Simon–Ando Decomposability and Fitness Landscapes

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■ Abstract

In this paper, we investigate fitness landscapes (under point mutation and recombination) from the standpoint of whether the induced evolutionary dynamics have a "fast–slow" time scale associated with the differences in relaxation time between local quasi–equilibria and the global equilibrium. This dynamical behavior has been formally described in the econometrics literature in terms of the spectral properties of the appropriate operator matrices by Simon and Ando (1961), and we use the relations they derive to ask which fitness functions and mutation/recombination operators satisfy these properties. It turns out that quite a wide range of landscapes satisfy the condition (at least trivially) under point mutation given a sufficiently low mutation rate, while the property appears to be difficult to satisfy under genetic recombination. In spite of the fact that Simon–Ando decomposability can be realized over fairly wide range of parameters, it imposes a number of restrictions on which landscape partitionings are possible. For these reasons, the Simon–Ando formalism doesn't appear to be applicable to other forms of decomposition and aggregation of variables that are important in evolutionary systems.

Keywords: Fitness Landscapes, Aggregation of Variables, Decomposability, Mutation, Selection, Dynamical Systems

■ Introduction

Ever since Wright's (1932) influential characterization of the evolutionary process as a population–level traversal of a genotype or phenotype "landscapes" where evolving populations are attracted to high fitness "peaks" separated from maladaptive "valleys," the metaphor has dominated evolutionary thinking at an intuitive level. However, relatively little has been done to develop a theory of fitness landscape structures as they relate to induced evolutionary processes. This is in part due to the lack of landscape models general enough to be compatible with empirical data. However, perhaps a more fundamental deficiency has been the absence of a theory mapping landscape topology to evolutionary dynamics.

Much of the work that has been done on landscape characterization has dealt with descriptions of statistical features such as autocorrelation over a random walk (Weinberger 1990, Fontana et al 1991, Stadler 1996), or heuristic descriptions of landscape "ruggedness" (Kauffman 1993), measures of neutrality (Ancel and Fontana 2000, Reidys and Stadler 2001) and topological descriptions of connectivity (Gavrilets and Gravner 1997). These landscape characteristics were chosen with the intuition that they should somehow correlate with evolutionary dynamics. For example, a "rugged" landscape can be thought of as having more local attractors (or rather, quasi–equilibria in a connected landscape) than a "smooth" landscape, while connectivity should relate to the ability of the evolving population to move between local peaks given potentially infinite time. However, most of these heuristic characterizations did not make an explicit link to the dynamical system properties correlated with the given measure.

In what follows, we investigate the possibility of characterizing fitness landscapes according to whether the state description induced by a particular landscape (or, rather, its corresponding mutation–selection operator) is decomposable and aggregable, or at least are decomposable and aggregable to a close approximation at the appropriate scale. We will begin by briefly defining what we mean by "decomposability" and "aggregability," while referring the reader to a more detailed treatment of these subjects in Shpak et al (2003).

In the broadest sense, aggregability of a dynamical system means that there exist macrostate variables (which are themselves functions of some subset of the microstate variables) which allow for a dynamically sufficient description of the system with fewer state variables than in the original dynami-

cal system. The ability to collapse subsets of state variables into an aggregate variable on each equivalence class reflects symmetries inherent in the selection and transmission processes specified by landscape topology and the mutation operators. From a purely computational point of view it is valuable to identify such symmetries, because they render otherwise computationally expensive analyses tractable by reduction of variables. In other words, from a practical standpoint, the advantage of a reduced state–space description are obvious: any reduction in the state space necessary for a dynamically sufficient description substantially simplifies both numerical and analytical treatments of the process in question.

In addition to the obvious significance of aggregation of variables from the perspective of computational complexity, the dynamical symmetries induced by a particular decomposable landscape shed light on the properties of the evolutionary process. The fitness landscape symmetries that make aggregation of variables possible may relate with hierarchy and modularity in the genotype–fitness map or other organizational constraints. Indeed, the general concept of aggregation has been widely applied to a range of biological models and problems, from classical notions of modularity in organismal design to modern notions of hierarchy in genetic architecture (Frenken et al 2000, Simon 1972 and 2000, unpublished).

System decomposability is often related to aggregation of variables but is in principle an independent property. It simply means that there exist (usually) non–intersecting subsets of variables which interact among themselves in some way that distinguishes their interaction from any other subset of variables. In other words, it implies the existence of self–contained "modules" of state variables in a dynamical system that are in some way independent or quasi–independent of the other microstate variables. Often these modules have associated aggregation rules that allow them to be characterized as "emergent" macrostate variables, but this need not be the case (Shpak et al, 2003).

In more formal terms, consider a discrete dynamical system (what follows is trivially generalizable to continuous systems) specified by a linear operator **A**, such that x(t+1)=**A**x(t). For convenience, we will denote x(t) as x and x(t+1) as y. We define aggregativity to mean that given a dynamical system with $(x_1 ... x_n)$ state variables, one can group subsets of the microstate variables into m<n macrostates $\boldsymbol{X}_1 = f_1(x_1 ... x_n) ... \boldsymbol{X}_m = f_m(x_1 ... x_n)$, where in the simplest scenario f is simply a linear combination of microstate values. These macrostates in turn must constitute a dynamically sufficient description, i.e. so that there exists an operator $\hat{A}$ such that X(t+1)=$\hat{\boldsymbol{A}}$X(t).

For a linear system specified by transition operator **A**, we require that there exists an aggrega-

tion operator **Q** such that there is an aggregate variable description Y=$\hat{A}$X, where Y=**Q**y and X=**Q**x. If y and x are state vectors of length n, for the aggregation **Q** to be non−trivial,it must be an mxn matrix (with m<n), and with $\hat{A}$ an mxm matrix. Such an aggregation of variables achieves a reduction of the state space dimension necessary for a dynamically sufficient description. **Q** is defined such that if $Q_{Ij}>0$, x_j is a member of the Ith aggregate class (the indices I,j refer to the element in the Ith row and jth column of the matrix **Q**, the use of upper and lower−case letters is simply to indicate that the non-zero indices j are within the Ith subset).

It was shown by Shpak et al that whenever such an aggregation exists, the aggregate dynamics operator $\hat{A}$ has the form

$$\hat{A} = QAQ^T (QQ^T)^{-1} \qquad (1.1)$$

It was also proven that even for systems which are not exactly aggregable, (1.1) gives the best approximation for the aggregate dynamics of X given the aggregation rule **Q**.

In the special case where the subsets defining the aggregate classes are mutually exclusive, the dynamical system is said to be decomposable as well as aggregable. The set of such subclasses is refered to as a partitioning, and the aggregation of variables on the partition have a **Q** matrix structure such that if $Q_{Ij}>0$ then $Q_{Kj}=0$ for all other K≠I. This means that the dynamical system in question is in some way "modular," i.e. variables contributing to a given macrostate variable do not contribute to others. Together, these rules specify an aggregation of variables which is also a decomposition. As discussed in the first section of Shpak et al (2003), decomposability and aggregativity are in principle independent of one another.

Contra the idealized representations of aggregation and decomposability presented above, most natural systems have a certain amount of communication (at least indirect) between variables across partitions. Indeed, when complete decomposability holds, the system is rather uninteresting in that it consists of non−interacting,self−contained subcomponents. One would expect a much more common scenario to be one where a dynamical system is said to be nearly decomposable if the aggregation via **Q** is dynamically sufficient as an approximation within some arbitrarily small error parameter $\epsilon<<1$, such that the linear operator **A** can be written as $\mathbf{A}=A^*+\epsilon\mathbf{C}$, where A^* is completely decomposable and **C** is an arbitrary n dimensional square matrix.

One such class of nearly decomposable dynamical systems occurs when the macrostate vari-

ables are specified as subsets which are nearly independent from the remaining state variables and exhibit local quasi–equilibria,at least over a certain time scale. We propose that such models may be of particular interest to population genetics from the standpoint of peak transitions in evolution. Such systems have a dynamic that is characterized by short–term clustering about local equilibria and long–term transitions towards the global equilibrium. It is hypothesized that the subsets of variables which exhibit local quasi–equilibria correspond to local fitness optima and their mutational neighbors (with the long time scale equilibrium being the mutation–selection balance over the entire landscape), and that such fitness landscapes induce "fast–slow"(e.g. Guckenheimer and Holmes 1981, Strogatz 1994) behavior.

Examples of nearly decomposable and aggregable natural systems include many well–known models in thermodynamics and statistical physics, which use macrostate variables such as temperature, pressure, and entropy as state variables. This permits a dynamically sufficient descriptions of particle ensembles which would be impossible to describe by tracking the microstates of the innumerable gas particles. In biology, aggregation of microstates into macrostates is (at least implicitly) the foundation for quantitative genetics, where the phenotype macrostates serve as (often approximate) state variables, and the corresponding microstates are the contribution to phenotype or mutational variance made by each individual locus (e.g. Bulmer 1970, Turelli and Barton 1994).

The purpose of this study is to demonstrate the applicability of aggregation methods in describing mutation–selection dynamics on model fitness landscapes, particularly the use of decomposability criteria to identify fitness landscapes which induce fast–slow evolutionary dynamics. It is hypothesized that those landscapes which are characterized by local quasi–equilibria are decomposable and aggregable into subsets of genotypes defining each quasiequilibrium. We begin with a general analysis of decomposability of linear dynamical systems, because of its simplicity and the fact that mutation–selection operators for haploid genotypes can be readily linearized.

■ Simon–Ando Decomposability and Fast–Slow Dynamics

Aggregativity and decomposability in what we will refer to below as "Simon–Ando" systems is only approximate, and as such the aggregate representations are only accurate over durations determined by the system dynamics (insofar as the near–aggregativity arises due to a time scale decoupling

between strong within–partitionclass dynamics and weak cross–class dynamics). We begin with a summary of Simon and Ando's results on fast–slow dynamical behavior as far as is necessary for understanding their relevance to what follows, while referring the reader to their papers and to Courtois (1977) for a more detailed discussion.

Consider a system of linear difference equations x(t+1)=**A**x(t) where **A** is an nxn transition matrix. Suppose that **A** can be rewritten as

(3.0) $\mathbf{A} = \boldsymbol{A}^* + \epsilon\mathbf{C}$

with $\boldsymbol{A}^*$ is a block diagonal matrix of the form:

$$\begin{pmatrix} A_1^* & 0 & 0 & 0 & 0 \\ 0 & \ddots & 0 & 0 & 0 \\ 0 & 0 & A_I^* & 0 & 0 \\ 0 & 0 & 0 & \ddots & 0 \\ 0 & 0 & 0 & 0 & A_M^* \end{pmatrix}$$

Each element $\boldsymbol{A_I^*}$ is a submatrix of dimension n_I (i.e. the number of elements in the partition class C_I) such that $n=\sum_{i=1}^{k} n_I$, while the corresponding partitions of the state vector x^* on which the submatrices operate are denoted as:

$$x^*(t) = \{x_i^*(t)\} = \{[x_{i_1}^*(t)],...,[x_{i_I}^*(t)],...,[x_{i_M}^*(t)]\}$$

where $x_{i_I}^*(t)$ is the subset of components of $\{x_i^*(t)\}$ where the indices given by $x_{i_I}^*(t)=x_i(t)$ for $x_i \in C_I$, with the lowest valued index with the partition being $i=\sum_{J=1}^{I-1} n_J + j$. In other words, the state vector $x_i^*(t)$ is divided into I=1...M subvectors of length n_I corresponding to the dimensions of $\boldsymbol{A_I^*}$. The values of $\boldsymbol{A_J^*}$ for J≠I have no effect on the behavior of $x_i^* \in C_I$. In this scenario, the system's behavior is fully specified by:

(3.1) $x_i^*(t) = \boldsymbol{A_I^{*t}}\, x_i^*(0)$

Due to the fact that there are non–communicating blocks in $\boldsymbol{A}^*$, the dynamical system determined by this matrix satisfies the requirements of complete partitionability: namely, that the system dynamics can be fully specified by applying transformation rules to each partition independent of the other.

In the system specified by $A=\boldsymbol{A}^*+\epsilon\mathbf{C}$, however, there is weak communication (scaling with ϵ <<1) across states, because **C** has nonzero off–diagonal (defined relative to A^*) entries. The existence of strong communication (approximated by the transition rates of A_I^*) for variables within partitions I,I and correspondingly weaker communication for variables across classes I and J (I≠J) leads to a fast–slow dynamic. Furthermore, as will be argued below, it allows one to (approximately) construct an aggregate dynamical system where the macrostate variables X_I are functions of the elements of the Ith strongly–communicating partition class of vertices $[x_{i_I}(t)]$.

At an intuitive level, approximate aggregation is possible because the distribution of variables $[x_{i_I}(t)]$ corresponding to partition class C_I tends towards a quasi–equilibrium very rapidly compared to the time required for the system as a whole to reach the global equilibrium. Consequently, for some intermediate time period, the subvectors $[x_{i_I}^*(t)]$ for each partition class will be in quasi–equilibrium determined by the corresponding transition operator $\boldsymbol{A}_I^*$, while an aggregate transition matrix of between–class transition rates can adequately approximate the transition dynamics between classes.

To see that this is indeed the case, consider the eigenvalues of each submatrix $\boldsymbol{A}_I^*$. Assuming that they are distinct, the n_I eigenvalues can be written in descending order so that $\lambda_{1_I}^* > \lambda_{2_I}^* > ...> \lambda_{n_{I_I}}^*$. Furthermore, the constituent blocks $\boldsymbol{A}_I^*$ of matrix $\boldsymbol{A}^*$ can be permuted so that the leading eigenvalues of each submatrix are arranged in the order $\lambda_{1_1}^* > \lambda_{1_I}^* >...> \lambda_{1_M}^*$ for the m submatrices (where $\lambda_{i_I}^*$ denotes the ith eigenvalue of the Ith block).

In order to describe the decoupling of dynamics between **A** and the $\boldsymbol{A^*}$ approximation, define a value δ^* such that:

(3.2a) $$\min_{i\neq j} |\lambda_{i_I}^* - \lambda_{j_I}^*| < \delta^*$$

The difference in eigenvalue magnitudes in the components of A^* are next compared to those of **A**, so that for any positive real number $\delta < \delta^*$ there is a sufficiently small ϵ>0 (as in eq. 2.0) such that for all i∈C_I

(3.2b) $$|\lambda_{i_I} - \lambda_{i_I}^*| < \delta$$

The differences in magnitude between δ and δ^* determine the characteristic time scale differences between the fast and slow dynamics. The fast system dynamics of $x_{i_I}(t)$ will be driven by the

eigensystem of the Ith subcomponent, hence being nearly identical to the behavior of $x^*_{i_I}$. In the short run (for a time span which scales exponentially with the magnitude of δ), the system behaves as a completely decomposable system specified by A^*. Given sufficient time, the subsystems settle into quasiequilibria given by the leading eigenvalue λ_{1_I} and the associated eigenvector of each submatrix, with the remaining (up to) $n_I - 1$ eigendirections being residual. The system x(t) as a whole consists of M quasiequilibria determined by their eigenvectors $\nu_{1_1} \ldots \nu_{1_M}$.

The system then becomes driven primirily by communication across quasi–equilibrium subcomponents, tending ultimately towards the eigendirection corresponding to the leading eigenvalue λ_1 of **A**. This can be seen by writing a spectral decomposition of the transition matrix **A** and its powers, i.e.

$$(3.3) \qquad \boldsymbol{A}^t = \lambda_{1_1}^t \, Z_{1_1} + \sum_{I=2}^{m} \lambda_{1_I}^t \, Z_{1_I} + \sum_{I=1}^{m} \sum_{i=2}^{n_I} \lambda_{i_I}^t \, Z_{i_I}$$

Where **Z** is the matrix of the product of left and right eigenvectors of **A**, i.e. $\mathbf{Z}=\mathbf{v}\tilde{\mathbf{v}}$ for $\lambda\mathbf{v}=\mathbf{A}\mathbf{v}$ and $\lambda\tilde{\mathbf{v}}=\tilde{\mathbf{v}}\mathbf{A}$, given an appropriate choice of normalization constants. **Z** satisfies the relation $\mathbf{AZ}=\mathbf{Z}\Lambda$ (with Λ a diagonal matrix of **A**'s eigenvalues ordered by descending absolute value).

The corresponding spectral expansion of $\boldsymbol{A}^{*t}$ (the completely aggregable approximation to $\boldsymbol{A}^t$) is

$$(3.3\,b) \qquad \boldsymbol{A}^{*\,t} = \sum_{I=1}^{m} \lambda_{1_I}^{*t} \, Z_{1_I}^* + \sum_{I=1}^{m} \sum_{i=2}^{n(I)} \lambda_{i_I}^{*t} \, Z_{i_I}^*$$

Where λ^*, $\boldsymbol{Z_I}^*$ are the eigenvalues and eigenvector products of $\boldsymbol{A}^*$. From the properties of near–decomposability, $\lambda^*_{i_J} \longrightarrow \lambda_{i_I}$ and $Z^*{}_{i_J} \longrightarrow Z_{i_I}$ if in (3.0) $\epsilon \longrightarrow 0$ (Simon and Ando 1961, pgs. 118–21). In the special case of stochastic matrix **A** and $\boldsymbol{A}^*$ (with every submatrix of the latter also stochastic), we also have the condition $\lambda_{1_1} = \lambda^*{}_{1_1} = \lambda^*{}_{1_J} = 1$.

For the above spectral decomposition, the jth component of the state vector $x_{j_J}(t) = A^t \, x_{j_J}(0)$ can be written as

$$(3.4) \qquad x_{j_J}(t) = \sum_{i=1}^{n} Z_{ij} \, \lambda_i^t \, y_i(0)$$

where $\mathrm{y(t)}=\boldsymbol{Z}^{-1}\,\mathrm{x(t)}$. By expanding and rearranging terms, is

$$(3.4\,a)\quad x_{j_J}(t) = \lambda_{1_1}^t Z_{1_1 j_J} y_{1_1}(0) + \lambda_{1_J}^t Z_{1_J j_J} y_{1_1}(0) + \sum_{I\neq J,\, I=2}^{m} \lambda_{1_I}^t Z_{1_I j_J} y_{1_I}(0) + \sum_{i_J=2}^{n_J} \lambda_{i_J}^t Z_{i_J j_J} y_{i_J}(0) + \sum_{I\neq j,\, I=1}^{m} \sum_{i_I=2}^{n_I} \lambda_{i_I}^t Z_{i_I j_J} y_{i_I}(0)$$

In order to satisfy the properties of near decomposability, $Z_{i_I j_J}$ must be orders of magnitude smaller than eigenvector components $Z_{i_I j_I}$ due to the significantly stronger within vs. between component couplings. Similarly, the completely aggregable approximation contains no cross–component terms (I,J) because the block–diagonal matrix has no cross–term communication. From the fact that $Z^*_{i_I j_J} = 0$, we write:

$$(3.4\,b)\quad x^*_{j_J}(t) = \lambda_{1_J}^{*t} Z^*_{1_J j_J} y_{1_1}(0) + \sum_{i_J=2}^{n_J} \lambda_{i_J}^{*t} Z^*_{i_J j_J} y_{i_J}(0)$$

The short term behavior induced by A^t (2.3) can be broken into intervals $T_1 < T_2 < T_3$ such that in the first two intervals (2.3b, 2.4b) are good approximations. That such a time–scaling exists follows from the Simon–Ando theorems, (Thms. 4.1 and 4.2 in Simon and Ando 1961, which we repeat here without proof):

Theorem 2.1:

Given Z and Z^* defined as in (3.3), for an arbitrarily small scalar quantity $\xi > 0$, there exists a sufficiently small $\epsilon < \epsilon_\xi$ (as in 2.0) such that

$$\max_{k,l} \left| Z_{kl}(i_I) - Z^*_{kl}(i_I) \right| < \xi$$
$$\text{for } 2 \le i \le n(I),\ 1 \le I \le N,\ 1 \le k, l \le n$$

Theorem (2.1) allows one to precisely bound the difference between the eigenvector components of the completely and nearly aggregable systems, and to combine this information with the ranking of eigenvalue magnitude in making predictions about the qualitative short–term versus long–term behavior of the system. Defining $\xi_{kl} = Z_{kl}(i_I) - Z^*_{kl}(i_I)$, following Simon and Ando we write

$$(3.5)\quad u_{ij} = \frac{\xi_{ij}}{\xi}$$

and

$$(3.6) \qquad \boldsymbol{Z} = \boldsymbol{Z^*} + \xi \mathbf{U}$$

This notation (together with the fact that for cross–component terms IJ the components $\mathbf{Z_{IJ}}$=0) allows us to rewrite the five terms of (2.4a) as

$$(3.7a) \quad x_{j_J}(t) = \xi \lambda_{1_1}^t u_{1_1 j_J} y_{1_1}(0) + \lambda_{1_J}^t Z_{1_J j_J} y_{1_1}(0) + \xi \sum_{I \neq J, I=2}^{m} \lambda_{1_I}^t u_{1_I j_J} y_{1_I}(0) + \sum_{i_J=2}^{n_J} \lambda_{i_J}^t Z_{i_J j_J} y_{i_J}(0) + \xi \sum_{I \neq j, I=1}^{m} \sum_{i_I=2}^{n_I} \lambda_{i_I}^t Z_{i_I j_J} y_{i_I}(0)$$

which we rewrite using the shorthand of Simon and Ando's equation (4.21),

$$(3.7b) \quad x_{j_J}(t) = \xi S_j^{(1)} + S_j^{(2)} + \xi S_j^{(3)} + S_j^{(4)} + \xi S_j^{(5)}$$

where the S terms are shorthand for the each of the respective terms in (3.7a).

Note that the first term (the leading eigendirection with corresponding leading eigenvalue λ_{1_1}) scales as ξ<<1 because it involves I,J cross–component interaction. Consistent with a qualitative account of system dynamics, the short term behavior of $x_{j_J}(t)$ is largely dominated by $S^{(2)}$ and $S^{(4)}$ (the only terms which appear in the completely decoupled system described by (2.4b)). For larger values of t, however, eventually $S^{(1)}$ comes to dominate as $\lambda_{1_J}^t << \lambda_{1_1}^t$ (and other terms) as t→∞ (and the global equilibrium is attained). The same applies for determining the time scale at which quasi–equilibria are attained within each Ith subcomponent ($S^{(2)}$ vs. $S^{(4)}$).

We can state this more precisely by delimiting time intervals over which some subsets of terms in (2.7) dominates over the others. This is made explicit in Theorem (4.2) in Simon and Ando,

Theorem 2.2a: (Within–Component Quasi–Equilibria)

Because $\lambda_{1J} > \lambda_{jJ}$ for j≥2, there exists a T_0 such that for t>T_o

$$(3.8) \qquad \frac{S_j^{(4)}}{S_j^{(2)}} < \eta_0$$

While for t>T_0 and some real number bound η, since from theorem 2.1 it follows that there exists a ξ for ϵ so that for T_0<t<T_1

$$(3.9) \qquad \frac{\xi\,(S_j^{(1)} + S_j^{(3)} + S_j^{(5)})}{S_j^{(2)} + S_j^{(4)}} < \eta_1$$

Theorem 2.2a means that for a sufficiently small elapsed time, the dynamics of x(t) is dominated by within–component interactions. The first inequality (3.8) describes the short–term within–component behavior before each partition class approaches its local quasiequilibrium. When S^2 dominates, the component is described as being in quasi–equilibrium.The second inequality simply states that for time less than T_1, the cross component terms of order ξ are negligible.

The next set of inequalities describe the behavior of cross–component (I,J) interactions. The first establishes a time limit at which cross–component interactions first become significant, the second the waiting time until the (global) leading eigendirection dominates:

Theorem 2.2b: (Cross–Component Equilibrium)

Given an ϵ which gives the bounds in Theorem 2.2a, given a bound η_2 there exist time $T_2 > T_1$ such that for T_2 <t,

$$(3.10) \qquad \frac{S_j^{(4)} + \xi S_j^{(5)}}{\xi S_j^{(1)} + S_j^{(2)} + \xi S_j^{(3)}} < \eta_2$$

for some value η_3, there exists a number $T_3 > T_2$ so that for t>T_3

$$(3.11) \qquad \frac{S_j^{(2)} + \xi S_j^{(3)} + S_j^{(4)} + \xi S_j^{(5)}}{\xi S_j^{(1)}} < \eta_3$$

The inequality (3.10) states that beyond time T_2, the cross–component terms start to dominate over the within–componentterms, while (3.11) suggests that given sufficient time t>>T_3, the leaning eigendirection (the direction of the global equilibrium) dominates all other terms.

The inequalities in Theorem 2 divide the fast–slow dynamics of x(t) into four stages. Consider an initial state vector x(0), in particularly the Ith component of the probability distribution $x_I(0)$.

Fort the entire time interval t<T_1, the behavior of $x_I(t)$ is closely approximated as $x^*_I(t)$, i.e. by the equations (3.4b). In the time interval 0<t<T_0, the distribution $x_I(t)$ is determined by the various eigendirections associated with $\boldsymbol{A_I}$, while during the time interval T_0 <t<T_1, the leading eigenvector of $\boldsymbol{A_I}$ dominates, and $x_I(t)$ is said to be in a state of local quasi–equilibrium.

When T_1 <t<T_2, cross component interactions with partition classes J≠I become significant.

Since prior to time T_2 the distribution $x_I(t)$ is at a quasi–equilibrium distribution closely approximated by the eigenvector Z_{1_I} (and the same is the true for all subcomponents J), the dynamics during the time intervals following T_1 can be approximated by assuming that the Ith component is in the equilibrium associated with $\boldsymbol{A^*_I}$, weighted by what initial proportion of the distribution was in the Ith component.

This is the property that allows for aggregation of variables approximations to be reasonably accurate representations for the dynamics of x(t). By treating the within–component distributions at quasiequilibrium as essentially static over the short term, each subcomponent distribution x_I can be treated as an aggregate variable X_I, and rather than tracking the interactions of individual elements i,j of the Ith and Jth component, the dynamics for $T_1 < t < T_2$ can be described by an aggregate matrix $\hat{\boldsymbol{A}}$ that describes net cross–component communication (as described in the following section).

During the time interval $T_1 < t < T_2$, the cross–component eigenvectors begin to dominate over the within–component eigenvectors, while for $T_2 < t$, the leading eigenvector of **A** dominates the distribution as it tends towards its global stable equilibrium (assuming that such exists). True fast–slow behavior occurs when T_2 is substantially (perhaps orders of magnitude) larger than T_0 by allowing a time scale decoupling between local quasiequilibria and global equilibration.

■ Aggregation of Variables and Decomposition in Simon–Ando Systems

In a nearly decomposable Simon–Ando system at time $T_1 < t < T_2$, the distribution in each component $x_I(t)$ is in quasi–equilibrium with nearly stationary within–partition class dynamics. Since for larger values of t cross–component (I,J) terms begin to dominate the system dynamics, the quasi–equilibrium distributions can be treated as macrostate variables with a time evolution determined by the sum total of transition rates across classes.

Given a transition matrix **A** which induces Simon–Ando dynamics, we construct a description of transition between macrostates (i.e. exchange rate between the K diagonal subcomponents in $\boldsymbol{A^*}$) by summing the indices A_{ij} across classes $i \in I$ and $j \in J$. Simon and Ando (1961) and Courtois (1977) derive an aggregate dynamics operator $\hat{\boldsymbol{A}}$ for a stochastic matrix **A** (their results apply readily to non–stochastic operators, apart from the leading block–eigenvalues not being equal to one) by arguing that in time interval $T_1 < t < T_2$, the normalized Ith component of $x_I(t)$ is approximately equal to the leading eigenvector (stationary distribution) of $\boldsymbol{A^*_I}$,

$$(3.12) \qquad \nu^*_{i_I}(1_I) \simeq \frac{x_{i_I}}{\sum_{i\in I} x_{i_I}}$$

We next construct a transition matrix which describes the dynamics of the transition probability between states J and I. In terms of conditional probabilities (and by abuse of notation where X=J denotes a transition to the Jth state), we have

$$P(X_{t+1} = I \mid X_t = J) = \frac{P(X_{t+1} = I, X_t = J)}{P(X_t = J)}$$

with $P(X_t = J) = \sum_{j\in J} x_{j_J}$ and $P(X_{t+1} = I, X_t = J)$ is the probability of leaving any state i∈I entering any state j∈J, which is the sum of $\boldsymbol{A}_{ij}$ transition probabilities weighted by the probability of being in the ith state, i.e. $\sum_{i\in I}\sum_{j\in J} x_{j_J} \mathbf{A}_{ij}$. Therefore,

$$(3.13) \qquad P(X_{t+1} = I \mid X_t = J) = \frac{1}{\sum_{j\in J} x_{j_J}} \sum_{i\in I}\sum_{j\in J} \boldsymbol{A}_{ij}\, x_{j_J}$$

with identical results (apart from a normalization constant) if one interprets the coefficients of **A** as rate terms rather than transition probabilities. From (2.9), we can approximate this expression as

$$(3.13\,b) \qquad P(X_{t+1} = I \mid X_t = J) \simeq \sum_{i\in I}\sum_{j\in J} \boldsymbol{A}_{ij}\, \nu^*_{j_J}(1_J)$$

For the completely decomposable system $\boldsymbol{A}^*$, by (3.13b) the transition rates are simply the elements of a diagonal matrix of leading right eigenvalues for each block, $\boldsymbol{P}_{II} = \lambda(1_I)$, $\boldsymbol{P}_{IJ} = 0$ for I≠J, with the former coefficient equal to unity for block–stochastic matrices.

This construction of aggregate dynamics implicitly assumes an aggregation operator **Q** which is a matrix of characteristic vectors, as in this formulation $X_I = \mathbf{Q}x = \sum_{i\in I} x_{i_I}$. However, a derivation of $\hat{\boldsymbol{A}}_{IJ}$ using the matrix of characteristic vectors according to (1.2) gives us something of the form (3.5), which is not equal to (3.13).

Alternatively, one could chose **Q** to be the matrix with rows $q_I = \nu^*_I(1_I)$, the leading eigenvectors of the block–diagonal submatrices of $\boldsymbol{A}^*$ to determine whether this choice of aggregation operator is consistent with (1.1). In this case, X_I would have to be normalized to produce a distribution as $\sum_{i\in I} \nu^*_I(1_I)\, x_{i_I}$ is not necessarily normal given x, ν_I^* normal. Furthermore, the resulting derivation of $\hat{\boldsymbol{A}}$

$$\hat{\boldsymbol{A}}_{IJ} = \sum_{i\in I}\sum_{j\in J} v^*_{i_I}\, \boldsymbol{A}_{ij}\, \frac{v^*_{j_J}}{\sum_{k\in J} v^*_{k_J}{}^2}$$

is only equivalent to (3.13) in the special case where each block submatrix of $\boldsymbol{A}^*$ has as its leading eigenvector a uniform stationary distribution.

This suggests that the standard expression (3.13) for the aggregate transition matrix in Simon–Ando systems does not generally satisfy the mean–square minimum of Theorem 1.1, nor is the $\hat{\boldsymbol{A}}$ used in Simon–Ando systems consistent with any choice of aggregation operators given (1.1). As discussed above, this does not mean that the expression for $\hat{\boldsymbol{A}}$ consistent with (1.1) should be preferred to a different aggregate matrix (3.10), as Theorem 1.1 only offers a heuristic for the construction of $\hat{\boldsymbol{A}}$ rather than a rigorous statement about the best approximation for aggregate dynamics. In fact, much of the numerical work related to Simon–Ando systems (Courtois 1977, Meyer 1989, Kafeety et al 1996, Deuflhard et al 2000) suggests that for strong time–decoupled systems with a large separation $T_2 - T_1$, the aggregation approximation for the dynamics of X is quite robust.

One of the differences between (3.13) and (1.1) is that the latter gives the least–square minimum estimate of $\|\mathbf{QA}x - \mathbf{AQ}x\|$ for x(t) over all times t, while (3.13) should give the best estimates for $X = \mathbf{Q}x$ for time intervals $t > T_1$. Some of our numerical results in the sections below suggest that for certain parameter landscapes (presumably, those where Simon–Ando decomposability might be a poor approximation), (1.1) gives reasonable estimates of aggregate dynamics where (3.13) fails. Conversely, (3.13) gives good estimates of the dynamics of $\mathbf{Q}x$ and the stationary distributions of the transition operator A in cases (presumably those which exhibit Simon–Ando dynamics) where (1.1) gives completely misleading estimates.

The relationships above suggest the time scales over which a Simon–Ando system is (to a close approximation) aggregable and decomposable, as the two properties are not necessarily congruent. During the time interval $t < T_0$, system dynamics are dominated by within–partition class processes, and thus the system dynamics can be described to a close approximation in terms of the within–partition class dynamics of x_I acted on by their respective $\boldsymbol{A}^*_I$.

For the time interval $T_0 < t < T_1$, because the within–component dynamics approximated by $\boldsymbol{A}^*$ still dominate, the system remains decomposable. However, the distributions within each partition are closely approximated by the eigenvectors $v^*_{1_I}$, hence in this interval the system is aggregable. In con-

trast, over the time interval t<T_0 the dynamical system was decomposable but not aggregable.

For T_2<t, cross–partition class communication becomes dynamically significant, thus $\boldsymbol{A}^*$ is no longer a good approximation for the system as a whole. The exchange rates across partitions have to be weighted by their quasistationary within–component distributions, so that the dynamical system in this time interval remains nearly aggregable in spite of the breakdown of decomposability.

The different behaviors over the defined time intervals illustrate the fact that for Simon–Ando systems where aggregation and decomposition are only approximate and time–dependent, the two properties are actually decoupled from one another. This is in contrast to the situation one encounters in dynamical operators that can be aggregated according to exact equitable partitions (Stadler and Tinhofer 1999, Shpak et al 2003). Those systems are exactly decomposable and aggregable over all time scales.

■ Mutation–Selection and Fitness Landscapes

A fitness landscape (V,ξ,f) consists of a vertex set of genotypes V, a transmission rule ξ that defines neighborhood relationship and/or a distance metric between vertices (genotypes) i,j, and a real–valued function f:V→$\mathbb{R}$ which assigns a fitness value to each genotype (Weinberger 1990, Jones 1992, Culberson 1992, Stadler 1994). In genetic systems, the relevant transmission rules are those that assign transition probabilities (edge weights) T_{ij} between genotypes i and j for mutation and recombination processes. We will first treat the simplest case, the fitness landscape specified by a mutation–selection process under single point mutation.

Consider a haploid asexual population, with k possible genotypic states. These can be interpreted as either k alleles at a single locus, or alternatively, k alternative multilocus genotypes. The state vector x(t) describes frequencies of ith genotype x_i(t), where $\sum_{i=1}^{k} x_i = 1$. To each genotype one assigns fitness value w_i, and define the mean population fitness as $\overline{W}=\sum_{i=1}^{k} x_i w_i$.

For the sake of simplicity, we assume that reproduction, mutation, and selection occur in non–overlapping generations. The probability that a j individual has an i offspring is given by the per–generation mutation rate μ_{ij}. This lets us define a row–stochastic mutation matrix **M** with entries:

$$(4.0) \quad \mathbf{M}_{ii} = 1 - \sum_{i=1}^{N} \mu_{ji}; \ \mathbf{M}_{ij} = \mu_{ij} \text{ for } i \neq j$$

Iteration of x(t) across a single generation is defined by an expression of the form:

$$(5.1) \quad x_i\,(t+1) = x_i\,(t)\,\frac{w_i}{\bar{W}} + \frac{1}{\bar{W}} \sum_{j=1}^{k} (\mu_{ij}\, w_j\, x_j - \mu_{ji}\, w_i\, x_i)$$

(see Crow and Kimura 1970, Ewens 1979, Burger 1998, Burger 2001, etc.).

The mutation–selection dynamics can be fully specified in the form of a matrix **A** operating on x, with

$$(5.2) \quad \mathbf{A}_{ij} = \mu_{ij}\, w_j \text{ if } i \neq j$$

$$\mathbf{A}_{ii} = \left(1 - \sum_{l=1}^{k} \mu_{il}\right) w_i$$

The mutation–selection matrix **A=WM**, where **M** is the mutation matrix (5.0) and **W** is a diagonal matrix of genotype fitness values $\mathbf{W}_{ii}$=w, $\mathbf{W}_{ij}$=0.

By definition $\overline{W}=\sum_{i=1}^{k} (\mathbf{A}x(t))_i$, thus one can write (5.2) as $x_i(t+1) = \frac{1}{\overline{W}}\mathbf{A}x_i(t)$. In its general form, one can describe the dynamics as:

$$(5.3) \quad x\,(t) = \mathbf{A}^t\, x\,(0) \Big/ \sum_{i=1}^{k} (\mathbf{A}^t\, x(0))_i$$

The same equations will describe evolution of a diploid population, if one defines w_i as a marginal fitness of genotype i, i.e. $w_i=\sum_{j=1}^{k} w_{ij}\, x_j$ and $\overline{W} = \sum_{ij=1}^{k} w_{ij}\, x_i\, x_j = \sum_{i=1}^{k} x_i\, w_i$.

It can be seen that eq. (5.3) is nonlinear due to the occurrence of terms containing x_i in $\overline{W}$. The characterization of a number of dynamical system properties is more straightforward if the equations can be linearized and expressed in matrix form. The decomposability criteria outlined in the first section only holds for linear systems.

A linearization of the coupled macromolecule synthesis models of Eugene (1971) by Jones et al (1976) and in Thompson and MacBride (1974). These are formally equivalent to the Crow–Kimura mutation–selection models, thus the treatment here is a transformation which is equivalent to that of Jones et al. Consider the transformed variable:

$$(5.4) \quad x(t) = y(t) \exp\left[-\int_o^t \frac{1}{\bar{W}}\, dt'\right]$$

$$\text{with } \bar{W} = \sum_{i=1}^{k} x_i(t')\, w_i$$

Substituting (5.4) into (5.1b) we obtain a linear difference equation. Note that this can be written in matrix form similar to (5.2) but without the nonlinear normalization term $\overline{W}$. This linearization is only valid for haploid genotypes (Thompson and MacBride 1974) because the diploid to haploid (gametic) transmission process is quadratic.

The linearization of the mutation–selection equations essentially changes the description of relative genotype frequencies to one of absolute frequencies (Baake et al 1997, Hermisson et al 2001) in an exponentially growing population rather than relative frequencies and requires the use of (absolute) Malthusian rather than Wrightean fitness parameters. One can transform back to the Wrightean relative frequency and fitness description with no information loss (by normalizing the absolute frequency vector), and the mutation–selection equations for haploids can be treated as a linear system to which the above definitions of decomposability are applicable.

In an absolute–frequencies based representation, the mutation–selection process can be fully specified as **A=WM**, i.e. as the product of a diagonal matrix of genotype fitness values and a stochastic mutation matrix (this is where the discussions in previous sections on the conservation of stochasticity in $\hat{\boldsymbol{A}}$ becomes relevant). Furthermore, when absolute frequencies are used and the nonlinear $\overline{W}$ term is removed, the linear operator **A** in (5.2) gives us the state equation for gene frequency change from one generation to the next.

The goal in constructing an aggregation–based description of mutation–selection processes is, given (5.1), to be able to construct either as an exact or approximate description

$$(5.5) \quad X_I(t+1) = X_I(t)\, W_I + \sum_{J=1}^{k} \boldsymbol{M}_{IJ}\, W_J\, X_J - \boldsymbol{M}_{JI}\, W_I\, X_I = (\hat{\mathbf{A}}\, X(t))_I$$

where X_I is the aggregate frequency of the Ith class of genotypes, M_{IJ} is some measure of net mutation rate from the Ith to the Jth class (usually as some weighted sum of cross–term mutation rates $\sum_{i\epsilon I, j\epsilon J} c_{ij}\, \mu_{ij}$, and W_I is some aggregate fitness value on the Ith aggregate class, i.e. $W_I = f(x_{I_1} \ldots x_{I_{n_I}})$ where $x_{I_i} \epsilon C_I$.

■ Landscapes on Hamming Graphs and Simon–Ando Decomposability

We now turn our attention to the question of whether Simon–Ando decomposability is applicable to a wide class of fitness landscapes. As stated in the introduction, one's intuition about landscape topography suggests that Simon–Ando like behavior might be fairly generic in multi–peaked landscapes where the peaks and surrounding high fitness genotypes are separated by broad, low fitness "valleys." We hypothesized that genotype frequency distributions would reach quasi–equilibria in the neighborhoods of local optima in the short run while slowly moving across the valleys towards the global mutation–selection equilibrium over a longer time scale.

The qualitative behavior and some of the mathematical structure associated with Simon–Ando dynamics has been observed in a variety of evolutionary models. The "epochal evolution" of the "Royal Road Genetic Algorithm" (van Nimwegen et al 1997) exhibits local quasi–steady states associated with the fixation of a subset of loci with a certain fitness effect, punctuated by stepwise transitions between these steady states in attaining the global optimum. Furthermore, the block–diagonal structure of fitness landscapes and its associated eigenstructure has been used by Schuster and Swetina (1988) and Wilke (2001a,b) to derive equilibrium distributions and determine global optima by identifying block components with the largest leading eigenvalues.

In asking how common Simon–Ando decomposability may be for generic mutation–selection systems, we work with a Hamming graph configuration space appropriate to the analysis of n–locus, two allele system where only point mutations are allowed in each generation. This representation can be generalized to multi–allelic systems and to models with a small but nonzero probability of multiple mutations per iteration (for example, a mutation matrix with coefficients determined by a Poisson or exponential probability of k mutations in each generation).

Recall that Simon–Ando aggregation and decomposability requires that the vertex set V be completely partitionable into $C=\{C_1 ... C_m\}$ such that every vertex x is an element of some class C_I. To be Simon–Ando decomposable, the partition classes are chosen such that intra–partitioncommunication is orders of magnitude stronger than interpartition communication. Applying the Simon–Ando aggregate description (3.13) to the mutation–selection equations (5.1 and 5.5), we have

$$\hat{\mathbf{A}}_{IJ} = \sum_{i\in I}\sum_{j\in J} \mathbf{A}_{ij}\, v^{*}{}_{j_J}\ (1_J) = \sum_{i\in I}\sum_{j\in J} \mathbf{M}_{ij}\, w_j\, v^{*}{}_{j_J}\ (1_J)$$

$$X_I\ (t+1) = X_I\ (t)\ W_I + \sum_{J=1}^{k} \mathbf{M}_{IJ}\ W_J\ X_J - \mathbf{M}_{JI}\ W_I\ X_I = \hat{\mathbf{A}}\ X_I\ (t)$$

where the aggregate variables and parameters are $X_I = \sum_{i\in C_I} x_i$, $W_I = \sum_{i\in C_I} w_i\ v^{*}{}_{i_I}\ (1_I)$, and $\mathbf{M}_{IJ} = \sum_{i\in I}\ \sum_{j\in J}\ \mathbf{M}_{ij}$. Using these parameters, it can be seen that $\sum_I\ \hat{\mathbf{A}}_{IJ} = W_I$.

It follows from the definitions of $\hat{A}$ and the condition for Simon–Ando (3.0) that for all classes J we obtain the following set of inequalities (noting that $W_J \le 1$, with the assumption that $\epsilon << \frac{1}{2}$)

(6.0)

$$\hat{\mathbf{A}}_{JJ} = W_J - \sum_{I\neq J} \hat{\mathbf{A}}_{IJ} >> W_J\ (1-\epsilon) \Longrightarrow$$

$$\hat{\mathbf{A}}_{JJ} >> \sum_{I\neq J} \hat{\mathbf{A}}_{IJ}$$

Rather than making this comparison for every class J, it is instructive to look at the limiting cases, i.e. the set with the highest cross–class communication rate and the one with the lowest within–class communication rate (using the indices 1 and 2 to denote these classes, respectively, and again applying the condition $\epsilon << \frac{1}{2}$):

(6.1 *a*)

$$\hat{\mathbf{A}}_{11} >> W_1\ (1-\epsilon) \Longrightarrow$$

$$W_2 - \sum_{I\neq 2} \hat{\mathbf{A}}_{I2} >> W_2\ (1-\epsilon) \Longrightarrow$$

$$\frac{\hat{\mathbf{A}}_{11}}{W_1} > (1-\epsilon) >> \epsilon > \frac{\sum_{I\neq 2} \hat{\mathbf{A}}_{I2}}{W_2}$$

For stochastic matrices, $W_1 = W_2 = 1$ for all J and the same class C_J that minimizes the left hand side maximizes the sum on the right hand side. In the general case, however, the class J which minimizes $\hat{\mathbf{A}}_{JJ}$ does not necessarily maximize $\sum_{I\neq J}\ \hat{\mathbf{A}}_{IJ}$, since a high mean partition fitness value leads to relatively high values for both within and cross–partition class communication rates. As a stronger condition than (6.1a), we propose

(6.1 b)

$$(\hat{\mathbf{A}}_{JJ})_{\min_J} >> \left(\sum_{I \neq J} \hat{\mathbf{A}}_{IJ}\right)_{\max_J}$$

where (6.1b)⟹(6.1a),(6.0) but not the converse. This inequality can be treated as a limiting case to determine whether a mutation–selection matrix **A** has a Simon–Ando partitioning, as it requires that the lowest–valued within–class communication rate to be greater than the largest–valued cross–class communication rate (the index J on both sides of 6.1b does not generally refer to the same class, the J on the left hand side refers to the partition class in which within–partition communication is minimal, the J on the right hand side refers to the partition class with maximal communication with outside classes). This criterion makes heuristic sense, as it follows from (3.0) that all cross–classterms should be of order ϵ, orders of magnitude smaller than the terms which dominate the within–class communication rates.

We propose two different classes of landscape decompositions as candidates for a Simon–Ando partitioning. The first example is the standard scenario of an adaptive peak and its immediate neighborhood, in the form of a radius κ, n–dimensionalball (with n the number of loci) centered about a local optimum x_{0_I}, to define the class $C_I = \{x | d(x, x_{0_I}) \leq \kappa\}$, with the number of neighbors within and outside the set determined by the topology of a Hamming graph. For the special case of κ=1, we have

(6.2 a)

$$\hat{\mathbf{A}}_{JJ} = \sum_{i,\, j \in J} (1 - (n-1)\,\mu)\, \nu_j^*\, w_j + (n-1)\, \nu_0^*\, w_0\, \mu$$

$$= \bar{W}_J\, (1 - (n-1)\,\mu) + (n-1)\, \nu_0^*\, w_0\, \mu$$

$$\sum_{I \neq J} \hat{\mathbf{A}}_{IJ} = \sum_{I \neq J} \sum_{i \in I} \sum_{j \in J} \nu_j^*\, w_j\, \mu = \bar{W}_J\, (n-1)\, \mu - (n-1)\, \nu_0^*\, w_0\, \mu$$

Similarly for κ=2, one needs to take into account "residue" terms for both the Hamming distance 0 and 1 classes with the factor n–2.The sum over the κ=2 terms gives a common factor with W_J. This suggests a general form for any value of κ<n

(6.2 b)

$$\hat{\mathbf{A}}_{JJ} = \sum_{i,\, j \in J} (1 - (n-\kappa)\,\mu)\, \nu_j^*\, w_j\, M_{ij} + \sum_{\{j \mid d(x_0, x_j) = \kappa\}} (n-\kappa)\, \nu_j^*\, w_j\, \mu$$

$$= W_J\, (1 - (n-\kappa)\,\mu) + (n-\kappa) \sum_{\{j \mid d(x_0, x_j) = \kappa\}} \nu_j^*\, w_j\, \mu$$

$$\sum_{I \neq J} \hat{\mathbf{A}}_{IJ} = W_J\, (n-\kappa)\,\mu - (n-\kappa) \sum_{\{j \mid d(x_0, x_j) = \kappa\}} \nu_j^*\, w_j\, \mu$$

The inequality (6.1b) compares the minimal valued within–class communication rate with the maximal–valued cross–class communication rate. We will denote these (respectively) as C_1 and C_2 with corresponding mean fitnesses W_1 and W_2. Using the values in (6.2b) to determine when (6.1) is satisfied, we get

(6.3)

$$W_1\, (1 - (n-\kappa_1)\,\mu) + (n-\kappa_1) \sum_{\{j \mid d(x_0, x_j) = \kappa_1\}} \nu_j^*\, w_j\, \mu \;>>$$

$$W_2\, (n-\kappa_2)\,\mu - (n-\kappa_2) \sum_{\{j \mid d(x_0, x_j) = \kappa_2\}} \nu_j^*\, w_j\, \mu$$

The subscripts below the κ values indicate the fact that C_1 and C_2 need not be partitions of the same size, because in general, an n–dimensional hypercube need not be fully partitionable into a set of balls of a fixed radius κ. Any hypercube where $2^n \neq 0$ mod (n+1) cannot be fully partitioned into radius κ –balls,and even hypercubes where n+1 does divide 2^n cannot always be subdivided into balls of a fixed radius. However, with the assumption that a single vertex is a trivial (radius 0) ball, some partitioning into balls of varying radii is always possible. In most cases, $\kappa_1 \neq \kappa_2$, though there are special cases (for example, if n=3, a partition into κ=1 balls about 000 and 111) where the lattice can be fully partitioned into balls of the same radius.

Because more terms are added to the left hand side term than those added to the right for larger values of κ, it is clear that a larger radius about any given point is more likely to give to a Simon–Ando partition. This suggests upper and lower bounds for each side of the inequality, as condition (6.3) will be satisfied for sufficiently small μ if the following relations hold (obviously, the converse need not be true for sufficiently large values of $(n-\kappa) \sum_{\{j \mid d(x_0, x_j) < \kappa\}} \nu_j^*\, w_j\, \mu$)

(6.4 a)

$$W_1\ (1 - (n - \kappa_1)\ \mu) >> W_2\ (n - \kappa_2)\ \mu \implies \frac{W_1}{W_2} >> \frac{(n - \kappa_2)\ \mu}{1 - (n - \kappa_1)\ \mu} \implies \frac{W_1}{n\ (W_1 + W_2) - \kappa_1\ W_1 - \kappa_2\ W_2} >> \mu$$

in the special case where $\kappa_1 = \kappa_2$, the inequality is

(6.4 b)

$$W_1\ (1 - (n - \kappa)\ \mu) >> W_2\ (n - \kappa)\ \mu \implies \frac{W_1}{W_2} >> \frac{(n - \kappa)\ \mu}{1 - (n - \kappa)\ \mu} \implies \frac{W_1}{(n - \kappa)\ (W_1 + W_2)} >> \mu$$

If we chose a sufficiently small per–site mutation rate μ (for small values of κ and W_1 and W_2 of roughly the same order, $\mu << \frac{1}{n}$), the time scale decoupling characteristic of Simon–Ando systems will be satisfied for a partition about a local optimum.

In most models of sequence evolution, μ is chosen to be of the order $\frac{1}{n}$, in which case Simon–Ando aggregation is not likely to give a very close approximation to the system dynamics. In order for the Simon–Ando approximation to hold, the mutation rate must be very low, implying that while there may be a time–decoupling across partitions, the within–class approach to equilibrium will also proceed very slowly. An interesting consequence of this result is that for sufficiently small mutation rates, a "flat" fitness landscape (i.e. one where W(x)=1 for all genotypes x) will be Simon–Anddecomposable for an arbitrary partitioning (provided that each partition is radius κ n–ball about any center vertex). In this special case at least, the time decoupling is due entirely to mutational connectivity within the partitions rather than any fitness differentials within or between partitions.

Our intuition suggested that a fitness landscape structure of several peaks with partition border regions defined by valleys would be necessary to achieve Simon–Ando, in fact this is not the case. A given mutation rate does place constraints on the maximal mean fitness differential across partitions, however, as setting $W_1 = 1$ and $W_2 = 1+S$ and rearranging terms in (6.4) implies:

$$S << \frac{1 - 2\ n\mu - \mu\ (\kappa_1 + \kappa_2)}{\mu\ (n - \kappa_2)}$$

again, when $\kappa_1 = \kappa_2$, the relation is

$$S << \frac{1 - 2\ \mu\ (n - \kappa)}{\mu\ (n - \kappa)}$$

Since the parameter is defined so that S>0, this constraint is only meaningful for $\mu(n-k)<1/2$ and $\mu<<1/n$. If these conditions are met, the inequality requires that the mean fitness differential across classes must be less than the term on the right hand side. This places a constraint on the choice of partitions, i.e. one cannot chose one class C_1 with a fitness substantially larger than that of C_2, at least not for biologically realistic values of μ. Consequently, if a fitness landscape consists of a relatively limited number of high–fitness vertices with the remaining genotypes a low–fitness valley, no partition class can be chosen to consist solely of low fitness genotypes. For example, any partitioning a two–peak landscape with high fitness vertices at (for instance) {00...0} and {11...1} and W(x)<<1 elsewhere must include one of the peaks, limiting the total number of possible partitions to two. The disadvantage of this constraint should be obvious: if the goal of the decomposition and partition approach is to reduce the effective number of state variables, one stands to gain comparatively little in terms of computational efficiency by partitioning a landscape into two blocks.

Furthermore, the above constraints on the value of S require that the differences in fitness betweenthe peaks in different partition classes must not be too great. If there were a large difference in fitness between two peaks, intuition suggests that offspring of the higher fitness region would saturate the entire landscape faster than the lower fitness local peak neighborhoods could attain quasi–equilibrium. This is confirmed by the result that a separation in fitness between partition neighborhoods is inconsistent with Simon–Ando dynamics.

It should be noted that these inequalities place no constraints on the internal structure of each partition class. Intuition might suggest that the "ideal" scenario for Simon–Ando decomposability would be a partitioning where each block consists of a center "peak" surrounded by lower fitness genotypes at the periphery, because we expect lower fitness genotypes at the edges of a partition to communicate with outside partitions at a lower rate than would high fitness vertices. Though certain within–partition class properties may certainly facilitate cross–class separation, as the example of a landscape with all genotypes having a fitness of unity illustrates, there need not be any constraints on within–partition class fitness distributions given a sufficiently low mutation rate.

The internal structure of the partition classes may become important for higher mutation rates, i.e. in situations where (6.4) is not satisfied while (6.3), as the more general condition, does hold for a

choice of partitions. While (6.4) only places conditions on the mean fitnesses of individual classes, the "residual" terms in (6.3), is

$$(n-\kappa) \sum_{\{j \mid d(x_0, x_j) < \kappa\}} \nu_j^* w_j \mu$$

In order for this term to have a significant effect on the relative magnitudes of the two sides of the inequality in (6.3), the product $\nu_j^* w_j$ must be large for $jld(x_o, x_j) < \kappa$. For example, in the case of $\kappa = 1$, the fitness and (consequently) the quasiequilibrium frequency of the center optimum must be significantly higher to compensate for the difference. In this situation, the standard "peak and valley" intuition does seem to be consistent with the requirements for decomposability.

An alternative partitioning we investigated in the context of Simon–Ando decomposition is one where each C_I contains members of an equivalence class characterized by common allelic states at any particular locus or subset of loci. One can interpret these equivalence classes as partitionings according to shared "character state" or "schema" identity (sensu Holland 1977, Goldberg 1989, Altenberg 1994). As examples, for a single locus schema, the equivalence classes are {0**...*},{1**...*}, for a two locus schema {00**..*},{01**...*},{10**...*},{11**...*}, where **...* represent arbitrary allelic configurations at the remaining loci and the schema loci are chosen to be the first κ for the sake of convenience. For a two allele system, there are 2^κ equivalence classes (where a decomposition based on the allelic identity at a single locus gives only two classes, while a multilocus schema can be interpreted as giving rise to "nested" sequential partitions over 1,2...κ site equivalence classes).

It should be obvious that for a κ–length schema, there are κ point mutations that put the offspring into another equivalence class versus n–κ possible mutations that remain inside the partition. Applying (6.1a) to these partitions,

$$(6.5) \quad \hat{\mathbf{A}}_{JJ} = \sum_{i,\, j \in J} (1-\kappa\mu)\, \nu_j^*\, w_j\, M_{ij} = W_J\, (1-\kappa\mu)$$

$$\sum_{I \neq J} \hat{\mathbf{A}}_{IJ} = W_J\, \kappa\mu$$

Note that both the internal and cross class communication rates are in this case independent of the total number of loci, being determined solely by the mutation rate and the number of sites defining a schema. Here we use C_1 and C_2 to denote the schema classes with the minimal intra–component

communication rate and maximal cross–partition class communication rate.

In order for Simon–Ando separation to apply, we need

(6.6)

$$W_1\,(1-\kappa\mu) >> W_2\,\kappa\mu \Longrightarrow \frac{W_1}{W_2} >> \frac{\kappa\mu}{1-\kappa\mu},\ \frac{W_1}{\kappa\,(W_1+W_1)} >> \mu$$

which, along with the expected constraint on mutation rate, implies a stronger separation for smaller κ (fewer loci defining fewer partitions). Rewriting (6.6) in terms of selection parameter S, where W_1 =1–S, W_2 =1, the inequality is equivalent to S<<$\frac{1}{1-\kappa\mu}$. For $\kappa\mu$~1/n, this is S<<$\frac{n}{n-1}$ (implying that for large numbers of loci, no more than a twofold difference in mean partition fitness is permissible).

The mean fitness W_J can be interpreted as the marginal fitness of the particular schema configuration defining the Jth partition class. For example, in a twofold landscape partition defined by 1**...* versus 0**...*, W_J represents the mean (marginal) fitness of allele 1 or 0 at the first locus. Because aggregability of the partition implies the (near) dynamical sufficiency of mean fitness and effective transition rate parameters, the condition (6.6) can be seen as indicating when schema can be treated as "units of selection" (see below). For this condition to be satisfied, the internal cohesion within an equivalence class must be greater than the communication from outside partitions, and as the inequality above indicates, this holds only when the mean (marginal) fitness of any particular schema configuration is of approximately the same order as the mean fitness of the other configurations.

A series of numerical experiments (computed using *Mathematica*, with programs available from the senior author on request) confirm that the landscapes induced by mutation–selection matrices satisfying (6.1b) are aggregable and decomposable. What is somewhat open–ended given the constraints on mutation rates and fitness differences in (6.4b) etc. is just how small the per–locus mutation rate μ has to be with respect to the ratio on the left hand side. It turns out that for certain landscapes, the Simon–Ando approximation to x_{i_I} (t) and $\nu_{i_I} * X_I$ (t) (and therefore, approximations of stationary distributions $\nu_{i_I} = \nu_{i_I} * \tilde{X}_I$, with $\tilde{X}$ the stationary distribution for $\hat{A}$) breaks down for all but very small mutation rates, while for others the results are robust for biologically realistic transition rates.

We begin with the special case of a system where the fitnesses of every genotype are identically set to unity. Using a five locus, two allele system as an example, we (for convenience) chose the equivalence classes to be all of the vertices within Hamming distance 2 from {00000} and {11111}

respectively. Clearly, the within–class quasi–equilibria ν_I^* will approximate uniform distributions irrespective of mutation rates, with the global distribution over the T_1 <t time interval approximated by the product of initial within–partition aggregate frequencies and the within–class uniform distributions. Choosing the mutation rate to be μ=0.01<<0.25, we compare the equilibrium genotype distributions ν_{i_I} (first eigenvector) of the mutation–selection matrix **A** to the aggregation of variables estimates $\nu_{i_I}{}^* \tilde{X}_I$ in Figure 1. The mean–square error is approximately 0.08, which is a reasonable approximation (and one which doesn't improve with lower mutation rates, reflecting the fact that 6.4b gives a sufficient but not necessary condition for time–separation).

In the next set of figures, we repeat the same calculations, but in this case we have multiplicative fitness functions about each local optimum, so that the fitness of any genotype is $W(x)=W_0(1-s)^{d_{\min}(x,x_0)}$ with x_0 the nearest local optimum and s=0.1. The mutation rate is set to μ =0.01, while the peak fitnesses are chosen to be {1,1} in Figure 2 and {1,0.9} in Figure 3. The first case corresponds to the "degenerate quasispecies" discussed by Eigen and Schuster (1989) and Schuster and Swetina (1988), with identical eigenvalues $\lambda_1=\lambda_2=.990181$ where the associated eigenvectors have most of their probability density about either peak (Fig 2a). The stationary distribution (plotted in Figure 2b) can be constructed as a weighted superposition of eigenvectors associated with the leading degenerate eigenvalue.

Aggregation of variables gives a very good approximation to the stationary distribution for this fitness landscape. The values of $\nu_{i_I}{}^* \tilde{X}_I$ are plotted against the stationary distribution in 2b. The mean–square error of ν versus $\nu_I{}^* \tilde{X}_I$ is of the order of 10^{-2}, a value that improves for lower values of μ (e.g. μ=0.001 gives errors of the order of 10^{-5}. This is consistent with our expectation, since the Simon–Ando approximation improves for lower transition rates.

The results are similar for the landscape where the two peaks differ in height, apart from the fact that the eigenspace is non–degenerate.The normalized leading eigenvector (corresponding to the equilibrium distribution) is plotted against $\nu_I{}^* \tilde{X}_I$ in Figure 3, again giving a close match with a mean–square error at the order of 10^{-2}. We note that the approximations are good whether we use the representation of aggregate transition rates (1.1) or (3.13).

The situation becomes more interesting in the case of two–peaked landscapes with nearly identical peak fitnesses. Consider a scenario where one peak has a fitness of unity while the other has a value close to unity, i.e. 0.999. It was shown by Schuster and Swetina (1988) and Wilke (2001b) that

for sufficiently high mutation rates the equilibrium distribution depends on the fitnesses of the immediate mutational neighbors of each peak. Namely, if the more fit peak is surrounded by relatively low fitness neighbors while the peak with slightly lower fitness has comparatively high fitness neighbors (corresponding to a "mutationally robust" or "genetically canalized" genotype, e.g. Wagner et al 1996), the equilibrium density will often be concentrated at the somewhat lower "plateau" rather than the sharp, isolated peak.

We replicated these results in Figure 4, which depicts the equilibrium genotype distribution for a fitness function defined by $W(x)=W_1(1-s_1)^{d_{\min}(x,x_1)}$ about the first peak and $W(x)=W_2(1-s_2)^{d_{\min}(x,x_2)}$ about the second peak, where $s_1=0.9$ and $s_2=0.1$ and x_1, x_2 are the local peak vertices (representing a fitness landscape with one sharp peak and a relatively flat fitness plateau). The fitness values are chosen such that the peak is slightly higher than the plateau, i.e. $W_1=1.0$, $W_1=.99$.

The first computations are for a relatively high mutation rate of $\mu=0.1$, which as expected gives a stationary distribution at the plateau. If we approximate the aggregate dynamics as (1.1), the estimate of the leading eigenvector is completely misleading, specifically, it predicts a stationary distribution concentrated at the peak. However, using (3.13) to estimate the leading eigenvector does predict a distribution concentrated at the "plateau," although it can be readily seen in Fig 4 that the match is not very close (the mean square error in this case is nearly 0.2). This is due to the fact that if we use $\mu=0.01$, the stationary distribution is still concentrated at the plateau and the aggregate distribution is somewhat improved, being just under 0.1.

For substantially smaller (and biologically unrealistic) mutation rates such as $\mu=0.001$, the stationary distribution is always concentrated at the highest peak (because, as Schuster and Swetina demonstrated, selection pressure in favor of the lower plateau is a second order effect that scales in proportion to mutation rate, when mutation rates are sufficiently low, peak genotype offspring rarely "encounter" their neighbors). For this case, Simon–Ando aggregation gives very good estimates (Figure 4b), giving square error values of the order of 10^{-3}. The estimates are good both for (1.1) and (3.13) as operators for the aggregate dynamics.

The applicability of Simon–Ando decomposability to these model landscapes has some interesting implications for the way one thinks about units of selection. It was suggested in Shpak et al (2003) that aggregation of variables offers a natural approach to identifying units of selection above the geno-

type level, in that aggregation methods involve partitioning the genotype space into coherently interacting subsets. Indeed, one criterion proposed for identifying units of selection is that of dynamical sufficiency (see Lewontin 1970, Wimsatt 1981).

While a case can be made that landscape partition classes behave as coherent entities, it doesn't seem to be the case that they must necessarily do so as a consequence of Simon–Ando dynamics. For example, Phase III of Wright's "shifting balance" model (1932) in which interdemic selection (aggregate competition between sets of genotypes composing more or less isolated peaks and their neighborhoods) is actually incompatible with a Simon–Ando model, because mean fitness differences between neighborhoods are in violation of (6.4b). Yet interdemic selection (as a special case of group selection) has been shown to be at least in principle a possible, if not necessarily an important, evolutionary force (Coyne et al, 1997) .

Similarly, the example of a landscape with an isolated high fitness peak competing against a lower fitness but more "robust" genotypes is a case in point, i.e. the parameter values where the plateau dominates the distribution are also those where the Simon–Ando approximation starts to break down due to relatively high mutation rates. Yet the long–term behavior of such a system can be predicted from the fact that the eigenvalues associated with the plateau are larger than those associated with the isolated peak under the right choice of parameters (Schuster and Swetina 1988, Wilke 2001), which suggests that in some sense of the word the competition is taking place between the peak and plateau as aggregate entities. This suggests that one can have higher–order entities that act coherently under selection whose aggregability is not necessarily a result of the fast–slow dynamics. As a case in point, competition between two–peaked landscapes was analyzed in the context of unweighted equitable partitions whose aggregativity was exact and not time dependent, contra Simon–Ando.

We now turn our attention to another issue in the units of selection question that can be elucidated by Simon–Ando aggregation and decomposition: the problem of character identification and schema–based identity classes.

■ Schema Partitioning and the Definition of Evolutionary Characters

In our earlier paper (Shpak et al 2003), we compared the formal property of landscape decomposability into equitable partitions defined by fitness and mutational distance equivalence classes to the character state decomposition models developed in Wagner and Laubichler (2000a,b). The latter form of decomposability defines equivalence classes in terms of identical allelic states at a locus or over subsets of loci (schema). It can be seen that in general equitable partitions need not correspond to schema equivalence classes.

However, there are cases where an equitable partitioning does correspond to a partitioning into schema equivalence classes. In the previous section we examined a partitioning defined by schema which for the appropriate choice of mutation rate and fitness function (6.6) satisfies the condition for Simon–Ando decomposability (which, in turn, is a special case of weighted equitable partitioning). Each schema equivalence class and its frequency can be interpreted as a "character state," and when the mutation–selection system is nearly decomposable, the frequencies of the equivalence classes are a dynamically sufficient descriptor of the evolutionary process. Since one condition for identifying units of evolution is determining whether the entities in question are dynamically sufficient, it is natural to equate selection on a schema class with selection for an independent character state.

What then is the relationship between Simon–Ando decomposability of schema partitions and the character partitionings of Wagner and Laubichler? To recapitulate Wagner and Laubichler's results (with changes made to the notation for consistency with this paper, as well as some formal adjustments for a discrete–time representation), define a set of genotypes $\{x_1 \ldots x_N\}$ with an associated frequency vector $p_i=\{p_1 \ldots p_N\}$. The equivalence classes $C^1=\{C_1 \ldots C_k\}$ and their associated frequencies $\pi_I=\{\pi_1 \ldots \pi_m\}$ are defined such that every genotype $x \epsilon C_I$ has an identical allelic state at a particular locus. More generally, the equivalence classes are defined as a set of genotypes identical over some arbitrary subset of sites, or a "schema" (sensu Holland 1975, Goldberg 1988, Altenberg 1995). One such equivalence class (defined as an allele at a single locus) for a 4–locus genotype would be the set of all genotypes C_1 of the form 0***, C_2 of those of the form 1***, defining partition C. In turn, another class of partitions C^2 will be defined by the allelic identity at the second locus, and so forth.

Wagner and Laubichler define the Cartesian product $C^1 \times C^2$ to be an oc (orthogonal compliment) partitioning if $C=C^1 \times C^2$, or more generally, $C=C^1 \times C^2 \ldots \times C^v$. For example, $C=C^1 \times C^2$ could be the Cartesian product of allelic variants at loci 1 and 2, respectively. The authors construct an oc–

partition by choosing a set of invertible functions F={f_{ij}|f:$C_i \to C_j$ } which maps every element in one equivalence class to the corresponding genotype in another class. For example, f could map 101 to 001, with *01 defining an (orthogonal) equivalence class with respect to the first locus. In the case where F is a family of transitive maps, i.e. s=f_{IJ}(x) and t=f_{JL}(u) implies t=f_{IL}(x), F defines a complementary (orthogonal) partitioning $\overline{C}$={$\overline{C_1}$...$\overline{C_k}$}, where every class is in the complementary partition is $\overline{C}$={s≃x if there is f_{IJ}∈F|s=f_{IJ}(x)}. This mapping specifies an equivalence relation because the functions in f are transitive and invertible (Rosen 1984, Bogart 1990), and consequently defines each genotype x as x=$C_I \cap \overline{C_J}$.

Given an oc–partitioning,Wagner and Laubichler have shown that for fitness functions satisfying the additivity condition and for "character" frequencies satisfying a generalized linkage equilibrium, the equivalence class frequencies π_I are a dynamically sufficient descriptor of evolution under a selection operator.

Carter (1997, unpublished) has shown that the equivalent condition in discrete time requires that all fitness functions are multiplicative across partitions, with w the Malthusian fitness parameter:

$$w(f_{IJ}(x)) = c_{IJ}\, w(x) \qquad (6.7)$$

In other words, the fitness differences between members of the same equivalence class (i.e. allelic state at a particular locus) are determined by a constant product term c_{IJ} determined by the rest of the genotype or character state configuration. This effectively excludes any type of nonlinearity due to epistasis in fitness functions. The other condition, of course, is generalized linkage equilibrium,

$$p_I(f_{IJ}(x)) = p_J(x), \text{ where } p_J(x) = \frac{p(x)}{\pi_J} \qquad (6.8)$$

with p(x) denoting the frequency of x while p_J(x) refers to the marginal frequency in the Jth partition. This definition is equivalent to the conventional linkage equilibrium condition p(x∈$\pi_I \cap \overline{\pi}_J$)=$\pi_I \overline{\pi}_J$.

It was shown in Carter's derivation that if these criteria are met, the selection equation on genotypes (here in discrete time)

$$p_i(t+1) = p_i(t)\, w_i \qquad (6.9a)$$

can be aggregated into a dynamically sufficient description as

$$\pi_I(t+1) = \pi_I(t)\, \bar{w}_I \qquad (6.9b)$$

The condition required for these to hold is that the within–class variances in fitness V_I be the same across partition classes $C_I = C_1 \ldots C_m$. This condition turns out to be generally stable only under multiplicative fitness and generalized linkage equilibrium.

In order to make a meaningful comparison between character partitioning under generalized linkage equilibrium and Simon–Ando, it is necessary to determine under which models of transmission (mutation) the within–class variances (and by extension, the generalized linkage equilibrium) are remain stable. In an unpublished manuscript, Altenberg (2002) proposed that for two orthogonal partitions C^1 and C^2 the following tensor product definition of generalized linkage equilibrium is stable under multiplicative fitness functions and mutation operators:

$$(6.10) \qquad x(t) = x^1 \otimes x^2 = (x_i{}^1 x_j{}^2)_{i=1\ldots N_1,\, j=1\ldots N_2}$$

where $\otimes$ is the Kronecker product operator $(A \otimes B)_{ij} = AB$. In vector form, the within–partition frequency distributions x are given by $x^1 = (\boldsymbol{I}_1 \otimes \mathbf{1}_2^T)x$ and $x^2 = (\mathbf{1}_1^T \otimes \boldsymbol{I}_2)x$, where **I** is an identity matrix and **1** is a vector of 1's corresponding to the number of orthogonal classes in the respective partitionings.

Rewriting the transition operator **A=WM**, with the diagonal fitness matrix **W** and **M** the mutation matrix, in order to satisfy the multiplicativity condition,

$$(6.11) \qquad W = W_1 \otimes W_2$$

and a similar structure for the mutation operator across two partitionings

$$(6.12) \qquad M = M_1 \otimes M_2$$

which can be extended to an arbitrary number of orthogonal partitions as $W = W_1 \otimes W_2 \ldots \otimes W_m$ etc. An interpretation of (5.6) is that mutation rates are independent at each locus (or partition) irrespective of the identity at the other loci.

To show that a Kronecker product model of mutation and fitness effects conserves partition independence and generalized equilibrium, note that

$$x(t+1) = (W \otimes W)(M \otimes M)(x^1(t) \otimes x^2(t)) =$$
$$(MW)\, x^1(t) \otimes (MW)\, x^2(t) = x^1(t+1) \otimes x^2(t+1)$$

implying that x,x are dynamically sufficient descriptors, since (5.7) implies that each equivalence class frequency trajectory can be represented as

$$x^1(t+1) = W_1 M_1 x^1(t),\quad x^2(t+1) = W_2 M_2 x^2(t)$$

This proves that generalized linkage equilibrium $x=x^1 \otimes x^2$ is stable given multiplicative fitness and mutation rate. The results can be summarized as saying that dynamical sufficiency of schema frequencies (i.e. "character decomposability") requires independent mutation rates and multiplicative fitness across partitions as well as multiplicativity of cross–partition class frequencies.

This is in contrast to the conditions under which a schema–based partitioning is decomposable according to the Simon–Ando criterion. Simon–Ando decomposition places no conditions on the frequency distribution apart from the requirement that the distribution within a partition class be in quasi–equilibrium (which, in general, would generate strong linkage disequilibria). Consequently, we can conclude that the two cases in which schema frequencies are dynamically sufficient as evolutionary "characters" are entirely independent of one another, suggesting at least two different sets of conditions (i.e. 6.6 versus 6.11–12 combined with linkage equilibrium) where schema can modelled as units of evolution.

If aggregativity and decomposability into classes defined by Hamming distance suggests units of selection above the genotype level, there are interesting conceptual implications for interpreting a partitioning based on schema equivalence classes. Traditionally, in any system where schema (e.g. allelic) frequencies are dynamically sufficient, evolution is thought of as occurring at a level below that of the genotype. In particular, when allele frequencies are a dynamically sufficient descriptor, it is often stated that the "gene" is the unit of evolution.

In reality, in both cases where schema frequencies are dynamically sufficient (i.e. the Wagner–Laubichler criterion and Simon–Ando), the aggregation and decomposition procedures are formally equivalent to the κ–ball partitions in that they involve treating sets of genotypes as aggregate entities. In other words, if we are to consider the case where κ–ball partitions are dynamically sufficient as selection on a set of genotypes ("group selection" in some broad sense), then it is not meaningful to think of the case of dynamically sufficient schema classes as selection below the level of the genotype. Quite the contrary, allelic or schema frequencies are simply a book–keeping shorthand for the frequencies of an aggregate class, and it is the symmetries or fitness equivalences within these classes that make the "gene frequency" shorthand possible. Far from confirming that selection occurs at the genic

level, the dynamical sufficiency of schema frequencies actually lends support to the idea of units of evolution above the genotype level.

■ Recombination and Simon–Ando Decomposability

The constraints on which mutation–selection systems have Simon–Ando dynamics are a general result of the neighborhood relations (specifically, the Hamming graph) induced by point mutation acting on Boolean or α–alphabet strings. It is natural to ask whether Simon–Ando dynamics can arise under different transmission operators, namely recombination. It has been shown elsewhere (Gitchoff and Wagner 1997) that the configuration space χ induced by recombination is a hypergraph with "edges" consisting of intermediate recombinant classes. Here we ask whether Simon–Ando decomposability can exist given a recombination–induced configuration space. It seems intuitive that Simon–Ando decomposability may be more difficult to achieve because a much wider spectrum of possible offspring genotypes can be produced under recombination than under point mutation, thus reducing the internal cohesion of any neighborhood class of genotypes.

Both the neighborhood relationships and the transition probabilities attached to these edges differ from any model of mutation in that they depend on which partner genotypes are present in the population. As a result, the transition rates A_{ij} are generally dependent on the probability of encountering of recombinant partner k in the population. Under random mating the transition rate from j to k is given by $A_{ij} = \sum_{k=1}^{n} x_k \, T_{jk \to i}$, where $T_{jk \to i}$ is the probability that a pairing of genotypes j,k produces recombinant offspring i. Under these assumptions the recombination–selection equations are

$$x_i\,(t+1) = \sum_{j=1}^{N} \sum_{k=1}^{N} w_j \, w_k \, x_j \, x_k \, T_{jk \to i} \tag{7.1}$$

Again, we use absolute frequencies and Malthusian fitnesses to avoid the complications of a mean fitness term in the denominator. If mating is nonrandom, the most general representation replaces $x_i \, x_j$ above with $\phi(x_i, x_j)$, which is the joint probability of the i,j pairing.

Under the action of a point mutation operator, the neighborhood sets of any genotype were definable as the point mutational neighbors (i.e. all i neighbors of j if $\mu_{ij} \neq 0$, or $\mu_{ij} < \epsilon << 1$), a similar definition of recombination neighbors based on $\sum_{k=1}^{n} x_k \, T_{jk \to i}$ is less straightforward because it depends

on the distribution of parental genotypes in the population. In general, a crossover operator involves a function on vertex (genotype) pairs χ:(V,V)→(V,V), in contrast to the mutation operator ξ:V→V.

The general structure of a recombination operator can be described as follows: given a length n string with a α–letter alphabet (α=2 for Boolean strings), we represent the crossover operator χ by denoting the kth site of genotype y as y_k, which gives us χ(y,z)=(u,v), $\forall$k:($y_k = u_k \wedge z_k = v_k$)$\vee$ ($z_k = u_k \wedge y_k = v_k$), i.e. at all sites k, the recombinant takes on the site identity of parent y while the sister (complementary) recombinant takes on the site identity of parent z. An arbitrary recombination operator R can be represented as a mapping from the set of vertex pairs onto the power set of V, i.e. R:(-V,V)→P(V), hence the P–structure terminology in Stadler and Wagner (1999).

For an operator R_1 associated with a single point recombination event, recombination at the kth point gives us (following the notation of Stadler et al 2000, Stadler and Wagner 1999):

$$R_1(\text{y,z}) = \chi_k(\text{y,z}) = \{(y_1 \ldots y_k\, z_{k+1} \ldots z_n), (z_1 \ldots z_k\, y_{k+1} \ldots y_n)\}$$

This definition of the offspring set can obviously be generalized to arbitrarily many crossover points. The limiting case given a high per–site recombination rate is one where any number of recombination points from none to all n loci are equally possible (i.e. "uniform crossover"), whereby each site k in a given offspring has an equal likelihood of coming from either parental genotype. The action of the uniform recombination operator R_U on two parental strings is described by:

$$R_U(\text{y,z}) = \{(v_1 \ldots v_n) : v_i = y_i \text{ or } z_i \ \forall\, i\}$$

Given a Hamming distance H(y,z)=d between the two parental sequences, it can be shown that the size of the recombination sets is (Gitchoff and Wagner, 1996):

$\|R_1(\text{y,z})\| = 2d$ when y≠z, 1 if y=z

$\|R_U(\text{y,z})\| = 2^d$

For the sake of computational simplicity, we will only examine the cases of uniform and single–point recombination, as they are the limiting cases under very high and relatively low crossover rates.

We now turn to the question of whether recombination systems can satisfy the conditions for Simon–Ando near–decomposability,i.e. whether there exist fitness landscapes that induce a fast–slow

dynamic and local quasiequilibria under the action of recombination. The existence of such quasi–equilbria implies that in principle an aggregation of state variables and parameters is possible, allowing the construction of dynamically sufficient representation of aggregate recombination dynamics

$$X_I\ (t+1) = \sum_J \sum_K W_J\ W_K\ X_J\ X_K\ T_{JK\to I}$$

where we define $X_I = \sum_{i\in I} \nu_{iI}^*$ and W_J as the mean fitness within the partition $\sum_{i\in I} w_i\ \nu_{iI}^*$, the "aggregate" recombination rate across partitions is estimated by $T_{\mathrm{JK}\to I} = \sum_{i\in I} \sum_{j\in J} \sum_{k\in K} \nu_{iI}^*\ \nu_{jI}^*\ T_{\mathrm{jk}\to i}$.

It should be noted that since (7.1) is a quadratic dynamical system (e.g. Rabinovich et al 1992, Rabani et al 1995), there is no reason to expect that either the inequalities defining Simon–Ando type properties or the aggregation rules for linear systems should apply here. However, since one of the defining properties of a Simon–Ando dynamic is the existence of local quasi–equilibrium distributions, if there exists such as distribution p^* for evolution under recombination and selection, then we can approximate p(t+1)=f(p(t)) as a linearization about p^*.

It is important to remember that any statements about the structure of the linearized transition operator **A'** do not allow one to make a statement about whether the recombination–selection system will have Simon–Ando type fast–slow dynamics. In order to do so, one needs information about the long–term behavior of the system, one in which the distribution of state variables can be quite far removed from any particular choice of distribution for the local linearization. So in stating that the linearized representation is "Simon–Ando" or that it satisfies (6.1b), the most that can really be said is that the local behavior of the system at some particular distribution is consistent with Simon–Ando in the short term (for instance, one can infer the near–stability of local quasi–equilibria).

However, we propose that the local linearization serves as a heuristically useful tool for identfying systems that are not Simon–Ando as well as those which satisfy the local quasi–equilibrium properties associated with the first phase of Simon–Ando dynamics. If even the local linearization fails to have Simon–Ando structure, then clearly the system will not have Simon–Ando type dynamics globally. Conversely, if the local linearization gives a transition operator consistent with Simon–Ando dynamics, then one can argue that at least the first stage of Simon–Ando decomposability, i.e. the existence of local quasi–equilibria,may be fulfilled.

Linearizing about the proposed quasi–equilibrium distribution, we obtain,

(7.2)

$$p_i(t+1) = f_i(p(t)) = \sum_{j=1}^{N} p_j w_j \sum_{k=1}^{N} p_k w_k T_{jk \to i}$$

$$p_i(t+1) \approx p_i^* + \sum_{j=1}^{N} \frac{\partial f_i}{\partial p_j}(p_j^*)(p_j - p_j^*) + O(2) + \ldots$$

$$= p_i^* + \left(\sum_{j=1}^{N} 2 w_j \sum_{k=1}^{N} p^*_k w_k T_{jk \to i} \right) (p_j - p_j^*)$$

in the transformed coordinate system with the perturbation state variables u=(p(t)–p^*), the state dynamics of u(t) are described in terms of the linear operator **A**' where

$$A'_{ij} = 2 w_j \sum_{k=1}^{N} p^*_k w_k T_{jk \to i}$$

can be evaluated given fitness and frequency distributions (as well as models of recombination) to determined whether the system locally induces fast–slow dynamical behavior.

Applying the corresponding sums on both sides of corresponding to inequality (6.1b) to **A**', we ask under which fitness functions and recombination rules the following will hold:

(7.3)

$$\left(\sum_{i \in J} \sum_{j \in J} 2 p^*_j w_j \sum_{k=1}^{N} p^*_k w_k T_{jk \to i} \right)_{\min J} >>$$

$$\left(\sum_{I \neq J} \sum_{i \in I} \sum_{j \in J} 2 p^*_j w_j \sum_{k=1}^{N} p^*_k w_k T_{jk \to i} \right)_{\max J}$$

for some distribution p^* (where min/max J refer to the classes J which respectively minimize and maximize the corresponding sides of the inequality). One can chose a "best case scenario" for this condition to be satisfied, namely, one where the fitness values for partition corresponding to the maximal value equal to those corresponding to the minimal value, without any assumptions about the structure of distribution p^* as a limiting case.

As for point mutation, we investigate the decomposability properties with respect to two types

of partitions; first the partitioning defined in terms of schema equivalence classes, second the radius κ n–dimensional balls around a fixed vertex point. For partitions defined by schema, the case of uniform (free) recombination is relatively straightforward to analyze, because the transition probabilities across schema depend only on the partial Hamming distances across the subset of loci defining the schema.

Specifically, if we rewrite (7.3) in the expanded form:

$$\sum_{i\in J}\sum_{j\in J} 2\, p^*_j\, w_j \sum_{k=1}^{N} p^*_k\, w_k\, T_{jk\to i} = \sum_{j\in J} 2\, p^*_j\, w_j \sum_{k=1}^{N} p^*_k\, w_k\, T_{jk\to i\in J}$$

and

$$\sum_{I\neq J}\sum_{i\in I}\sum_{j\in J} 2\, p^*_j\, w_j \sum_{k=1}^{N} p^*_k\, w_k\, T_{jk\to i} =$$

$$\sum_{j\in J} 2\, p^*_j\, w_j \sum_{K}\sum_{k\in K} p^*_k\, w_k\, T_{jk\to i\notin J} = \sum_{I\neq J}\sum_{j\in J} 2\, p^*_j\, w_j \sum_{K=0}^{n_s}\sum_{k\in K} p^*_k\, w_k\, T_{jk\to i\in I}$$

where for an allelic alphabet of size 2 there are 2^{n_s} partition classes C_I given n_s loci defining a schema, each class containing 2^{n-n_s} genotypes. Through abuse of notation, the indices K correspond to partial Hamming distance classes where all members of the Kth partition are of partial Hamming distance K to the schema loci in the Jth class (with K=0 corresponding to the Jth class itself). Under free recombination, for any two recombinant genotypes j,k with partial Hamming distances K=d_s the probabilities $T_{jk\to i\in J}=(\frac{1}{2})^{d_s}$, while This is simply the probability that in any pairing of distance d_s over the schema loci all of the parental types in schema class J are transmitted to the offspring. Therefore, we have

$$\hat{A}_{JJ} = 2\sum_{j\in J} p^*_j\, w_j \sum_{K=0}^{n_s}\sum_{k\in K} p^*_k\, w_k \left(\frac{1}{2}\right)^K = 2\, W_J \sum_{K=0}^{n_s}\left(\frac{1}{2}\right)^K W_K = 2\, W_J{}^2 + W_J \sum_{K=1}^{n_s}\left(\frac{1}{2}\right)^K W_K$$

$$\sum_{I\neq J}\hat{A}_{IJ} = 2\sum_{j\in J} p^*_j\, w_j \sum_{K=0}^{n_s}\sum_{k\in K} p^*_k\, w_k \left(1-\left(\frac{1}{2}\right)^K\right) = 2\, W_J \sum_{K=0}^{n_s}\left(1-\left(\frac{1}{2}\right)^K\right) W_K$$

it can be seen that for any choice of W_1 and W_2 (defined as before as the mean fitnesses of partitions C_1 and C_2, the subsets with the minimal within–class and maximal cross–class communication rates,

respectively), the Courtois inequality will not be satisfied under free recombination, because the magnitude of $\sum_{I\neq 2} \hat{A}_{I2}$ will be of the same order as that of $\hat{A}_{11}$. If on the other hand we posit a situation where each genotype has a certain probability ρ of undergoing recombination in every generation versus probability $1-\rho$ of reproducing through selfing, with overall genotype transition rates

$$p_i(t+1) = f_i(p(t)) = (1-\rho)\, p + \rho \left(\sum_{j=1}^{N} p_j\, w_j \sum_{k=1}^{N} p_k\, w_k\, T_{jk\to i} \right)$$

which, linearized about p gives the local transition operator A' as

$$A'_{ij} = \rho \left(2\, w_j \sum_{k=1}^{N} p^*{}_k\, w_k\, T_{jk\to i} \right) \qquad i \neq j$$

$$(1-\rho) + \rho \left(2\, w_j \sum_{k=1}^{N} p^*{}_k\, w_k\, T_{jk\to i} \right) \qquad i = j$$

From the above, the within and cross class transition rates are approximated by:

$$\hat{A}_{JJ} = W_J \left[(1-\rho) + 2\,\rho \sum_{K=0}^{n_s} \left(\frac{1}{2}\right)^K W_K \right]$$

$$\sum_{I\neq J} \hat{A}_{IJ} = 2\,\rho W_J \sum_{K=0}^{n_s} \left(1 - \left(\frac{1}{2}\right)^K\right) W_K$$

Analogous to mutation–selectionsystems with very low mutation rates, it is relatively easy to satisfy (6.1b) given a sufficiently small value of ρ, except in cases where $W_2 >> W_1$. This is to be expected because of the way the model is formulated; as with mutation, offspring in each generation tend to remain in the same partition as parents simply because for very low ρ each genotype produces offspring identical to itself. This form of internal stability is the trivial limiting case for which strict sense "Simon–Ando" decomposability can apply even on a flat fitness landscape (though the degree of inequality is certainly enhanced by the right choice of mean fitness differentials).

For single point recombination the combinatorics of the problem become much more problematic. While under free recombination only the partial Hamming distances between recombinants are needed to calculate the probability of remaining in the parental partition, in the case of single (or 2...n–1 point) recombination requires information about which particular loci determine the partial Hamming

distances and their lengths apart on the chromosome. For example, under single point recombination the probability that a recombinant between {11000,00000} produces an offspring outside the 11*** equivalence class is less than the same for a schema defined by 1****1, i.e. {10001,00000} because there are more possible recombination events that could produce offspring outside the 1****1 class than for 11***.

If the equivalence classes are defined by a single locus, calculating the within and cross–partition class transition rates $T_{jk\to i\in J}=\frac{1}{2n}$ (for j∈J and k∉J), as the probability of recombination occurring at that particular locus is simply the reciprocal of the number of loci, and given that a recombination even occurs there one half of the progeny will be of the parental type. For a schema defined by two loci, $T_{jk\to i\in J}=\frac{1}{2n}$ for a partial Hamming distance of unity, while for a partial Hamming distance of two, the probability of obtaining a parental recombinant is $\frac{n-D}{2n}$, where D is the number of loci separating the schema elements. In the case where $d_s(j, k) = 0$, it is obvious that $T_{jk\to i\in J} = 1$.

From this we can calculate both sides of the Courtois inequality for the two locus schema under single point recombination. The relevant equivalence classes with respect to a particular schema class have the partial Hamming distances 0,1,2 based on how many schema loci have different allelic states than the parent genotype (the same procedure with one fewer partial Hamming class can be used to calculate the terms in the trivial case of a single locus schema).

Below W_2 and W_2 are the mean fitnesses of the partial Hamming distance 1,2 classes with respect to partition J:

$$\hat{A}_{JJ} = 2 \sum_{j\in J} p^*_j w_j \sum_{K=0}^{2} \sum_{k\in K} p^*_k w_k T_{jk\to i\in J} = 2 W_J \left[W_J + \frac{1}{2n} W_1 + \frac{n-D}{2n} W_2 \right]$$

$$\sum_{I\neq J} \hat{A}_{IJ} = 2 W_J \left[\left(1 - \frac{1}{2n}\right) W_1 + \frac{n+D}{2n} W_2 \right]$$

The Courtois inequality is not readily satisfied in this case. While $\sum_{I\neq J} \hat{A}_{IJ}$ can be minimized by assuming $W_J >> W_0, W_1$, the inequality requires a comparison of $\hat{A}_{JJ}$ minimal over all J to $\sum_{I\neq J} \hat{A}_{IJ}$ maximal over all J. Thus minimizing W,W with respect to the maximum value for $\sum_{I\neq J} \hat{A}_{IJ}$ also reduces the magnitude of $\hat{A}_{JJ}$, because the partition J which minimizes the latter is by definition in the 0,1 partial Hamming classes with respect to J_{max}. From this we can conclude that

(local) Simon–Ando is not likely to occur under single point recombination in the absence of some model which restricts the frequency of recombination itself.

It should be apparent that for longer schema, calculating these transition probabilities will require information about which schema loci constitute the partial distances as well as pairwise (chromosome length) distances for each of those loci. As such, we have no closed form solution for within and cross–partition class transition rates under single–point recombination, though these calculations should be fairly straightforward numerically for sufficiently short schema.

Turning now to partitioning defined by Hamming distance κ radii with respect to some choice of reference vertices (the first type of partitioning investigated in the context of mutation–selection systems), chose partition C_J as the set of genotypes within Hamming distance κ of x_0. To calculate $\sum_{i\in J} A_{ij}$, the probability that the progeny i of j∈J are elements of the same partition, one needs the following set of Hamming distances: d_{0j} (distance between reference vertex and parent j), d_{0k} (distance between reference vertex and parent k), and d_{kj}.

From these quantities one can calculate the "shared" distance from the reference vertex to both parents: $k_{jk}=(d_{0k}+d_{0j}-d_{jk})/2$ (i.e. if the reference vertex consists of all 0's, k_{jk} denotes the number of shared 1's in both parent sequences). In turn, the Hamming distance from the reference genotype to the offspring is $d_{0i}=k_{jk}+m_{jk}$, with m_{jk} being the number of offspring loci with allelic states different from the reference vertex which have been inherited from either parent j or k (but not both). This quantity has a binomial distribution given free recombination,

$$P(m_{jk}) = \binom{d_{jk}}{m_{jk}} \left(\frac{1}{2}\right)^{d_{jk}}$$

from which one can derive the probability that offspring i will be within Hamming distance κ of the reference vertex (and thus within the partition),

$$T_{jk\to i\in J} = P(d_{0i} \le \kappa) = \sum_{k=0}^{\kappa-k_{jk}} \binom{d_{jk}}{k} \left(\frac{1}{2}\right)^{d_{jk}}$$

Unfortunately, there is no actual closed form solution for this partial sum, which evaluates to the following, where H_{21} is the Kummer confluent Hypergeometric function of the second kind, i.e. $H_{21}(a,b,c,z)=\sum_{k=0}^{\infty}(a)_k (b)_k/(c)_k z^k/k!$,

$$P\,(d_{0\,i} \le \kappa) = 1 - \frac{d_{jk}\,(2^{-d_{jk}})\,d_{jk}!\,H_{21}\,(1,\ 1+\kappa-k_{jk}-d_{jk},\ 2+\kappa-k_{jk},\ -1)}{(2+\kappa-k_{jk})!\,(d_{kj}-\kappa+k_{jk})}$$

In terms of calculating the within and cross–partition class transition rates for the κ–radius partitioning, the probability of remaining within C_J is given by:

$$\hat{A}_{JJ} = 2\sum_{j\in J} p^*_j\, w_j \sum_k p^*_k\, w_k\, T_{jk\to i\in J} = 2\sum_{j\in J} p^*_j\, w_j \sum_k \sum_{r=0}^{\kappa-r_{jk}} p^*_k\, w_k \binom{d_{jk}}{r} \left(\frac{1}{2}\right)^{d_{jk}}$$

To compute the cross–class communication rates, one needs to define other equivalence classes in terms of Hamming distances to some set of reference vertices, i.e.

$$\sum_{I\neq J} \hat{A}_{IJ} = 2\sum_{j\in J} p^*_j\, w_j \sum_k p^*_k\, w_k\, T_{jk\to i\notin J} =$$

$$2\sum_{j\in J} p^*_j\, w_j \sum_k \sum_{r=\kappa-r_{jk}+1}^{d_{jk}} p^*_k\, w_k \binom{d_{jk}}{r} \left(\frac{1}{2}\right)^{d_{jk}}$$

which, as for the sum over values within the κ radius, has no closed form but evaluates to a multiple of the Hypergeometric function H_{21}:

$$P\,(d_{0\,i} > \kappa) = \sum_{k=\kappa-k_{jk}+1}^{d_{jk}} \binom{d_{jk}}{k} \left(\frac{1}{2}\right)^{d_{jk}} =$$

$$\frac{2^{-N}\,(1+d_{jk})!\,H_{21}\,(1,\ 1+\kappa-k_{jk}-d_{jk},\ m+\kappa-k_{jk},\ -1)}{(2+\kappa-k_{jk})!\,(d_{kj}-\kappa+k_{jk})}$$

Unfortunately, there is no way to collect $p_j w_j$ terms for partitions thus defined and derive a result in terms of the mean fitnesses of each class. The reason for this is that while for uniform recombination schema–based equivalence classes, each value $T_{jk\to i}$ is equal for all k∈K, allowing one to factor out a $\overline{W}_J$. For recombination across Hamming–distance based equivalence classes, $T_{jk\to i}$ will differ according to one's choice of k. This is another reason why there is no closed–form expression for the within versus cross–class communication rates for this partition. Consequently, as far as we can determine the only way to evaluate whether any Hamming distance based partitioning is consistent with

Simon–Ando is by numerical computation on a case–by–casebasis for each fitness function.

The situation is of course even more problematic for single–point (or multipoint) recombination, in that the offspring classes have to be averaged over all parental types of given Hamming distances d of one another, as the probability of any offspring type depends not only on the Hamming distances but on the lengths separating individual loci.

However, the analysis of uniform recombination suggests one result that almost certainly applies to most recombination–selection systems. Because most modes of recombination allow the production of offspring outside the parental partition at relatively high rates (as long as all possible parental pairings are permitted with equal probability), it implies that in general achieving the conditions for Simon–Ando with recombination in each generation is unlikely. One rather trivial way of achieving a much higher rate of within–partition versus cross–partition class communication is to reduce the frequency of recombination events, i.e. as in the scenario investigated above, have probability ρ of sexual reproduction and $1-\rho$ of selfing. For $\rho<<1$, most offspring are identical to their parents and hence by default remain in whatever partition they belong in.

A more interesting model which we leave as an open–ended question is what happens under assortative mating. If instead of random mating we assume that there is some pairing probability function f(p_j,p_k) that depends on the pairwise Hamming distances between j,k or on the partial Hamming distances between relevant schema–defining loci, it should be obvious that if the parents tend of both be members of the same partition there will be a bias in producing offspring which are members of this partition. This is a more interesting scenario than the facultative recombination model because it allows for a non–trivial internal transmission dynamic within and across partitions, as well as relating conceptually to the origin of species through assortative mating mechanisms (Bush 1982, Kondrashov and Minna 1986).

■ Discussion: Future Directions

The question of just how "common" fitness landscapes with transition operators consistent with (3.0) and by necessity (6.1) relative to the entire space of possible fitness landscapes might be can be addressed from a number of directions. A natural approach would be to define a "landscape space" for an n–locus system, i.e. as a Fourier function space f:V:→ℝ,

$$(9.1) \qquad f(v) = \sum_{k=1}^{N} a_i \phi_k(v) + a_0$$

where $\phi_k(x)$ is a rule mapping each k–tuplet subset genotype v onto a real–valued contribution to fitness. Representing each k–tuplet as $\sigma_1 \sigma_2 ... \sigma_k$ where $\sigma_i = \pm 1$, we have a straightforward representation of epistatic interactions as Walsh function components (Weinberger 1992, Stadler 1994, Stadler et al 1998). Given a k–subset of loci π_k and summing over all $\binom{n}{k}$ possible k–products:

$$\phi_k = \sum_{x=1}^{\binom{n}{k}} \prod_{i \in \pi_x} \sigma_i$$

Now given a parameter space $\{a_0 ... a_n\}$, we have a well–defined fitness function space in this way, we can ask what proportion of landscapes in this universe have a partitioning which satisfies (6.1). Given the intractable dimensionality of this function space, a more reasonable starting point might be simply to ask which orders of epistatic interaction (i.e. fitness functions f=ϕ, given "elementary landscapes" sensu Stadler 1994) tend to produce the desired landscapes.

An alternative method would be to characterize "valley" landscapes in terms of landscape autocorrelation (Stadler 1994). Landscape autocorrelation has been related to orders of epistatic interaction, there is a straightforward relationship between the statistical characterization and the underlying epistatic rules that we can make use of. Such an approach may be fruitful because the conditions necessary for valley landscapes seem to require strong local fitness function autocorrelation (producing localized neighborhoods of high fitness genotypes) and globally low autocorrelation (leading to separation of the high fitness partitions by valleys).

Work on landscape connectivity by Gavrilets (Gavrilets and Gravner 1997, Gavrilets 1999) suggests that high levels of connectivity are a generic property of high–dimensional systems while separation by broad valleys requires rather specialized conditions on the fitness functions. So whether decomposable systems prove relevant is probably significant empirically than theoretically. We know

that they can be constructed even though most landscapes probably are not of this form, the question remains whether this more restricted class of landscapes is common enough for aggregation of variables methods to be at all useful in analyzing mutation–selection systems.

Therefore, what one is ultimately interested in is not whether random landscapes satisfy Simon–Ando or the "valley" generalization, but whether fitness landscapes in nature (i.e. real genetic systems) tend to have the structure in question. This is a more complicated question to address given the difficulty of measuring fitness in any but the most artificial systems, though a good starting point may be the growing literature on RNA and protein landscapes defined in terms of the polymer's performance of a given catalytic function.

It may be that Simon–Ando decomposability (defined by 3.0 and 6.1) may be too restrictive, and that even if the transition operator for a fitness landscape cannot be represented in this form it may still have some of the desired aggregation and decomposability properties. If what we are interested in general is the existence of classes of genotypes on a fitness landscape which behave as quasi–independent entities over a certain time scale, there may be a more general class of operators with the desired dynamical property. What is more, finding such an alternative representation as a generalization of Simon–Ando may be of value even in describing systems which are consistent with the stronger criterion, in that the alternative representation may allow for a greater reduction in the state space necessary for a dynamically sufficient representation.

A partitioning consistent with (3.0) is restrictive in that it requires that every vertex be a member of a partition where every element communicates strongly with some of the vertices that are members of the same subset (see closure theorem 6.2). Consequently, a strict Simon–Ando partitioning allows for only as many partitions are there are local optima, thus a two–peaked landscape can only be partitioned into two subsets, at least one of which has a large number of constituent microstates. This does not permit a substantive reduction of state space unless there are a large number of peaks. Furthermore, because the within versus cross–partition class communication rates for partitions of arbitrary topology do not generally have closed form solutions, we proposed the use of κ–ball partitions to simplify the aggregation calculations. As noted above, however, a generic landscape need not be partitionable into κ–balls of fixed radius. It is necessary to allow partitions of varying radius, in many cases including trivial "partitions" which consist of a single vertex. If many such vertices remain in the complement to the κ–ball partitioning, it becomes apparent that the original goal of an aggregate representa-

tion is only partially satisfied.

Here we investigate the possibility of treating the "remainder" vertices in a landscape which is not fully partitionable as a self–contained aggregate entity in its own right independent of its topology or fitness distribution.What we propose below in preliminary form is a weaker version of Simon–Ando decomposition that would allow one to make partitions around the optima and to have another partition (or any number of partitions) corresponding to the low–fitness genotypes separating the two peaks.

The somewhat less restrictive "block triangular" form discussed in Ando and Franklin (1963) would still impose the same constraints on landscape partitioning, while alternative aggregation of variables techniques (such as the bounded aggregation methods of Courtois 1984, 1989) also don't give representations consistent with the partition classes and their complements used in our class of models. Here we analyze a fitness landscapes with a matrix structure where part of the lattice is partitionable into Simon–Ando components while a substantial complement set of vertices remains which is not a Simon–Ando partition according to definition (6.1).

The classical view of Wrightean landscapes postulates low fitness "valleys" of arbitrary width (with any number of steps separating high fitness regions). In this case, with a proper arrangement of rows and columns, where an arbitrary number of diagonal "submatrices" are also of order $\epsilon<<1$

$$\begin{pmatrix} A_1 & \epsilon & \epsilon & \epsilon & \epsilon \\ \epsilon & \ddots & \epsilon & \epsilon & \epsilon \\ \epsilon & \epsilon & A_I & \epsilon & \epsilon \\ \epsilon & \epsilon & \epsilon & \ddots & \epsilon \\ \epsilon & \epsilon & \epsilon & \epsilon & E \end{pmatrix} = \boldsymbol{A}^* + \epsilon \boldsymbol{C} \tag{8.0 a}$$

where E is a square matrix of order ϵ values of arbitrary dimension, corresponding to a decomposition $\mathbf{A}=\boldsymbol{A}^*+\epsilon\mathbf{C}$ where $\boldsymbol{A}^*$ consists of block diagonal matrices up through the Kth partition and zeros elsewhere.

Investigating the dynamical properties of operators with a structure consistent with (8.0) is beyond the scope of this paper, but it can be seen intuitively that there should be short term quasi–equilibria associated with each A as there were in the Simon–Ando case, with the complication that communication across the partition classes occurs via indirect paths through E rather than exclusively through direct cross–class communication. One can also consider the limiting case where there is no direct communication between classes A_I and A_J

$$(8.0\,b) \qquad \begin{pmatrix} A_1 & 0 & 0 & 0 & \epsilon \\ 0 & \ddots & 0 & 0 & \epsilon \\ 0 & 0 & A_I & 0 & \epsilon \\ 0 & 0 & 0 & \ddots & \epsilon \\ \epsilon & \epsilon & \epsilon & \epsilon & E \end{pmatrix} = \boldsymbol{A}^* + \epsilon \boldsymbol{C}$$

so that any aggregate description of the cross–term dynamics between A and A depends on the rate of transit through the intermediate "valley."

On a final note, we return to an observation we made in the introduction, namely, that aggregation of variables (at least implicitly or conceptually) has found numerous applications in evolutionary biology. An approach in many ways complimentary to ours has been undertaken by a number of groups (Frenkel et al 2000, Watson 2002), where partitioning according to strong versus weak coupling is used to represent epistatic interactions. In their case, the Simon–Ando partitions correspond not to clusters of genotypes but rather to clusters of interacting genes. Whether or not there is between decomposability of epistasis rules and landscape decomposability as defined in this paper remains to be answered.

■ Dedication and Acknowledgements

We dedicate this paper to the memory of the late Dr. Herbert Simon (1916–2001),with whom the senior author had the privelege of corresponding with in the last year of his life, and whose original research inspired this project.

We express our gratitutude to Joachim Hermisson for his advice on recombintaion models and for his collaboration on related projects. The authors also thank the following people for their assistance and commentary on both technical and conceptual aspects of this paper: Sean Rice, Junhyong Kim, Robert Dorit, Ashley Carter, Pierre–Jacques Courtois, Claus Wilke, and Richard Watson.

■ Figure Captions

Figure 1:

Shows a plot of the exact stationary distribution (uniform at 1/32 for each genotype) against the Simon–Ando eigenvector estimate for a 5 locus, 2 allele fitness landscape with every genotype fitness W(x)=1.0. The 32 genotypes are arranged in the order of Boolean numbers, i.e. 00000,10000,...11111.- The mutation rate per locus is set to 0.01. While the order of magnitude estimates are correct, the Simon–Ando approximation for any particular genotype deviates due to the fact that edge vertices in each partition class are set as "boundaries" in the approximation.

Figure 2:

The following plots are for the mutation–selection matrix induced by a bimodal fitness landscape. In a 5 locus, 2 allele system, the genotypes 00000 and 11111 have fitness values set to 1.0. The Hamming distance one genotypes have a fitness of 0.9, while the Hamming distance two neighbors (with respect to either peak) are set to 0.01. Mutation rate is again μ=0.01.

a) This symmetric, bimodal fitness landscape has degenerate leading eigenvectors with identical λ =0.999 eigenvalues. The normalized degenerate eigenvectors are shown above.

b) The stationary distribution for this bimodal landscape is plotted against togehter with the estimated distribution derived from the eigenvectors of the Simon–Ando partition matrices.

Figure 3:

The fitness landscape is the same as the above, except that one peak was set to a lower fitness (W(11111)=0.9, W(00000)=1.0) value to illustrate directional selection. The corresponding unimodal leading eigenvector is closely approximated by Simon–Ando aggregation.

Figure 4:

The fitness landscape in this set of computations has two peaks of almost equal fitness: W(00000)=1.0 and W(11111)=0.99. However, the peak with somewhat lower fitness has mutational neighbors with fitness values approximately equal to 0.9 while the higher peak has single–point mutational neighbors

with a fitness of about 0.1. The Hamming distance two neighbors with respect to both peaks are again set to 0.01, with μ set to 0.01. For this parameter range, the stationary distribution's probability density is concentrated about the more "mutationally robust" genotype, i.e. the one with the higher fitness neighbors. While this pattern is qualitatively predicted using the Simon–Ando approximation, it can be seen from the graph that the prediction is rather poor.

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■ Figures

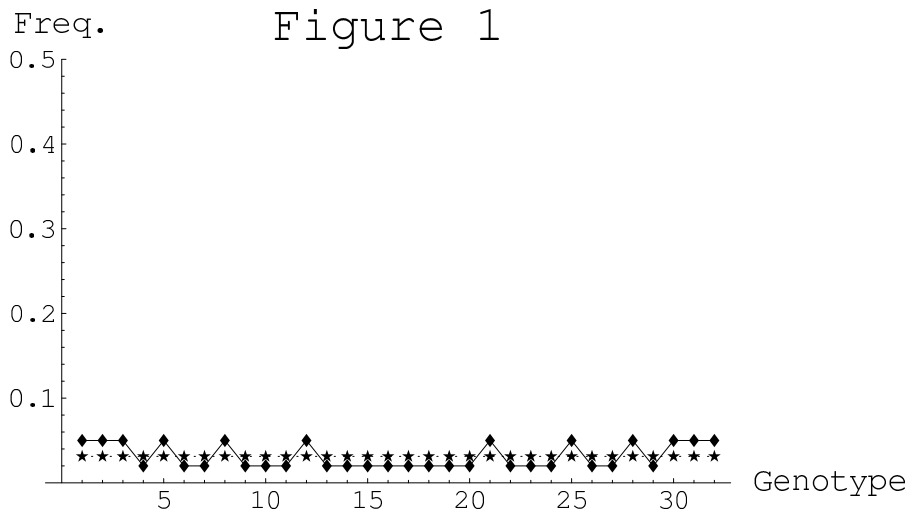

Figure 2a

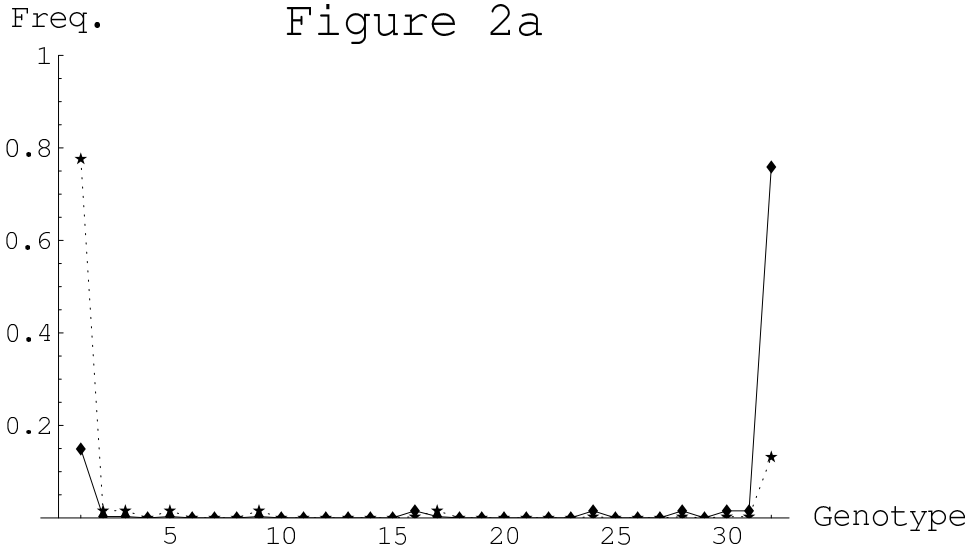

Figure 2b

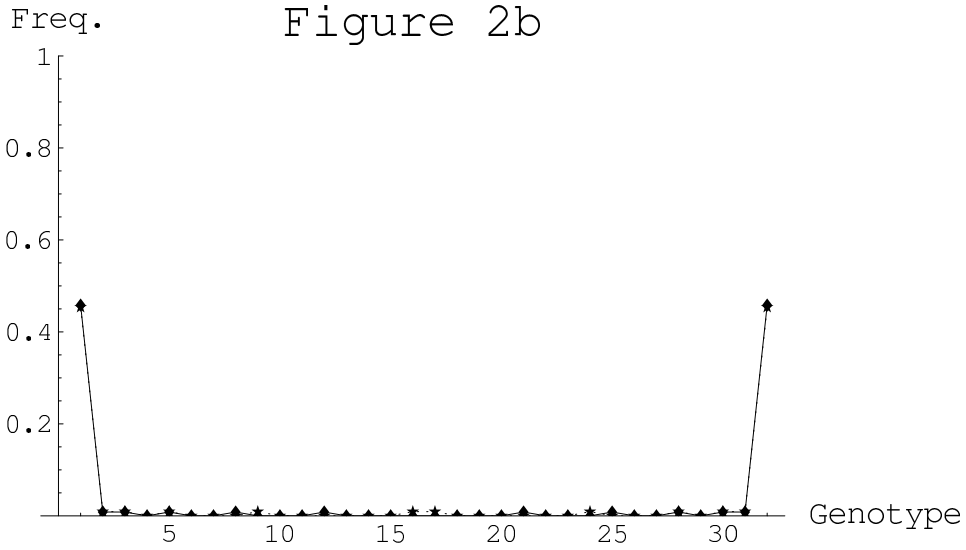

Figure 3

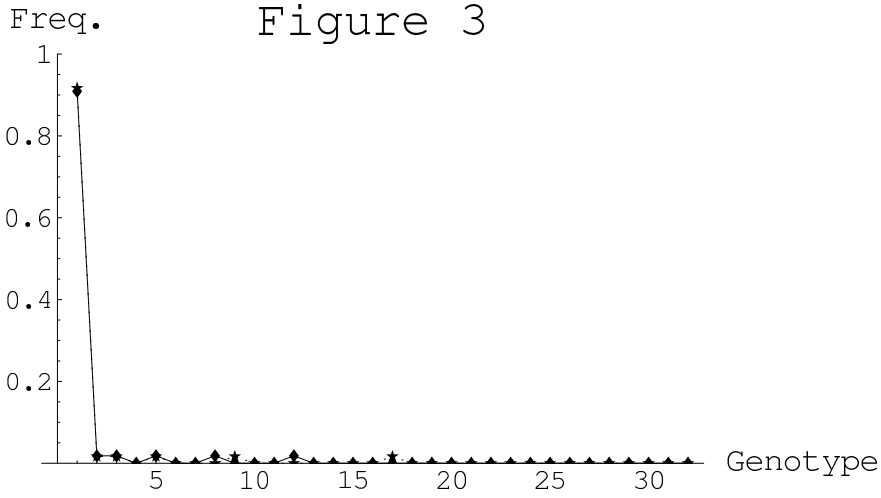
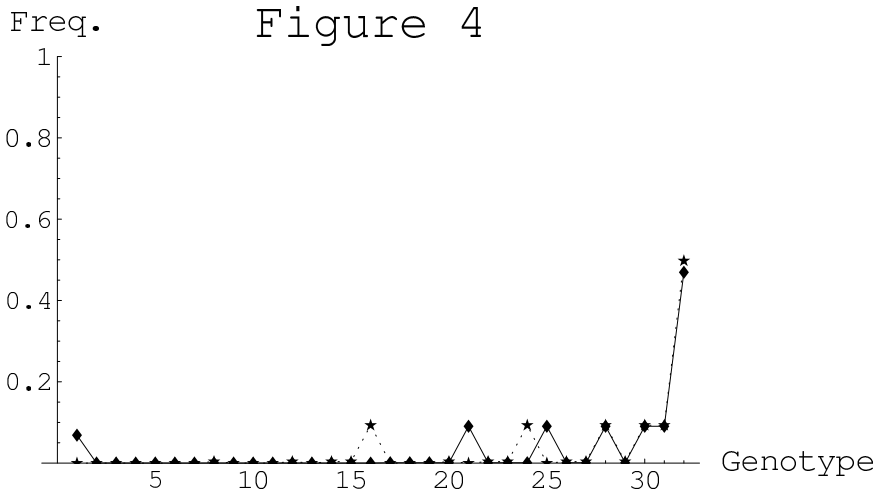
Figure 4