrix.

Thus the extent of migration involved in $\rm M_1$ is effectively the outcome of two stages of exchange (and/or) immigration with one stage corresponding to $\rm M_2$.

It is generally anticipated that two operations of gene flow spread the effects of the local selection forces engendering the workings of a more homogeneous population. This is not a valid general conclusion. Where M_2 and M_3 entail excessive movement possibly cancelling each other then M_1 can reflect less movement than M_2 or M_3 separately. Indeed, by Definition 3, M^2 is more mixing than M, but the extreme example

$$M = \begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix} \quad \text{and} \quad M^2 = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

shows that M^2 may involve no exchange of population while M entails a total exchange. Accordingly, there are essential limitations on the amount of mobility ascribed to M_2 and M_3 in order that M_1 reflect genuinely more mixing than M_2 . The exact requirements on M_2 and M_3 are embodied in the condition (2.28) below which imposes a constraint on the magnitude of movement and mixing satisfied in many biologically reasonable contexts. These include cases of stepping stone migration, the examples of (1.8) and others.

We have established a precise result enabling us to compare

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the influence of different levels of mixing with respect to the existence of protected polymorphisms and this is now stated formally. Further interpretations and implications are set forth in Section 3.

Result I. Suppose each M_{i} in (2.27) admits the representation

$$M_{i} = F_{i}P_{i}G_{i}$$
 , $i = 1, 2, 3$ (2.28)

where F_i and G_i are positive definite diagonal matrices with P_i a positive semi definite matrix (cf. the discussion of (2.11)). If M_1 is more mixing than M_2 such that (2.28) holds, then for any selection matrix D we have

$$\rho(M_1D) \leq \rho(M_2D)$$
 (see (2.4)). (2.29)

Thus, where the multi deme population determined by the migration selection parameter set $\{M_1, D\}$ entails A-protection then with the migration pattern M_2 (which is less mixing than M_1 in the sense of Definition 3) and the same selection structure of D, protection of the A-allele is, a fortiori, assured.

In particular, if M possesses the representation (2.28) then for each integer $\,k$, we have

$$\rho(M^{k+1}D) \leq \rho(M^{k}D) . \qquad (2.30)$$

It is important to underscore the fact that the relation (2.29) is not universally correct with respect to any <u>two</u> <u>comparable migration patterns</u>. In fact, consider a system of 2-subpopulations having equal deme sizes with homogeneous migration matrix

$$M = \begin{pmatrix} 1-\gamma, \gamma \\ \gamma, 1-\gamma \end{pmatrix}$$

It is elementary to check that M $_{\gamma_1}$ is more mixing than M $_{\gamma_2}$

in the sense of Definition 3 if and only if $\gamma_1 > \gamma_2$. However, for any $D = \begin{pmatrix} d_1 & 0 \\ 0 & d_2 \end{pmatrix}$, $\rho(M_{\gamma}D)$ decreases to a minimum attained when $\gamma = \frac{1}{2}$ and afterwards increases. Of course, M_{γ} for $\gamma > \frac{1}{2}$ does not fulfill the requirement of (2.28). The significance of these examples is tantamount to the phenomenon that where the migration structure induces excessive oscillatory mixing then the possibilities for a protected polymorphism are diminished.

The hypotheses underlying Result I are satisfied for the homogeneous stepping stone forward migration matrix of any number of demes provided $m \leq \frac{1}{4}$ allowing for a general prescription of deme sizes.

(ii) Rates of homing

The following criterion for comparison of two migration patterns seems natural.

Definition 4. Let M⁽¹⁾ and M⁽²⁾ be two (backward) migration matrices. If for each i

 $m_{ij}^{(2)} \ge m_{ij}^{(1)}$ for all $j \ne i$ (2.31) <u>then it is suggestive to say that</u> $M^{(2)}$ <u>is more mobile than</u> $M^{(1)}$.

The relation (2.31) tells us that after migration the number of inhabitants in locality P_i originating from any other locality other than P_i is larger for the migration mode $M^{(2)}$ as against $M^{(1)}$ and this property holds for all i.

A set of matrices comparable in the sense of (2.31) incorporates the one parameter family

 $M^{(\alpha)} = (1-\alpha)I + \alpha M$ (M is a fixed stochastic matrix). (2.32) The Deakin migration pattern (1.7) is a very special

example of (2.32) with $M = ||e_i c_j||$, $(e_i \equiv 1)$. We can interpret $1-\alpha$ as the innate propensity of an organism to actively home, independent of selection and deme sizes. A proportion α of the population follows the migration pattern M. When $\alpha = 0$ all demes are strictly isolated and when $\alpha = 1$ the migration behavior of the total population per generation is summarized by M.

It is trivial to check that $M^{(\alpha_2)}$ is more mobile (in the sense of Definition 4) than $M^{(\alpha_2)}$ if and only if $\alpha_1 > \alpha_2$.

Allowing for dispersal rates varying with the deme origin we obtain an n-parameter family of matrices

$$\begin{pmatrix} \underline{\alpha} \\ \underline{m}_{ij} \end{pmatrix}^{(\underline{\alpha})} = (1-\alpha_{i})\delta_{ij} + \alpha_{i}m_{ij} , \quad i,j = 1,...,n$$

$$(M = ||m_{ij}|| , \underline{\alpha} = (\alpha_{1},...,\alpha_{n})).$$

$$(2.33)$$

Obviously the matrix $M^{(\underline{\alpha})}$ is more mobile than $M^{(\underline{\beta})}$ constructed with dispersal parameter sets $\underline{\alpha} = (\alpha_1, \alpha_2, \dots, \alpha_n)$ and $\underline{\beta} = (\beta_1, \dots, \beta_n)$, respectively, if $\alpha_i \ge \beta_i$ for every i.

To what extent does "more mobility" enhance the maintenance of a protected polymorphism? Comparison of the migration structure $M^{(\underline{\alpha})}$ and $M^{(\underline{\beta})}$ with n genuine parameters is formidable and does not point to a coherent relationship. In fact, decreasing only the first component α_1 <u>need not</u> ameliorate the occurrence of protected polymorphisms.

For the case of a uniform dispersal rate (the model of (2.32)), we find in substantial generality, independent of the selection gradient, that the likelihood in favor of a protected polymorphism becomes stronger as the degree of mobility diminishes (α decreases).

The following general result is correct.

Result II. Consider the one parameter family of migration matrices (2.32) where M has the form (2.28). Let D be a diagonal matrix with positive terms on the diagonal induced by the spatial array of aa-selection coefficients (see (2.4)). Then

$$\rho(M_{\alpha}D) = \rho(\alpha)$$

is a decreasing function of α .

It follows that if a protected polymorphism exists for a level of homing $1-\alpha_0$, and migration structure $M^{(\alpha)}$ then a protected polymorphism is assured for any higher level of homing. This finding is consistent with the small parameter theory of Karlin and McGregor [1972].

3. DISCUSSION

In explaining polymorphisms and clines, emphasis is usually given to changes in selective factors between and within environments. It is also widely recognized that in many natural situations migration may play an important, even a dominant, role. The following theme recurs in many works concerned with population genetics: The ongoing process of evolution probably requires adjustment to a constantly varying environment and to the combination of characteristics that survive from the different populations. Important sources of variability in natural population can be genes and gene complexes transferred from other populations. Also widely recognized is that differentiated populations retain the ability for exchange of genetic material. Put in a more descriptive language, spatial and temporal variation in environment are considered to be highly involved in the maintenance of genetic variation in populations (Darlington [1957], Wright [1968], Dobzhansky [1967]). The results reported in

Section 2 bear a variety of implications pertaining to the theme cited above.

Through a series of mathematical models the representations of genetic variability in a subdivided population acted on by migration selection forces has been recently studied by a number of authors including Deakin [1966], [1972], Prout [1968], Maynard-Smith [1970], Christiansen [1974], [1975], Strobeck [1974] and others. The existence of "stable polymorphic equilibria" has been mostly confirmed by showing that each allele is protected against disappearance. (This method used for the confirmation of polymorphism is reliable only in the context of two alleles.) All the above theoretical works confined attention to very special models mostly variations on the Wright Island model. The discussion of special examples are undoubtedly of some separate interest and may fit some natural situations. But even here, complete exact results on protection for the important stepping stone cline models are as yet unavailable. (In this connection see Karlin and Richter-Dyn [1976].)

1. It is commonly stated that a spatial and temporal environmental variation and increased population subdivision enhance the occurrence of polymorphism. The theory expounded in this work and its detailed development in Karlin [1976] circumscribes somewhat the scope and validity of this contention. For this purpose it is essential to delimit carefully the concept when two environmental selection gradients can be compared with reference to their degrees of heterogeneity (this is not always well defined). Such comparisons must take proper account of the migration structure coupled to the spatial selection gradient.

Various authors have emphasized that "average heterozygosity seems to increase with increasing environmental

variability". Most <u>averages</u> are usually computed by weighting equally likely over space and/or time. We have determined in Section 2 that it is unnatural when constructing the average to improperly scale the effects of deme sizes, differences in local migration rates and the spectrum of selection influences. Formulas (2.12) and (2.6) indicate possible appropriate weightings.

2. A precise sense in which more heterogeneous selection gradients engenders more polymorphism is the intent of Principle I, now restated (see Section 2 for its detailed formulation). If the environment \mathcal{E} (characterized by the aagenotype spatial selection coefficient array $\{s_i\}_{i=1}^n$) is <u>more heterogeneous than environment</u> $\mathcal{E}' \approx \{s_i'\}_{i=1}^n$ with respect to the migration structure M in accordance with Definition 2, then protection of the A-allele is more likely with \mathcal{E} <u>over</u> \mathcal{E}' .

The above assertion appears to be true in substantial generality. We have accomplished its validation for several important models but we do not have a complete classification. The comparison of soft versus hard selection fits perfectly the framework of Definition 2. We have established in a number of cases, including the migration selection cline setting, that Principle I applies with hard selection corresponding to a less heterogeneous environment vis a vis soft selection. However, the conclusion that protection for hard selection entails protection for soft selection is not universally correct. Some restrictions on the nature of the migration structure are essential.

3. Recent theoretical studies show that with temporally fluctuating selection intensities the extent of polymorphism

increases, see Gillespie [1973], [1974], Hartl and Cook [1973], Karlin and Lieberman [1974]. Bryant [1974] has reviewed some of the literature on temporal and spatial selection heterogeneity related to natural enzyme polymorphisms. He dwells on the relative roles of spatial and temporal environmental variation and claims on the basis of mathematical work of Haldane and Jayakar [1963] and some work of Charlesworth and Giesel [1972] and Giesel [1972] that the conditions for polymorphic stability in the presence of temporal variation are more stringent than for spatial variation. Bryant goes on to conclude that "the major trend of genetic variation seems intimately associated with temporal variation in the environment, while the remaining trends in some cases may be related to other parameters, including spatial heterogeneity".

This conclusion is not concordant with our findings reported in Section 2. With population subdivision and moderate migration flow a sufficient condition for the existence of, say, protection of the A-allele is

$$\sum_{i=1}^{n} v_{i} \frac{1}{1+s_{i}} \ge 1$$
 (*)

where $\{s_i\}^n$ consists of the spatial array of aa-genotype i=1 selection coefficients among the n localities and the components of (v_1, v_2, \dots, v_n) reflect the influence of migration and varying deme sizes (see (2.23) and (2.12)).

For a cyclically (e.g. seasonal) varying set of selection effects $\{s_i\}_{i=1}^n$ of period length n a sufficient condition for protection is

$$\prod_{i=1}^{n} \left(\frac{1}{1+s_{i}} \right)^{\vee_{i}} > 1 \qquad (\star\star)$$

where v now relates to the variable population sizes over successive generations.

The generalized arithmetic geometric mean inequality

$$\sum_{i=1}^{n} \mathbf{v}_{i} \frac{1}{1+s_{i}} > \prod_{i=1}^{n} \left(\frac{1}{1+s_{i}}\right)^{\mathbf{v}_{i}}$$

shows that protection of the A-allele is more easily maintained with spatial as against temporal variation in selection coefficients. This suggests that <u>spatial rather than</u> temporal heterogeneity of the environments is a more powerful force for polymorphism. For temporal heterogeneity the determining factor is a generalized geometric mean of fitness values while in spatial heterogeneity a generalized arithmetic mean of fitness values is critical. It should be emphasized that we are comparing the same average levels of selection in the two cases.

The contrast is more manifest with small cumulative selection effects, $(\sum_{i} |s_i|$ small), then (*) is essentially equivalent to

$$\sigma^{2} > s_{v} \text{ with } \sigma^{2} = \sum_{i=1}^{n} v_{i} (s_{i} - s_{v})^{2} \text{ and}$$

$$s_{v} = \sum_{i=1}^{n} s_{i} v_{i}$$
(†)

while (**) reduces to

١

$$\frac{\sigma^2}{2} > S_v \quad . \tag{(*)}$$

Thus with temporal fluctuating selection intensities the inequality (*) (by a factor $\frac{1}{2}$) brings less likelihood of protection.

Hartl suggested an intuitive argument for the above conclusion. In the circumstance of cyclic temporal selection

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variation, once fixation occurs in a generation then fixation persists thereafter. Whereas in the presence of spatial selection variation even with fixation in one locality for a generation, still the alternative type can be reintroduced by migration from other localities.

An accurate assessment of the significance and descrip-4. tions of the degree of homogeneity or heterogeneity in gene frequency patterns correlated to the environmental selection gradient and population structure could only come from a determination (qualitative or explicit) of all the stable equilibria, their domains of attraction and the dynamic behavior of the process. This is undoubtedly a formidable analytic task. We had some success on this objective for the cline stepping stone model (Karlin and Richter-Dyn [1976]). The evaluation of $\rho(DM)$ (see (2.4) for the definition) does give some information concerning the gene frequency patterns that are possible in the general case. To wit, if $\rho(DM)$ is substantially larger than 1 then certainly in some locality, at least one, we could expect a significant frequency of the A-allele. If $\rho(DM)$ is close to 1 but still exceeding 1 then the A-allele is protected but generally represented throughout the population in small frequency. The early discussion of Section 2 gives quite good lower estimates of ρ for several important cases of migration patterns.

5. It is also of interest to contrast migration structures as to their degrees of mixing and isolation. Two such concepts were introduced in part C of Section 2 and analyzed. The influence of migration structure on the maintenance of a protected polymorphism and its characteristics can be divided into four categories according to the extent of migration flow; very small, small to moderate, moderate to uniform

mixing, and strongly oscillatory movement. In each case, based on the analysis of Section 2, a number of qualitative inferences are highlighted and discussed.

(i) <u>Very small migration flow.</u> In this circumstance, the degree of environmental heterogeneity coupled to the initial frequency state plays a decisive role in the evolutionary development of the population:

(a) With selection forces favoring different genotypes in

different niches (demes), a preponderance of one or other alleles predominate in each deme. The average level of heterozygosity is low but the level of polymorphism is large. The emerging gene frequency arrays are considerably heterogeneous. The exclusive contingency of avoiding polymorphism for any sets of initial conditions is that a single allele has selective advantage throughout the population range (cf., Karlin and McGregor [1972a], [1972b]).

(b) With a homogeneous selection gradient involving local

heterozygote advantage, a relatively homogeneous polymorphic frequency state is achieved expressing a high average heterozygosity.

(c) A mixture of underdominance, directional and overdominant

spatially varying selection expression can produce a wide variety of stable polymorphic and/or fixation states and the actual equilibrium established depends sensitively on the initial frequency state.

(ii) <u>Small to moderate outbreeding or mobility rates.</u> Result II (Section 2) tells us that the strength of a protected polymorphism increases with the extent of isolation of demes. It is important to caution that this result applies in general form only if the rate of outbreeding is diminished

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uniformly independent of the deme sites. A decrease of dispersal at a particular deme while the other dispersal rates are kept constant, can engender the opposite effect making fixation more likely.

Increasing strength of protection means that the fixation states are more repellant and that each allelic frequency is represented with substantial frequency in at least one deme. There appears to be no relationship between the strength of a protected polymorphism and the form of the polymorphic equilibrium. With low migration rates we would expect considerable heterogeneity in gene frequency. For moderate migration, more monomorphic outcomes are revealed unless substantial heterozygote advantage is operating in each deme.

(iii) <u>Moderate to uniform mixing migration rates.</u> The contribution of the demes substantially blend in all respects. The outcomes now depend in a complex manner on all parameters of the model producing both fixation and polymorphic possibilities with fixation occurrences usually more frequent unless other forces are involved. With local heterozygote advantage a usually unique global polymorphism is maintained independent of the nature of gene flow.

(iv) <u>Strongly oscillating migration patterns.</u> Protection is now again more likely than with uniform mixing. There appears to be a threshold level of medium migration flow such that the maintenance of a stable polymorphism is minimal at that rate of migration.

6. Several authors have recently appealed to Levins [1968] to help explicate the influence of fine versus coarse grain environmental expression pertinent to genetic variability. Although this theory is regarded as mathematically based, it is principally graphical and descriptive in

character. One commentary of this theory is that a very mobile organism experiences many different conditions, the average of which is similar for all members of a population. The effective environment is accordingly fine grained signifying little uncertainty and therefore the organism may well fix on a given genotype adaptive to the bulk of its experiences. For relatively immobile population, the environment experiences is likely to be uncertain and therefore the adaptive strategy of the population is to maintain substantial variability with different alleles predominant over appropriate ranges of the population.

The tenuous contact of these concepts with our work is that a migration pattern with substantial flow has indeed decreased opportunities for polymorphism. More precisely, Result II provides an analytic assertion that with increasing outbreeding (or mobility), the manifestation of multiple phenotypes and genotypes is reduced. There are restrictions on the validity of Result II. The reduced mobility must apply essentially uniformly over the whole range of species.

A different approach to the evaluation of degrees of mixing is the substance of Result I in paragraph C of Section 2.

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