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Population Dynamics in a Spin-Glass Model of Chemical Evolution

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Summary. We introduce a simple model describing the evolution of a population of information-carrying macromolecules. We discuss the asymptotic dependence of the variability of the population on different parameters, representing the severity or the fluctuations of the environment. We show the existence of a transition separating a neutralist evolutionary regime from a trapped one. We investigate the dependence of the evolutionary behavior of the population on the correlation properties of the fitness landscape.

Key words: Prebiotic — Self-organization — Spin-glass — Neutralism

1. Introduction

We introduce and discuss in this paper a simple model of evolution at the molecular level. Our aim is to clarify the issues involved in some of the recent approaches to chemical evolution, and in particular to the emergence of information-carrying macromolecules. The only mechanisms envisaged are mutation and selection; mutation is taken to be completely random, whereas selection operates according to the fitness value of the individual. Fitness depends on the individual alone, who competes, as it were, against an immutable environment. "Struggle for life" is only indirectly embodied in a fixed population constraint. The model is investigated by qualitative and analytic arguments and by computer simulations.

The original motivation was to understand the long-time behavior of models introduced to explain the origin of biological information (Anderson 1983; Tsallis and Ferreira 1983; Rokhsar et al. 1986; see also Peliti 1989). We find nevertheless that our attempt can be interpreted within a slightly wider scope. Whereas the model is explicitly defined under strict simplifying assumptions to make its treatment feasible, we believe that most features of its behavior are common to a class of models that share its fundamental architecture: namely, the existence of point mutations exclusively, and the dependence of fitness on the nature of the single individual. The features we believe to be common to all such models are:

i) the survival, in the long run, of a single molecular quasi-species; this prevents, within the assumptions of the model, the eventual coexistence of distinct molecular species; and
ii) the existence of either neutralist (Kimura 1983) or adaptive regimes, according to the values of the parameters entering the definition of the model.

Some other features might also be valuable: the dependence of the average fitness of the population on a parameter defining the sloppiness (Dyson 1985) of the selection mechanism; and the transition from a wandering (neutralist) to a trapped evolution regime, corresponding quite closely to a gelation transition in models of disordered systems (Mézard et al. 1987). A key role is played in our approach by the concept of the correlation of a fitness landscape, whose importance has been emphasized by Kauffman and Levin (1987) and Kauffman (1988). We shall sketch the consequences of a varying fitness correlation on the behavior of the model.

As we have mentioned, we mainly conceive as

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evolving entities information-carrying polymers such as protopolynucleotides. We assume that some replication mechanism of moderate efficiency exists. This justifies the consideration of not too large "genome" sizes. Nevertheless the same questions could be asked and the same model could be applied (with minor modifications) to other situations. In particular, the conclusion that the fluctuation instability prevents this class of models from describing the diversity of life forms applies in general.

The model is defined in section 2. The properties of the fitness function, and in particular the correlation concept, are discussed in section 3. Section 4 contains the results concerning the apparently trivial case in which the death probability is independent of the individual. Section 5 contains the results of the simple case in which selection is sharp and the fitness function is rugged. More general cases, with sloppier selection rules and correlated fitness landscapes, are considered in section 6. Section 7 contains a brief discussion. Appendix A contains the discussion of a class of random functions with tunable correlation. Appendix B contains the derivation of a simple but important technical result needed in section 4.

2. The Model

The model we consider has been inspired by those introduced by Anderson (1983) and Rokhsar et al. (1986). We have striven to reach a maximum of simplicity in order to highlight the effects of mutation and selection alone in a given fitness landscape.

First of all, we have chosen to work with a fixed population size M. This is motivated mainly by computational simplicity in the simulations. Nevertheless we do not feel that it imposes too much of a restriction on the model. A more realistic constraint would be a fixed resource flux. However, it is known that differential equation models of populations evolving under constant flux constraints behave essentially like those under constant population size conditions (see, e.g., Küppers 1983). They are in general more difficult to solve. The effect we neglect is the possible variation in population size due to variation in the average fitness. Although this effect is important, the computational complications introduced by relaxing the fixed population constraint have convinced us to keep it.

Present-day information-carrying macromolecules are chains of monomers, each of which may be one of 4 (for nucleic acids) or 20 (for proteins) types. Mutation and selection processes may already appear when the choice is restricted to just two types (standing, e.g., for purine or pyrimidine). This simplification has already been introduced by the authors referenced above and by Abbott (1988). We define therefore the configuration of a given individual α ($\alpha = 1, 2, \ldots, M$) by a set $\mathbf{s}^\alpha$ of N binary variables:

$$\mathbf{s}^\alpha = (s_1^\alpha, \ldots, s_N^\alpha);$$
$$s_i^\alpha = \pm 1,\ \alpha = 1, \ldots, M,\ i = 1, \ldots, N \qquad (2.1)$$

We assume that the size N of the "genome" is fixed. This is a very drastic limitation, which we are planning to relax in future work. However, it allows us to consider a "genome space" defined once and for all as the space of all the 2^N possible genome configurations. This space has the topology of an N-dimensional hypercube. It is endowed with a natural notion of distance, i.e., the *Hamming distance*, d_H, equal to the number of entries s_i that are different in the two configurations $\mathbf{s}$ and $\mathbf{s}'$:

$$d_H(\mathbf{s}, \mathbf{s}') = \frac{1}{2}\sum_{i=1}^{N}(1 - s_i s_i') \qquad (2.2)$$

Equivalently, one may consider the *overlap*, $q(\mathbf{s}, \mathbf{s}')$, between the two configurations, defined by

$$q(\mathbf{s}, \mathbf{s}') = \frac{1}{N}\sum_{i=1}^{N} s_i s_i' = 1 - \frac{2d_H}{N} \qquad (2.3)$$

We shall sometimes say that two configurations, $\mathbf{s}$ and $\mathbf{s}'$, whose Hamming distance is equal to ν, are "ν mutations away" from each other.

One should not lose sight of the shortcomings of our choice to have a fixed genome size N. It implies that we are in fact focusing on the effects of point mutations, and that we do not consider all processes that may lengthen or shorten the genome. These processes, which include in particular gene duplication, are undoubtedly important in the long run. On the other hand, the simulations of a more complex model performed by Rokhsar et al. (1986), while showing a fast growth of polymer length N in the early stages, appear to imply that this growth becomes much slower at later times. The fast-growing phase could be described by a simpler model, like the one introduced by Tsallis and Ferreira (1983; see also Tsallis 1989). We assume that we are considering a time scale in which all polymers contained in the population have reached an almost constant length.

We do not explicitly consider the mechanism of replication. If we take, e.g., template replication, the net effect of a two-step cycle is to produce a new copy of the original chain, maybe with some replication errors (mutations). If we want to implement the fixed population constraint, it is more convenient to separate the mutation from the replication steps. We introduce, therefore, random mutations in a population of fixed size, and we perform error-

less replication to fill in the gaps generated in the selection step. To cut down the arbitrariness, we assume that all mutations are equally likely. Genome dependence will appear only at the selection step.

Selection involves the evaluation of a fitness function, $H(\mathbf{s})$, defined on genome space. We defer to the next section the discussion of $H(\mathbf{s})$. We suppose only that an individual with higher values of H has a smaller probability of being removed at any selection step than those with lower values of H. We can therefore define a *death probability*, $p(H)$, as a monotonically decreasing function of H, interpolating between 1 and 0 as H increases from $-\infty$ to $+\infty$. A form of this function has been suggested by Rokhsar et al. (1986):

$$p(H) = \frac{1}{1 + e^{\beta(H - H_0)}} \tag{2.4}$$

The coefficient β is a *sharpness parameter*, and H_0 is a *threshold*. When $\beta \to \infty$, the death probability is 1 for all configurations $\mathbf{s}$ such that $H(\mathbf{s}) < H_0$, and 0 otherwise; i.e., survival is cut sharply at the threshold. When $\beta < \infty$, the cut is more gentle, or, in other words, selection is sloppier. If $\beta = 0$, the death probability is always equal to ½. Higher values of H_0 correspond to more exacting environments. Smaller values of β correspond to the existence of mechanisms that partially disconnect survival from fitness (e.g., strongly fluctuating environments or error-correcting developmental programs).

We are thus led to the definition of the following mutation–selection mechanism in three steps:

i) *mutation:* a fraction τ of the NM units (i, α) present in the population is chosen at random, and its state is changed:

$$s_i^\alpha \to -s_i^\alpha \tag{2.5}$$

we shall assume that τ is a small number—its actual magnitude will be discussed later;

ii) *selection:* the fitness function $H(\mathbf{s})$ is evaluated for each individual α as a function of the configuration $\mathbf{s}^\alpha$ of its genome; the individual is then removed from the population ("dies") with a probability p given by eq. (2.4);

iii) *replication:* as a consequence of the previous step, a number M' of individuals will have died (we neglect the small probability that the whole population is annihilated in one go); to keep the population size constant, one chooses M' times an individual among the surviving ones and makes a copy of it.

The succession of the steps i–iii is called a *generation*. Adaptation only affects step ii. One might of course envisage more general scenarios, where not all mutations are equally likely, or where the replication probability is not equal for all surviving individuals. We think however that our model reduces arbitrariness to a bare minimum, still keeping sufficient generality to describe a set of reasonable evolution processes.

3. The Fitness Function

We now turn to a discussion of the fitness function, $H(\mathbf{s})$. Quite independently of the nature of the individuals that make up our population—be they polymers in the prebiotic soup, or genes coding for homologous proteins in a given species—we expect that their fitness will be the outcome of a complex interaction with the environment. It is difficult to build up a satisfactory theory that associates an explicit fitness value with any given sequence $\mathbf{s}$.

If we imagine that our sequences represent protopolynucleotides, one may consider several contrasting effects by which the nature of a sequence may affect its own replication efficiency. If two subsequences are complementary to each other, for example, the chain may fold on itself like a hairpin, and become therefore less likely to reproduce. On the other hand, the same effect may yield a more compact coil, which is presumably more resistant to environmental degrading agents.

Because the actual fitness function is unknown, the best we can do at the present time is to draw it at random from a certain class of functions, which we may try to specify a priori. One hopes that the qualitative behavior of the model will depend only on the statistical properties of the fitness function, which are the same for almost all realizations within the given class.

One important requirement is that the fitness function should exhibit a large number of optima. This point has been emphasized by Anderson (1983). Only in this way, in fact, can one explain the coexistence of both stability and diversity in information-carrying macromolecules. This condition can be achieved if there is a sufficient degree of *frustration* among the different interactions involved (Toulouse 1977), i.e., if several competing interactions coexist that cannot all be satisfied at the same time. As we mentioned above, it is likely that actual fitness functions do involve such competing effects. This has led Anderson (1983) to introduce as a model fitness function the energy function (Hamiltonian) of random ferromagnets (spin-glasses), where the coexistence of ferromagnetic and antiferromagnetic interactions leads to frustration and to the coexistence of a large number of optima.

We have considered a more general class of functions in order to analyze the effects of a varying

degree of correlation of the fitness landscape. This landscape may be smooth or rough according to the higher or lower degree of correlation existing among the random values of $H(\mathbf{s})$ relative to different configurations. The landscape correlation measures how the fitness values of neighboring sequences $\mathbf{s}$ and $\mathbf{s}'$ are different from each other on average.

The smoothest landscape has only one optimum, and allows one to define at each configuration $\mathbf{s}$ a direction of steepest ascent, pointing toward that optimum. Such is the landscape considered by Dyson (1985). As the degree of correlation decreases, the number of optima increases, and the path length connecting any given sequence $\mathbf{s}$ to the nearest optimum decreases. On the other hand, in the same limit, the values of the fitness of these optima become smaller and smaller, and become typically of the order of the mean of $H(\mathbf{s})$. We may expect therefore that the behavior of evolving systems does depend on the correlation of the fitness landscape.

Kauffman and Levin (1987; see also Kauffman 1988, 1989) have introduced a class of fitness functions with tunable correlations in an evolutionary context. A basically equivalent class of functions was introduced in the context of the theory of disordered systems by Derrida (1980, 1981). We can exploit their results to define a number of possible fitness landscapes whose degree of correlation may be changed at will.

We define in Appendix A a class of fitness functions $H_K(\mathbf{s})$, whose correlation decreases as the integer parameter K increases. These functions are analogous to the NK model introduced by Kauffman (1988, 1989). For $K = 2$, one recovers the spin-glass fitness function introduced by Anderson (1983). In the limit $K \to \infty$, one obtains a completely uncorrelated (or *rugged*) fitness landscape, such as that discussed by Kauffman and Levin (1987). This function is known, in the context of statistical physics, as the Random Energy Model (REM) (Derrida 1980, 1981).

Although the REM is easiest to think upon, it probably is not suitable to describe actual evolutionary processes. Kauffman and Levin (1987) argue that a certain degree of correlation is needed to avoid the *complexity catastrophe*, related to the fact that, in a rugged fitness landscape, most local optima have fitness values close to the mean. We have therefore also considered a rather correlated fitness function (first introduced in this context by Anderson 1983), namely the "spin-glass" function

$$H_2(\mathbf{s}) = \sum_{\langle i,j \rangle} A_{ij} s_i s_j \tag{3.1}$$

The sum runs over all distinct pairs of units, and the A's are independent, identically distributed random variables for each such pair. This form has the advantage of being well studied (see, e.g., Mézard et al. 1987). Although it is rather correlated, it exhibits a relatively large number of local optima (at least if N is sufficiently large).

To summarize, we have considered the following two possibilities for $H(\mathbf{s})$:

i) the REM, completely uncorrelated, in which $H(\mathbf{s})$ assumes an independent value for each configuration $\mathbf{s}$. We take it to be uniformly distributed between -1 and 1;
ii) the "spin-glass" function defined by eq. (3.1). We have taken the A's to be equal to $\pm a$ with equal probability, with $a^2 = N(N-1)/2$. In this way, the one-level probability distribution function $P(E)$ is approximately a Gaussian of zero mean and with variance equal to one.

4. The $\beta = 0$ Case

It is very instructive to start by investigating the simple case in which the sharpness parameter β appearing in eq. (2.4) vanishes. The model then reduces to a special case of the diffusion-reproduction processes investigated by Zhang et al. (1989). We may then translate their results in our language.

If we let $\beta = 0$ in eq. (2.4), we obtain that the death probability p equals ½ for each of the M individuals, independently of its configuration $\mathbf{s}$. Therefore, at each generation, roughly half of the individuals are removed ("die"). Because the remaining ones are reproduced to fill in the gaps in the population, we are in a situation in which, at each generation, any individual faces death or reproduction with equal probability. Moreover, we may conceive the effects of mutations as forcing the surviving individuals to perform a random walk on the hypercube of possible configurations.

Let us assume that the M individuals present at the beginning occupy random positions on the hypercube. As some of them die and others are reproduced to take their place, the population organizes into *families*, composed of the descendants of one of the original individuals.

In fact, after a number of generations of the order of M, all surviving individuals will belong to the same family, with a probability arbitrarily close to one. This result can be obtained in the easiest way by a simple mean-field argument, although a rigorous derivation should not be unattainable.

Let us start from a well-known result of the theory of branched processes, rederived in Appendix B. If a population of variable size contains at time $t = 0$ exactly M individuals, and each of them has equal probability λdt of either dying or producing an offspring during the short time interval dt, then the

probability that the population is extinct at time t is given by

$$p_0(t) = \left(\frac{\lambda t}{1 + \lambda t}\right)^M \tag{4.1}$$

If λt is sufficiently large, this expression may be approximated by

$$p_0(t) \simeq 1 - \frac{M}{\lambda t} \tag{4.2}$$

Therefore, after a time t^* proportional to M/λ, $p_0(t)$ will exceed any given confidence threshold. The constant of proportionality may be very large in some cases. In our search for truly asymptotic behavior, we will however consider this constant to be a number of order one. We shall see later some situations in which this assumption is not warranted.

Let us go back to our original situation, with a fixed population size M and death probability $p = ½$. Let us assume that at any given time there are F families (i.e., groups of individuals having one of the original individuals as a common ancestor). On the average, each such family will have M/F members. Because of the above result, each such family will almost certainly disappear if we wait a number of generations proportional to the size of the family, i.e., to M/F. Therefore, over a time interval Δt, the number F of families decreases by ΔF, where

$$\Delta F = -F \cdot \left(\frac{F}{M}\right) \Delta t \tag{4.3}$$

yielding

$$F \sim \frac{M}{t} \tag{4.4}$$

This argument is very rough, a probably misses some logarithmic factors. Nevertheless it is warranted to draw the conclusion that F will be equal to 1 after a number of generations proportional to M (and inversely proportional to the death probability). Let us denote by T this number of generations. Let us remark that fluctuations in family size make, if anything, the process *faster,* because smaller families are more likely to disappear.

This *fluctuation instability* is in our opinion an essential feature of the class of models we are considering, in which the only interactions among individuals are either reproduction or competition for common resources. In fact, the only features needed to derive this result are a death probability that never vanishes, and a bounded population size (what makes the death and reproduction probabilities equal on average). However, the time needed to obtain a one-family population increases when the average death probability decreases.

Let us now consider the population a very long time after the beginning. It is all made up of one family; indeed, by reckoning back of the order of M generations, we can identify the common ancestor of the whole population. Therefore each individual α will have accumulated at most τNT mutations since it branched off the common ancestor. We assume that this number is much smaller than the size N of the genome. Given two individuals, α and β, their mutual overlap $q^{\alpha\beta}$ is defined by

$$q^{\alpha\beta} = q(\mathbf{s}^\alpha, \mathbf{s}^\beta) \tag{4.5}$$

In the population we are discussing, this overlap is bounded by

$$1 \geq q^{\alpha\beta} \geq 1 - 2\tau T \tag{4.6}$$

We may visualize the population as forming a small cloud in some region of genome space. Such a structure is called a *quasi-species* (Eigen and Schuster 1979). However, the region occupied by the population varies as time goes on. We may identify the center of the cloud (which we are tempted to call the *wild type*) by $\mathbf{s}^W = (s_i^W)$, where

$$s_i^W = \frac{1}{M} \sum_\alpha s_i^\alpha \tag{4.7}$$

and the sum runs over all members of the population. The wild type mutates as fast as a single individual. Indeed, it is reasonable to expect that the wild type configuration is close to that of the common ancestor, T generations back. When time t increases by Δt, the common ancestor will have undergone $\tau N \Delta t$ mutations. This will be the new location of the center of the population.

This argument may be made more quantitative as follows. The average number of mutations undergone by the wild type over one generation is given by

$$D = \frac{1}{4} |\Delta \mathbf{s}^W|^2 = \frac{1}{4} \sum_i (\Delta s_i^W)^2 \tag{4.8}$$

where $\Delta \mathbf{s}^W = (\Delta s_i)$ and

$$\begin{aligned} \Delta s_i^W &= s_i^W(t + 1) - s_i^W(t) \\ &= \frac{1}{M}\left[\sum_\alpha s_i^\alpha(t + 1) - \sum_\beta s_i^\beta(t)\right] \end{aligned} \tag{4.9}$$

Let us neglect the small number of mutations taking place in the one generation we are looking at. Then the variation $\Delta \mathbf{s}^W$ is essentially due to the replacement of "dead" individuals by copies of the "surviving" ones. We have, therefore

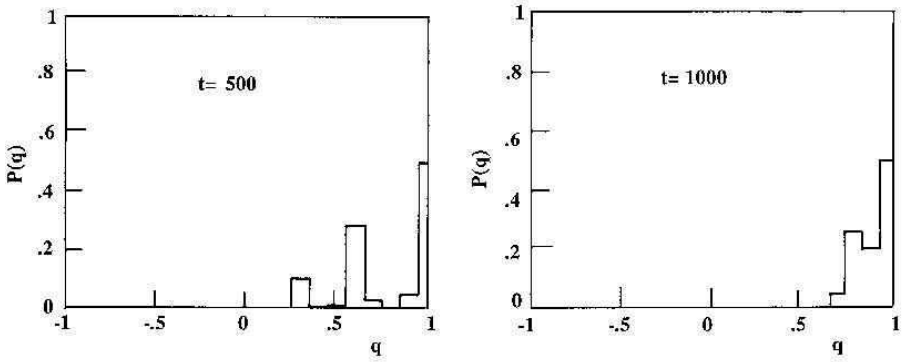

Fig. 1. Histogram (20 bins) of the mutual overlaps q at $\beta = 0$. Population size $M = 200$, genome size $N = 20$. Mutation rate $\tau = 0.25\%$. These data remain the same in all simulations reported here. After t = 500 generations the population is formed by three subpopulations. There is only one subpopulation at $t = 1000$, although a new one is splitting out.

$$\Delta \mathbf{s}^W = \frac{1}{M} \sum_{\alpha} (\mathbf{s}^{\alpha'} - \mathbf{s}^{\alpha}) \tag{4.10}$$

where the sum runs over all "dead" individuals, and we assume that the individual α is replaced by a copy of individual α'. We can estimate the difference $\mathbf{s}^{\alpha} - \mathbf{s}^{\alpha'}$ by recalling that α and α' both belong to the population at time t, and have therefore branched off the common ancestor T generations back. Therefore they may differ at most by $2\tau NT$ mutations. The difference $\mathbf{s}^{\alpha} - \mathbf{s}^{\alpha'}$ is therefore a vector with at most $2\tau NT$ nonzero entries, each such entry being equal to ± 2. For each entry of $\Delta \mathbf{s}^W$ we obtain therefore the sum of $(M/2)2\tau NT$ terms with a random sign, hence a contribution of the order of $\sqrt{\tau NMT}$. Recalling that T is proportional to M we see that the factors M cancel in eq. (4.10), and that in fact D is proportional to τN, just as for a single individual.

To summarize, when $\beta = 0$ the population organizes as a single quasi-species, with a comparatively small dispersion around a "wild type," which keeps on mutating at a frequency independent of the population size. To highlight this behavior one may describe the composition of the population at any given time t by means of the *overlap matrix* $q^{\alpha\beta}$: $\alpha, \beta = 1, 2, \ldots, M$, where $q^{\alpha\beta}$ is defined in eq. (4.5). The entries $g^{\alpha\beta}$ will always belong to the interval $[-1, 1]$. We report in Fig. 1 the histogram of q for a population evolving at $\beta = 0$ at a varying number of generations. A single quasi-species produces a histogram with a single peak located near $q = 1$. In presence of two quasi-species one sees a secondary peak, located close to the average overlap between the two subpopulations. The number of peaks increases rapidly as the number of quasi-species increases. In practice, it is hard to identify more than three quasi-species. One sees that, although after 500 generations (for a population size of 200) three relatively close, but different, quasi-species are present, all but one have disappeared after 1000 generations. The process is however a dynamic one, as is witnessed by the small shoulder at $q = 0.75$, which corresponds to a small subpopulation that is differentiating.

5. The $\beta \to \infty$ Case

The other simple limit is $\beta \to \infty$. As we discussed in section 2, this implies that all individuals whose fitness is smaller than the threshold die; the others survive and are reproduced. It is most simple to start by considering a rugged fitness function (i.e., the REM). This case has been the subject of a preliminary investigation by the us (Amitrano et al. 1988). We report here a more detailed discussion.

It is useful to visualize the genome configurations whose fitness is lower than H_0 as "forbidden" sites on the hypercube. They are randomly interspersed among the "allowed" sites, whose fitness exceeds H_0. The fraction x of allowed sites is a function of the threshold H_0:

$$x = \int_{H_0}^{\infty} dE P(E) \tag{5.1}$$

where $P(E)$ is the single-level distribution defined in eq. (A.3). Let us focus on one allowed site. Only a fraction x of its N neighbors (i.e., of the configurations that are a single mutation away from the site we are looking at) will be allowed on average. As a consequence, at any given mutation step, any individual will have a probability equal to $\tau N(1 - x)$ to step on a forbidden site—and to be eliminated at the next step. This has the consequence that even fit individuals have a nonvanishing probability of dying at each generation. This implies that the con-

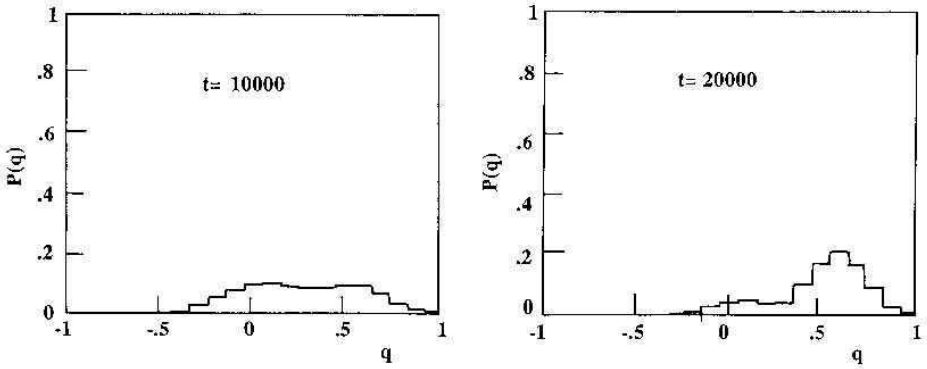

Fig. 2. Histogram of q for the REM model at $\beta = 20$ and $H_0 = 0.25$. Notice the longer time scale. The quasi-species is more widely distributed, and one may notice a small peak at $q = 0$ corresponding to a small splitting subpopulation.

clusions reached in the previous section also hold for this case. The population will therefore be made of a single quasi-species if one waits long enough.

The main difference from the previous case lies in the fact that the common ancestor of all surviving individuals at any given time must have wandered only on allowed sites. If the fraction x of allowed sites is close to 1, this will only slightly reduce the mutation speed of the wild type. However, as the environment becomes more exacting, and x decreases, the mutation speed will become smaller and smaller. It is possible to argue that, if the threshold H_0 exceeds a critical value H_c, this speed will essentially vanish in the long run. The critical value H_c is related to the critical value of x for percolation on the hypercube (Campbell et al. 1987).

For the sake of argument, let us assume that the only sites accessible from any given configuration in one-mutation steps are its nearest neighbors (i.e., the N sites that are one mutation away from the given one). Two allowed configurations will be accessible from each other if they are nearest neighbors, or if it is possible to draw a path from one to the other that touches only allowed configurations, always jumping from nearest neighbor to nearest neighbor. Mutually accessible configurations arrange into *clusters*. The statistics of clusters on a hypercube, as a function of the fraction x of allowed sites, have been recently investigated by Campbell et al. (1987). For large values of x most of the allowed sites belong to the largest cluster. When x drops below a *percolation threshold*, x^*, all clusters become comparatively small, and the fraction of allowed sites belonging to the largest cluster becomes practically zero. Similarly, when x is large, the largest cluster contains configurations arbitrarily different from one another; as x drops below x^*, all configurations in any given cluster become closer and closer to one another. This effect may be measured by the *average overlap*, $\bar{q}$, of the largest cluster. It is defined by

$$\bar{q} = \frac{1}{n} \sum_{s} q(\mathbf{s}, \mathbf{s}_0) \tag{5.2}$$

The sum runs over all n configurations $\mathbf{s}$ belonging to the largest cluster, with an arbitrarily chosen configuration $\mathbf{s}_0$ as the reference point. The behavior of $\bar{q}$ is approximately given by

$$\bar{q} = \begin{cases} 0, & \text{if } x > x_c^* \\ \dfrac{x_c^* - x}{x_c^*}, & \text{if } x \le x_c^* \end{cases} \tag{5.3}$$

where the threshold x_c^* is slightly different from x^*, but rapidly approaches it as N increases. A good estimate of x_c^* for large N is given by Gaunt et al. (1976):

$$x_c^* \sim x^* \sim \frac{1}{z} + \frac{3}{2z^2} + \frac{15}{4z^3} + \frac{83}{4z^4} + \ldots \tag{5.4}$$

where $z = N - 1$. This estimate is obtained by considering percolation on a Cayley tree with N branches at each node.

Because the population is restricted to wandering only on a connected cluster, the evolution of its genome configuration will bear traces of the extension of the cluster. A good measure of this property would be the self-overlap of the wild type with itself over a varying number of generations T:

$$Q(T) = \frac{1}{N} \sum_i s_i^W(t) s_i^W(t + T) \tag{5.5}$$

This quantity will in general fluctuate as t varies; however, as $T \to \infty$, it will approach values of the order of $\bar{q}$. If $x > x^*$, because $\bar{q} = 0$, we shall have $Q(T) \to 0$ as $T \to \infty$; i.e., the population loses memory of its initial genome configuration. Otherwise, $Q(T)$ will vacillate around the average $\bar{q}$ as the population wanders on the allowed cluster.

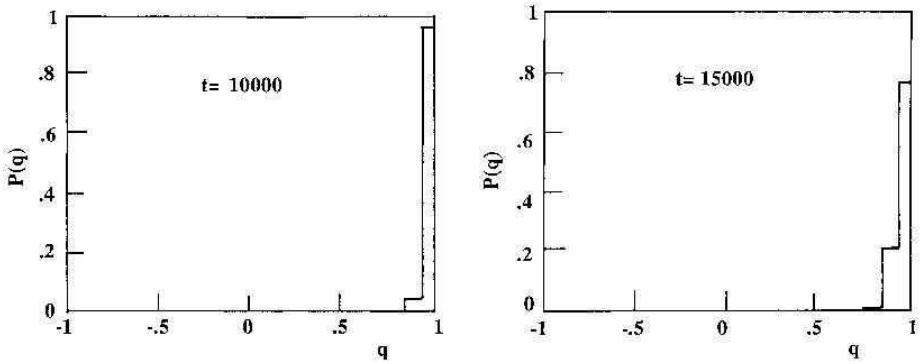

Fig. 3. Histogram of q for the REM model for $\beta = 20$ and $H_0 = 0.95$. The quasi-species is very sharply distributed. Subpopulations occasionally develop, as one may notice from the small shoulder for $t = 15{,}000$.

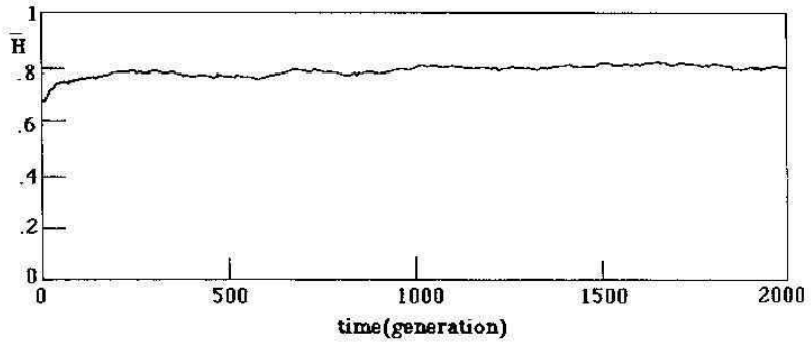

Fig. 4. Average fitness $\bar{H}$ for the REM model for $\beta = 20$ and $H_0 = 0.25$.

We have taken for granted in this argument that the quasi-species wanders on the largest cluster. This is warranted by the overwhelming extension of this cluster when $x > x^*$; on the other hand, if $x < x^*$, most sites belong to clusters with similar values of $\bar{q}$ and the result still holds with high probability.

Figure 2 shows the overlap evolution for a low value of the threshold H_0, corresponding to a fraction, $x = 37.5\%$, of accepted sites. One sees a comparatively widely spread quasi-species that occasionally develops into separate subpopulations, as witnessed by a peak in the histogram at $q = 0$. By comparison, Fig. 3 shows a typical configuration for $H_0 = 0.95$, corresponding to $x = 2.5\%$. Here again, shoulders occasionally develop, as one sees to be the case for $t = 15{,}000$. Notice the much longer time scale with respect to the $\beta = 0$ case.

It is interesting to remark that at $\beta = \infty$ there is no direct "selective advantage" for higher values of the fitness, once they are above threshold. This is strictly true only if the fitness landscape is not correlated. When β is not strictly infinite, however, there is a small selective advantage due to the exponential "tail" in the death probability. A similar effect holds for correlated fitness landscapes, as it is less likely that a configuration with a higher fitness value be surrounded by forbidden configurations. This entails a weak trend toward adaptation. However, this trend will have visible consequences only after a number of generations inversely proportional to the differential in the death probability. If this time is so long that meanwhile all members of the population will have undergone some mutations, there will be no net selective effect. In this situation, the evolution is *neutralist* in the sense that the average value, $\bar{H}$, of the fitness does not increase with time. We report in Fig. 4 the average values of the fitness $\bar{H}$ for a population of size $M = 200$ evolving at $\beta = 20$, $H_0 = 0.25$ in the REM. After 1000 generations, $\bar{H}$ reaches a value of 0.8 and keeps fluctuating around it. This value of $\bar{H}$ slightly exceeds the median of the allowed values of H because of finite β effects. Indeed, as β decreases, the selective advantage mentioned above increases, and $\bar{H}$ increases as a consequence. Figures 5 and 6 contain the results of a simulation with $\beta = 5$. The increased tolerance turns out to yield a substantially larger asymptotic value of $\bar{H}$. This corroborates the guess that adaptation requires a tolerant selection mechanism.

It is interesting to remark that adapting mechanisms emerge also at $\beta = \infty$ in correlated landscapes. In this situation, in fact, configurations that have high fitness values are more likely surrounded by

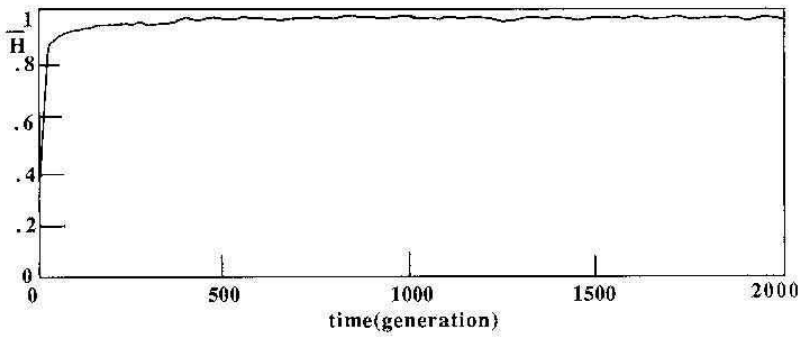

Fig. 5. Average fitness $\bar{H}$ for the REM model for $\beta = 5$ and $H_0 = 0.25$.

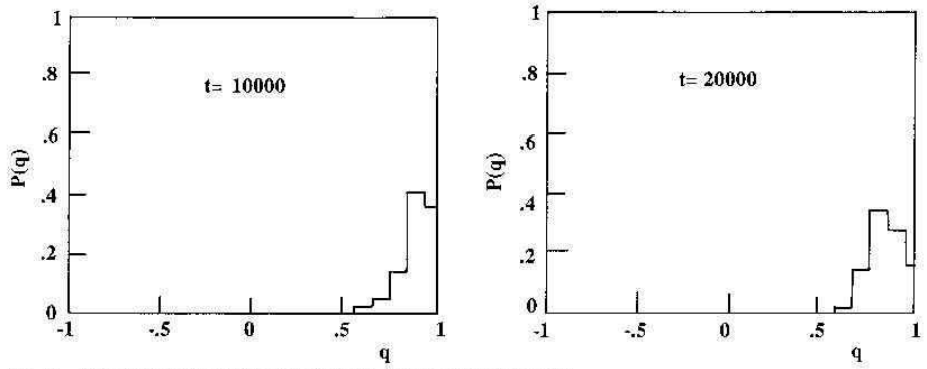

Fig. 6. Histogram of q for the REM model for $\beta = 5$ and H_0 0.25.

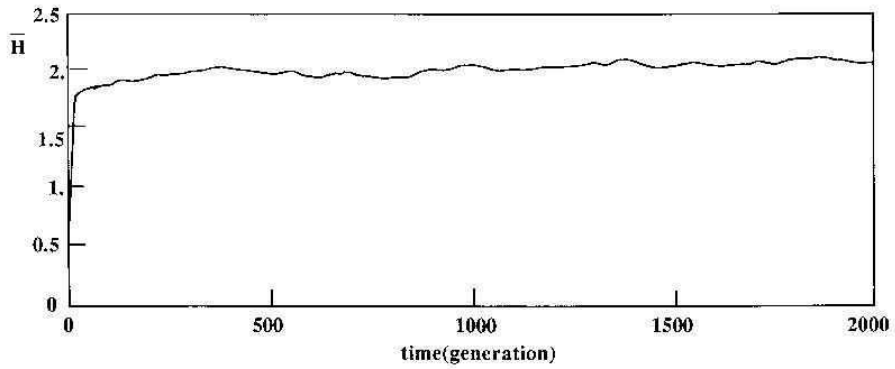

Fig. 7. Average fitness $\bar{H}$ for the spin-glass model for $\beta = 20$ and $H_0 = 1$. One notices that typical values of $\bar{H}$ are much larger than the threshold.

other fit configurations; therefore, the effective death probability, which depends on the probability that a mutation leads to an unfit configuration, is correspondingly smaller. This effect is stronger when the fitness landscape is more correlated. Figure 7 reports the results of a simulation performed on the spin-glass model with $\beta = 20$ and with a threshold value $H_0 = 1$. One should remember that, in this case, the one-level probability distribution is approximately a Gaussian distribution of zero mean and variance equal to one. Typical values of H are therefore of order one, whereas the simulations show much higher values of $\bar{H}$ even at such high values of β.

6. Finite β

As we have just mentioned, the effects of a finite value of β are similar to those of a correlated landscape. This is slightly surprising, because one might argue that finite values of β blur the boundary be-

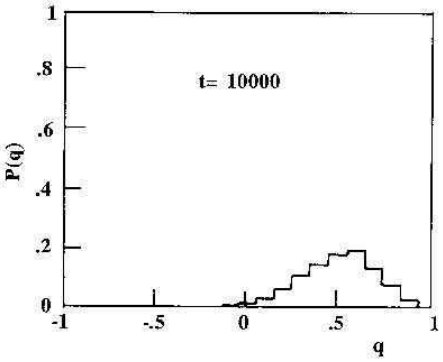

Fig. 8. Histogram of q for the spin-glass model for $\beta = 10$ and $H_0 = 1$. One notices the wider spread of the quasi-species with respect to the REM model.

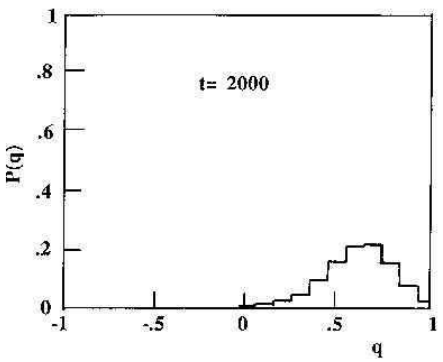

Fig. 9. Histogram of Q for the spin-glass model for $\beta = 3$ and $H_0 = 1$. One notices the smaller spread with respect to the previous figure.

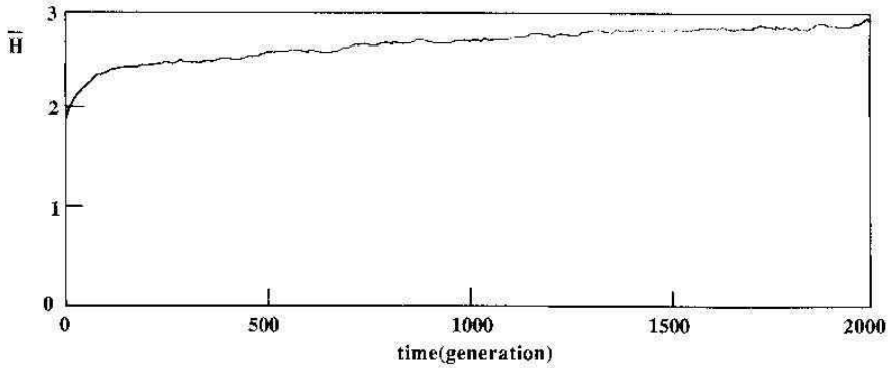

Fig. 10. Average fitness $\bar{H}$ as a function of t for the spin-glass model, for $\beta = 3$ and $H_0 = 1$. Notice the high values of $\bar{H}$ and the continuing adaptive trend.

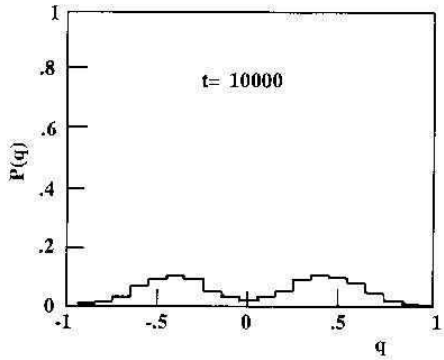

Fig. 11. Histogram of q for the spin-glass model for $\beta = 5$ and $H_0 = 1.25$. Notice the persistence of two "opposite" subpopulations.

tween allowed and forbidden configurations, whereas increasing correlation would tend to make this boundary sharper. In fact, the two effects go in the same direction, which is to smooth the boundary and to improve adaptation. Finite values of β blur the boundary in the region (whose width is of order β^{-1} in terms of H) where $p(H)$ varies rapidly with H, but the location of this boundary becomes correspondingly smoother, at least if the landscape is not fully uncorrelated.

Therefore, as soon as $\beta < \infty$, we expect the population spread to decrease and the adaptation (as measured by the value of $\bar{H}$) to increase, and this in a more marked way as the correlation of H increases. We report in Figs. 8 and 9 the histogram of q for the spin-glass model, with a fixed value of the threshold ($H_0 = 1$) and with varying values of β. It is remarkable that, even for β as small as 3, the dispersion of the subpopulation is quite large, as shown by the broad peak in the histogram around $q = 0.5$. The corresponding plot of $\bar{H}$ is shown in Fig. 10. The adaptive trend does not appear to saturate even after 2000 generations. In other cases one may observe the persistence of separated subpopulations for a large number of generations, thus vindicating (at least partially) the initial motivation of Anderson for introducing the spin-glass fitness function. One such instance is represented in Fig. 11. The two populations occupy opposite regions of

configuration space (i.e., one is close to the "reverse image" of the other: $\mathbf{s}' = -\mathbf{s}$). Therefore they do not really correspond to different quasi-species. One may however envisage different situations—in particular with larger values of N—in which different quasi-species may coexist for very long times. These situations are metastable, although the number of generations needed to obtain a single surviving quasi-species is approximately inversely proportional to the death frequency, and may become very long for highly correlated landscapes.

These features make a detailed investigation of the general case (varying correlation, finite β) very challenging.

7. Discussion

The main conclusions reached here are the following:

i) The fluctuation instability prevents the eventual stabilization of coexisting, well-defined molecular quasi-species in all models in which the interaction between different individuals is reduced to the competition for common resources; it follows that a candidate for chemical evolution needs the introduction of some interaction mechanism at its very definition.

ii) Models of this kind may exhibit either neutralist or adaptive behaviors depending on the nature of the fitness landscape and on the values of the relevant parameters. In any case, the transition between neutralist and adaptive regimes is not sharp (at least for the relatively moderate genome lengths we have considered).

iii) It is important to probe the correlation of the fitness landscape in which a given system is evolving. Models in which the selective advantage is proportional to the number of correctly placed bases in the genome have a very highly correlated landscape and lead to a rather trivial evolutionary behavior. The same probably applies when the selective probe corresponds to a small number of independent phenotypic traits. Complexity of the interaction between individual and environment corresponds to less correlated landscapes.

One might consider the possibility of probing landscapes with different correlations by varying the selection mechanisms in experiments of evolution in vitro like those of Orgel (1979). Replication speed in $Q\beta$-polymerase–$Q\beta$-RNA systems probably corresponds to a highly correlated landscape, in which only the detailed RNA configuration near the recognition site (and the chain length) is probed. Resistance to replication inhibition should make the landscape more corrugated, by increasing the number of selected traits. An empirical measure of landscape roughness could be the fluctuation in the number of concomitantly variable bases (see, e.g., Fitch and Markowitz 1970). This is probably not completely unattainable in experiments of selection in vitro.

We hope that our investigation will encourage some researchers to pay increased attention to analogous abstract evolution models, which may be useful in defining more sharply the questions that evolutionary theory is required to answer.

Note added. Dr. S. Leibler has kindly drawn our attention to the recent review paper by M. Eigen, J. McCaskill, and P. Schuster, Molecular quasi-species, J Phys Chem 92:6881–6891 (1988), where very similar ideas are explored in the context of a *deterministic* model.

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Appendix A

We define in this appendix a class of fitness functions, denoted by $H_K(\mathbf{s})$, whose degree of correlation depends on the integer parameter K.

Let us denote by N the set of indices $\{1, 2, \ldots, N\}$. For any integer K, $K \leq N$, let us define the random function $H_K(\mathbf{s})$ by

$$H_K(\mathbf{s}) = \sum_{i_1 \ldots i_K} A_{i_1,\ldots,i_K} s_{i_1} \ldots s_{i_K} \tag{A.1}$$

where the sum runs over all subsets I of N composed of exactly K elements, and where, for each such subset I, A_I is an independent random variable. We shall assume for simplicity that all A_I's are identically distributed, and that the probability distribution $p(A)$ of the A's is even: i.e., for any $I \subset N$ one has

$$p(-A_I) = p(A_I) \tag{A.2}$$

Let us define the one-level probability distribution function $P(E)$ as the probability density that any given configuration $\mathbf{s}$ has a fitness H equal to E:

$$P(E) = \langle \delta[E - H(\mathbf{s})] \rangle \tag{A.3}$$

where δ is Dirac's delta function and the average is taken with respect to the probability distribution of the A's. In order to compute the statistical properties of this class of function, it is convenient to introduce the corresponding characteristic function $G(k)$, i.e., the Fourier transform of $P(E)$:

$$G(k) = \int dE P(E) e^{ikE} \tag{A.4}$$

Characteristic functions have the convenient property that the characteristic function of the sum of two independent random variables is equal to the product of the corresponding characteristic functions.

By exploiting this fact, it is easy to show that

$$G(k) = \prod_I \Gamma_I(k) \tag{A.5}$$

where the product runs over all sets I of K indices, and $\Gamma_I(k)$ is the characteristic function of A_I:

$$\Gamma_I(k) = \int dA_I p(A_I)\, e^{ikA_I} \tag{A.6}$$

To derive eq. (A.5), we have exploited eq. (A.2) and the fact that

$$\tau_I = \prod_{i \in I} s_i = \pm 1 \tag{A.7}$$

Because the A's are identically distributed, it follows from eq. (A.5) that

$$\ln G(k) = \binom{N}{K} \ln \Gamma(k) \tag{A.8}$$

Because it is well known that $\ln G(k)$ is the generating function of the cumulants of H_K, eq. (A.8) may be read as a relation between the cumulants of H_K and those of A_I:

$$\langle H_K^m(\mathbf{s}) \rangle_c = \binom{N}{K} \langle A_I^m \rangle_c \tag{A.9}$$

In particular, if $p(A_I)$ is a Gaussian distribution of zero mean and of variance given by

$$\langle A_I^2 \rangle = \frac{J^2}{\binom{N}{K}} \tag{A.10}$$

we obtain

$$\langle H_K^2(\mathbf{s}) \rangle = J^2 \tag{A.11}$$

independent of both N and K, while all other cumulants vanish. Therefore, in this case, $H_K(\mathbf{s})$ is distributed according to a Gaussian distribution of zero mean and variance J^2.

A measure of the correlation between values of $H(\mathbf{s})$ for different configurations is given by

$$C(\mathbf{s}, \mathbf{s}') = \langle H(\mathbf{s}) H(\mathbf{s}') \rangle \tag{A.12}$$

where $\mathbf{s}$ and $\mathbf{s}'$ are two different configurations. Because $\langle H(\mathbf{s}) \rangle$ vanishes for any configuration $\mathbf{s}$, we expect that $C(\mathbf{s}, \mathbf{s}')$ vanishes when the corresponding values of $H(\mathbf{s})$ are independent. A simple calculation shows that, if $K \ll N$, one has

$$\langle H_K(\mathbf{s}) H_K(\mathbf{s}') \rangle = \langle A_I^2 \rangle \frac{N^K}{K!} [q(\mathbf{s}, \mathbf{s}')]^K \tag{A.13}$$

where $q(\mathbf{s}, \mathbf{s}')$ is the overlap of the two configurations, defined by eq. (2.3). In particular, for a Gaussian $p(A_I)$, with the variance given by eq. (A.10), one has

$$\langle H_K(\mathbf{s}) H_K(\mathbf{s}) \rangle = J^2 [q(\mathbf{s}, \mathbf{s}')]^K \tag{A.14}$$

Equation (A.13) shows that if the overlap between two given configurations decreases, i.e., if they become more and more different, the correlation $C(\mathbf{s}, \mathbf{s}')$ decreases at the same time; this takes place faster and faster as the value of K increases. In the limit $K \to \infty$ (which should of course follow a suitably defined limit $N \to \infty$) the correlation vanishes whenever the overlap between the two configurations is less than one, i.e., whenever they are different for the state of any finite fraction of their units.

We have thus defined a class of fitness functions $H_K(\mathbf{s})$ whose correlation decreases as the value of K increases. These functions are analogous to the NK model introduced by Kauffman (1988, 1989). The quantity K may be interpreted (as suggested by Kauffman and Levin 1987) as the number of genome units that collectively determine a phenotypic trait that falls independently under the edge of selection. The limit $K \to \infty$ corresponds to the rugged fitness landscape of Kauffman and Levin (1987) and to the Random Energy Model (REM) of Derrida (1980, 1981; see also Ruelle 1987). For this model, the value $H(\mathbf{s})$ of the fitness function is an independent random variable for each of the 2^N configurations $\mathbf{s}$.

Appendix B

We calculate here the extinction probability for a population of initial size equal to M, in which each individual has equal probability λdt of either dying or producing an offspring during any short time interval dt. Let us denote by $p_n(t)$ the probability that the population size is equal to n at the time instant t. The stated condition is equivalent to the following differential equation for $p_n(t)$:

$$\frac{dp_n(t)}{dt} = \lambda[(n+1)p_{n+1}(t) + (n-1)p_{n-1}(t) - 2np_n(t)] \tag{B.1}$$

The initial condition corresponds to

$$p_n(0) = \delta_{nM} \tag{B.2}$$

We define the generating function $\Gamma(z, t)$ by

$$\Gamma(z, t) = \sum_{n=0}^{\infty} z^n p_n(t) \tag{B.3}$$

Because of eq. (B.2), we have

$$\Gamma(z, 0) = z^M \tag{B.4}$$

On the other hand, eq. (B.1) implies that $\Gamma(z, t)$ satisfies the partial differential equation

$$\frac{\partial \Gamma}{\partial t} = \lambda(z-1)^2 \frac{\partial \Gamma}{\partial z} \tag{B.5}$$

This equation may be easily solved by the method of characteristics. Let $\zeta(t; z)$ be the solution of the ordinary differential equation

$$\frac{d\zeta}{dt} = \lambda(\zeta - 1)^2 \tag{B.6}$$

which satisfies the initial condition

$$\zeta(0; z) = z \tag{B.7}$$

Explicit calculation yields the following expression for $\zeta(t; z)$:

$$\zeta(t; z) = \frac{z - (z-1)\lambda t}{1 - (z-1)\lambda t} \tag{B.8}$$

The solution of eq. (B.5) reads

$$\Gamma(z, t) = \Gamma(\zeta(t; z), t = 0) \tag{B.9}$$

The probability $p_0(t)$ that the population is extinct at time t is given by

$$p_0(t) = \Gamma(z = 0, t) \tag{B.10}$$

The above calculation yields $p_0(t) = \Gamma(\zeta(t; 0), 0)$, where

$$\zeta(t; 0) = \frac{\lambda t}{1 + \lambda t} \tag{B.11}$$

Letting eq. (B.11) into eq. (B.4) we obtain

$$p_0(t) = \left(\frac{\lambda t}{1 + \lambda t} \right)^M \tag{B.12}$$

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