Exact solution of the quasispecies model in a sharply peaked fitness landscape

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We reconsider Eigen's quasispecies model for competing self-reproductive macromolecules in populations characterized by a single-peaked fitness landscape. The use of ideas and tools borrowed from polymer theory and statistical mechanics allows us to exactly solve the model for generic DNA lengths d. The mathematical shape of the quasispecies confined around the master sequence is perturbatively found in powers of $1/d$ at large d. We rigorously prove the existence of the error-threshold phenomena and study the quasispecies formation in the general context of critical phase transitions in physics. No sharp transitions exist at any finite d, and at $d\rightarrow\infty$ the transition is of first order. The typical rms amplitude of a quasispecies around the master sequence is found to diverge algebraically with exponent $\nu_{\perp}=1$ at the transition to the delocalized phase in the limit $d\rightarrow\infty$. [S1063-651X(97)13709-6]

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I. INTRODUCTION

In recent years there has been an increasing interest in theoretical physics with respect to new interesting phenomena for which the general approach of statistical mechanics has turned out to be extremely powerful. Typical examples are represented by earthquake modelization [1], forest-fire propagation models [2], financial systems and stock markets dynamics [3], portfolio theory [4], and population dynamics [5].

In the large context of biological models of evolution, the so-called *quasispecies model*, as first introduced by Eigen [6], has to be considered the paradigm of all systems describing the dynamics of competing macromolecular organisms. It mostly relies on Darwinian's natural selection principle as the best suited general theory to explain the evolution of ''prebiotic'' complex structures. In general it is believed that this principle has not only guided species to their present level of evolution, but also acted at a molecular level in order to create the first living beings. The complexity of life as it is still represents a hard challenge for the scientists. The natural questions arising in this context are usually: (i) how is it possible that among the huge number of possible (stable) molecular structures, natural selection has chosen the ones appropriate for the appearance of life on our planet? (ii) Why is this final state so stable and perfect despite the number of possible casual mutations that can occur during evolution? If we count the number of different alternative DNA sequences that one obtains by modifying a chain of given length, we would discover that it is so huge that we are necessarily forced to admit that the majority of the chemical combinations has never been tested by natural evolution.

In this article we reexamine Eigen's model in the simplest formulation, with a sharply peaked fitness landscape on a lattice. By means of a mapping to an equilibrium problem, we solve the model under very general assumptions, and we discuss the consequences of our results in more realistic situations.

The remainder of this paper is organized as follows. In Secs. II and III we give a short survey of the quasispecies model as first formulated by Eigen and co-workers. Sections IV and V are devoted to the introduction of our simplified lattice model. More specifically, we will show how the Eigen's equations can be mapped into the statistical mechanics of directed polymers in a random medium. In Sec. VI we introduce the effective transfer matrix associated to the system. It will be used to get some preliminary analytical results. Sections VII and VIII contain the basic ingredients towards a full solution of the problem: the dual space method and the characterization of the error-threshold phenomenon as a thermodynamic phase transition. Finally, in Sec. IX, we get the complete solution of the model after summation of the associated partition function. The critical properties at the error threshold are calculated. A survey of the main results and a comparison with previous approaches are finally summarized in Sec. X.

II. THE QUASISPECIES MODEL

In order to look for a mathematical transcription of Darwinian theory we must first resume the basic statements of natural selection. (i) Life came about through evolution; (ii) evolution is the result of mutations for thermodynamic systems out of equilibrium; (iii) mutations are due to incorrect reproductions or errors during the process.

The selective principle, sometimes called ''survival of the fittest,'' is actually opposed to coexistence among individuals. Even though the fitness landscape had strong fluctuations, evolution would not proceed very far if it were based on correlations among species instead of competition. Without a true competition for life, evolution would have needed a much larger time (perhaps larger than the life of the Universe) to explore the advantageous mutations among the huge number of different choices in the fitness landscape.

Darwinian principle is nothing but a sort of deterministic process of selection of the fittest individuals with the implicit assumption that an advantageous mutant can occur *by chance* during reproduction. This is, however, not the whole story. As demonstrated by Eigen and co-workers in their famous work on macromolecular evolution [6], some guidance principle towards the advantageous mutants does exist, as fitter DNA chains have a greater chance to appear than do

disadvantageous ones. In Darwinian models evolution is guided towards the peaks of the fitness landscape, that is, even though no correlation exists between a mutation and the fitness of the resulting mutant, there is a tendency provided by the fact that the distribution of mutants is fitness dependent and (statistically) not all mutations have the same probability to occur.

We say that two mutants belong to the same quasispecies (see discussion below) if at each position of the DNA chain the found symbol is the prevailing one. In a virus chain, 10^4 single position errors can be present. If their probability is uniform, the wild-type sequence would be, on average, exact with a probability of about 0.9999. In other words, at each site of a DNA chain one could find the same nucleotide by averaging among all the individuals of a given group with an error of the order $\sim 10^{-5}$, even though each mutant can have its own sequence, which is different from those of the others. The target of the selection is therefore not a single individual, but a set of mutants whose DNA chain is close, in the statistical sense above defined, to that of a wild-type sequence.

Let us now introduce Eigen's model. Imagine that each individual is defined by a DNA chain and consider all individuals having a chain of the same length d. For each site of the chain in the primary structure, we can have k different nucleotides, which appear in a random manner. In a DNA or RNA structure they can be of four different types (G, A, C, U). Alternatively, to simplify the problem, we can decide to distinguish only among purines (R) and pyrimidines (Y); in the latter case we assume $k=2$. The total number of possible sequences of purines and pyrimidines is given by $M=2^d$, and results in an extremely large number of choices. A single ribosomal RNA (for which $d=120$) is one of 10^{72} possibilities, and a viral genome (typically $d\sim 5000$) is one of among the $M\sim 10^{3000}$ alternative sequences. For more complex forms of life this number increases wildly and one can appreciate the order of magnitude of the typical numbers involved in the system. In the statistical mechanics language, these systems must be represented in a discrete phase space with volume of the order of $10^{10^{4,5}}$.

In order to mathematically define affinity among individuals, we need a quantitative measure suitable for mathematical description. This can be achieved by introducing the *Hamming distance* D_H. It is defined as follows: given two individuals I_i and I_j, each having its own sequence of length d, their Hamming distance is given by the number of different positions that are occupied by different basis (G, A, C or U). Two individuals having a smaller D_H than another couple are also more biologically affine.

A correct classification of mutants according to their Hamming distance requires a space of dimension d in which each dimension consists of k sites. Mathematically, the configuration space Ω is a d-dimensional hypercubic lattice in which each side contains k identical sites. In the simplest case of only two kinds of bases ($k=2$) each site has a 1-to-1 correspondence with binary sequences. Therefore each point of Ω represents a given wild type and its neighbors represent the mutants with closest biological affinity. We assign to each site $\mathbf{x}\in\Omega$ a variable, or discrete field $\mathcal{Z}(\mathbf{x})$, giving the relative concentration of wild-types of kind $\mathbf{x}$ in the total population.

The topological structure of Ω has interesting properties. By increasing the dimension d, the number of different ways by which two points in Ω at distance L can be connected increases much faster (as $L!$) than the number of points having that distance, whose number goes as 2^L. This has the effect that, if d is large, an enormous number of sites are confined among them with a relative small Hamming distance. Biologically this means that in the ''genome space'' Ω, even small mutations (e.g., one-basis error reproductions) can explore, after a short time, a big region in the whole accessible space, of total dimension 2^d. Moreover, as the number of different paths is of the order $L!$, a given chain can easily transform into another one by avoiding unfavorable ways (e.g., disadvantageous sites).

Finally, in the very general situation, we must assign to each site in Ω a variable identifying the fitness of that given sequence. This quantity must be a frozen variable; that is, its value must be conserved during evolution, as it schematically represents the quality of reproduction of that particular DNA sequence. From the mathematical point of view, the fitness landscape is represented by a rough function and defined by quenched random variables. This has the effect of rendering the solution of the model a very hard task, as in the spin glass problem [7].

In his simpler formulation the sequences are self-reproductive; i.e., individuals reproduce themselves asexually, and mutants appear through mutations of their respective parents. We then introduce a random variable with uniform distribution in $[0,1]$, the *copying fidelity* q_i. From experimental observations, the typical values of q_i are very close to 1; that is, the probability that a given reproduction process creates a mutant different from the original parent is very small. From simple combinatorics we get that the probability that successive consecutive mutations bring a sequence I_i to a different I_j (whose reciprocal Hamming distance is D) will be

$$Q_D = q^d\left(\frac{1/q-1}{k-1}\right)^D. \tag{1}$$

The mutation matrix $\mathbf{Q}=(Q_{i,i}|i,j=1,2,\ldots,k^d)$ has elements $Q_{i,j}$ giving the probability of mutation between I_i and I_j. The reader should note that this approach allows for different single-base mutations per time step.

Let us introduce the dynamics by considering the following hypothesis. (i) Sequences reproduce themselves in a constant fashion and, if any individual is present with concentration $n_i(t)$, the rate of change of the population is given by $\dot{n}_i(t)$. (ii) Sequences generate by asexual reproduction with erroneous replication and the rate depends linearly on the relative concentration.

The most general natural evolution equation for the concentrations $n_i(t)$ of the sequence I_i, will then be given by [6]

$$\dot{n}_i(t)=\sum_{j=1}^{k^d} W_{ij}n_j(t), \quad \text{with} \quad W_{ij}=Q_{ij}A_j-\delta_{ij}D_i. \tag{2}$$

In the above formula we have introduced the rate matrix **W**, which contains both diagonal and off-diagonal terms. A_i are autocatalytic amplification factors, that is, the relative rates of replication of the individual I_i. They equally describe the *fitness*, as favorable DNA chains generate a higher number of offspring. The diagonal terms W_{ii} $(i=1,\ldots,k^d)$ correspond to reproduction processes involving perfect replication of sequences, while off-diagonal terms correspond to mutations of the original ancestor. In order to maintain the total population constant, one has to take into account external constraints causing the spontaneous death of individuals. This can be simply achieved by summing to the diagonal terms the *decay rate* D_i of I_i (counting the number of deaths per unit time). Its inverse is the average lifetime.

It is worth pointing out that both A_i and D_i are (in general) quenched variables in the equations. Each wild-type I_i is supposed having a given fitness and decay rate, fixed by external condition and by genetic information. These parameters must be considered as ''frozen'' during evolution.

III. GUIDED EVOLUTION AND ERROR CATASTROPHE

Eigen and co-workers were able to show that this simplified level of description is indeed well defined if the concentrations $n_i(t)$ are not too high, and the replication rates $dn_i(t)/dt$ linearly depend on the concentrations themselves. At higher densities, the solution saturates and the creation of new templates happens in more complex forms (for a review see [6]). Even taking into account these effects, the proposed model can be shown to stay valid at a qualitative level of description, as the system still has rates that linearly depend (in average) on the concentrations. There are, however, situations in which a linear model cannot describe the actual reproduction mechanisms. A virus can, for instance, reproduce in the early stages of an incoming infection at much higher rates than those described by Eigen's linear model.

We are now ready for a deeper investigation of the Eigen's model. To this aim it is advantageous to introduce a rescaled quantity

$$x_i(t)=\frac{n_i(t)}{\sum_{j=1}^{k^d} n_j(t)}, \tag{3}$$

which represents the fractional population variable. In its complete form we should add to Eq. (2) a term that takes into account changes in the population caused by transport effects. To this aim one usually introduces a general ''flux'' term $\phi(t)$ to fix a restriction on the total number of individuals. We can thus write the kinetic equations as

$$\dot{x}_i(t)=\sum_{j\neq i} W_{ij}x_j(t)-\phi(t)x_i(t). \tag{4}$$

If one neglects $\phi(t)$, the above equation simplifies into a high-dimensional linear differential system whose matrix **W** is diagonalizable. As, moreover, **W** is definite positive, Frobenius theorem applies, that is, the maximum (or *dominant*) eigenvalue λ_0 is positive and nondegenerate, and has a corresponding positive eigenvector. It gives the net production rate of sequences in the stationary state, and the corresponding (positive) eigenvector $(x_1,x_2,\ldots,x_N)$ is associated to the relative concentrations of individuals in the total of the population. Formally, the full stationary solution is a superposition of uncoupled modes and in the limit of large times the evolution is associated to the eigenvector corresponding to λ_0.

It can be shown that the average eigenvalue $\overline{\lambda(t)}$ acts as a threshold: modes corresponding to $\lambda_i>\overline{\lambda(t)}$ grow indefinitely during evolution, while modes with $\lambda_i<\overline{\lambda(t)}$ die out. Each normal mode corresponds, in the original variables $x_i(t)$, to a set of sequences (or a ''clan'') with high biological affinity. A clan is uniquely defined by an eigenvector and its associated eigenvalue. It competes for selection with all other clans and the target of evolution is the group corresponding to λ_0. If viewed in the original space, a clan is represented by a set of sequences distributed around the one corresponding to the largest diagonal term W_{ii}, which will be called the *master sequence* (MS). The mutants of the MS are grouped around it in such a way that only their averaged sequence equals that of the MS itself, which will be thought of as the most abundant individual in the set (though variances can be very large around the MS). This set is called *quasispecies*.

The picture that emerges from the above considerations is that of a huge number of individuals transforming into one another during evolution. After some time all individuals will be found to be close to a limited number of MSs, as less favorable ones have already died out. The characteristic time necessary to reach a unique MS starting from a flat distribution in the space of sequences is not infinite, despite the enormous number of sites in the system. This is due, as previously pointed out, to the topological structure of Ω, in which points very far apart can be reached in few steps and are linked to each other by a tight network of different paths. As a consequence, a given sequence will almost certainly find a more favorable region in the rugged landscape by performing a walk in Ω that avoids passing through high potential barriers where it would stay pinned for a long time.

This principle of *guided evolution* depends on the off-diagonal terms of the matrix **W**. If they are zero, no mutations occur and the global population is stationary. If they are too big with with respect to the diagonal terms W_{AA}, the ''diffusion'' in Ω is overenhanced and the stationary state is dominated by a random creation and annihilation of all sequences. In this situation the typical spatial amplitude of a quasispecies becomes of the same order of d and no MS can be uniquely defined. We would reach the same final state if the fitness landscape would be flat, i.e., $A_i=\text{const}\ \forall i$. As a consequence, we deduce that a critical value of the error rate q_c may exist such that if $q<q_c$ the class of sequences classified as fittest becomes so large that it cannot be sampled by any biological population.

This phenomenon was indeed shown to exist for a large variety of fitness landscapes [6] and it is now well accepted as the intrinsic and outstanding feature of the quasispecies model. A rough estimate of q_c (usually called *error threshold*) can be achieved by noting that in order for a given sequence I_i to be competitive with other mutants, its exact replication rate W_{ii} must be larger than the average produc-

tion rate of the mutants $\overline{E_{j\neq i}}$. On this basis it is possible to show [6] that the condition reads

$$W_{ii} > \overline{E_{j\neq i}} = \frac{\sum_{j\neq i} E_j \overline{x_j}}{\sum_{j\neq i} \overline{x_j}}, \tag{5}$$

where $\overline{x_j}$ are the stationary relative concentrations of the mutants. Since, by definition, $W_{ii}=A_iQ_0-D_i$ and $Q_0=q^d$ is the probability of exact replication, we find that the critical threshold reads

$$Q_0 > \frac{\overline{E_{j\neq i}}+D_i}{A_i} = \frac{1}{\sigma}. \tag{6}$$

Hence it follows that, in order to have localization around the MS, the length of the sequences must not exceed the critical value

$$d_{\max} = -\frac{\ln\sigma}{\ln q} \sim \frac{\ln\sigma}{1-q} \quad \text{for} \quad 1-q \ll 1. \tag{7}$$

Once both q and σ are fixed, we have a strong restriction on the maximum possible length, which allows selection to find the optimal MS. The above condition can be equally rewritten in terms of the autocatalytic rate as

$$A_i > (\overline{E_{j\neq i}}+D_i)\left(\frac{1}{q}\right)^d \sim e^{ad}. \tag{8}$$

The last inequality can be expressed by saying that in order to maintain a given quasispecies stable around a MS one needs the corresponding selective advantage (or fitness) to exceed a given threshold. What is surprising is the functional dependence of this threshold on the length of the sequences: since typically d if the order of $10^{3,4}$, the minimum A_i requested is enormous.

IV. TOWARDS A SOLVABLE MODEL OF EVOLUTION

A full complete solution of Eigen's model is not achievable by analytical methods, and despite past extensive work [8–10], no exact solutions are available in the literature. An important exception is represented by a slightly different model, introduced by Baake *et al.* [11] in which one allows mutation and selection to go on in parallel. That system, whose links and differences with the original Eigen's model were exhaustively discussed by the authors, can indeed be mapped to a quantum system of lattice spins at equilibrium. This observation allows for analytical approaches for several representative fitness landscapes.

Another important result in this context was achieved by Leuthäusser [9], who first showed the link between the quasispecies model and the statistical mechanics of lattice surface systems. In the last section we will come back to this mapping, mainly in connection with the results of our work.

Our goal is to introduce a simplified version of Eigen's equations, which, although being well suited for analytical approach, still retains the basic fundamental features of the general system. In particular we will consider a model in discretized time, as in [9] and, after having exactly solved the problem for generic sequence lengths d, we will prove that the transition from a localized quasispecies to a random distribution of individuals is equivalent to a first-order phase transition. The mapping is based on the observation that the system allows a simple representation in terms of equilibrium statistical physics. Similar ideas were already introduced in [9], where the main idea was to map the ordinary differential equation (4) into a multidimensional Ising-like spin system at equilibrium. However, due to the complex form of the ''effective'' Hamiltonian resulting from the mapping, which contains a complicated interaction term depending on the selective advantages A_i, this approach is of very poor utility, in practice. Tarazona [10] performed, on this basis, a series of interesting computations with different fitness landscapes and found a rich resulting scenario.

Our idea is to introduce a different mapping of Eigen's equations to an equilibrium statistical system, which, in our opinion, is simpler and more natural than the one used in [9]. By means of this new mapping, in fact, we can directly relate Eq. (4) to a well-known problem in statistical mechanics, that is, directed polymers in random media (DPRM) [12]. Due to the large amount of work done in this domain in the past years [13], a mapping to DPRM is important for many reasons. First of all, the physics of DPRMs has applications in a large variety of physical phenomena, and it would be at least interesting to compare all these systems with the evolutionary dynamics proposed by Eigen. On the other hand, due to the large amount of analytical and numerical work done in the directed polymers context, we have a solid background that can be used to understand, on a more rigorous basis, the physics behind the quasispecies model.

In particular, in this paper, we will concentrate on the characterization of the error-threshold phenomenon as a phase transition, and the calculation of the critical exponents involved (we will be restricted in this paper to considering the simplest, nontrivial scenario). Anticipating future conclusions, the error-threshold transition turns out to be equivalent to a depinning phase transition of a directed polymer by a bulk potential [13]. For the sake of completeness, in the last section, we will discuss our results with respect to those obtained by previous approaches.

In order to introduce our model, we first formulate some general hypotheses. (1) We consider sequences defined by a two-state basis (e.g., Y and R); that is, we take $k=2$. Each sequence of length d is made of a combination of ''0'' and ''1'' bits and Ω is the unitary hypercubic lattice $\{0,1\}^d$. (2) The fitness landscape is flat but one point (take the origin $\mathbf{0}$) has higher fitness. In other words we consider a single-peaked distribution of selective advantages, by taking $A_i=b$, if $\Omega \ni \mathbf{x} \neq \mathbf{0}$ and $A_i=a>b$, if $\Omega \ni \mathbf{x}=\mathbf{0}$. (3) The decay rates are zero, i.e., $D_i=0$, $\forall i=1,2,\ldots,k^d$. We have numerically verified that this assumption does not affect our final conclusions. (4) We consider evolution in discretized time. Eigen's model is (formally) similar to a system of coupled master equations in the variables $x_i(t)$ if we interpret $x_i(t)$ as the ''probability to find a localized quasispecies around the MS I_i at time t.'' If we imagine considering the time as a multiple of a small interval (or *waiting time*) τ, i.e., $t=N\tau$, we can write that

$$\dot{x}_i(N\tau) = \lim_{N\to\infty} \frac{x_i((N+1)\tau) - x_i(N\tau)}{\tau}$$

$$\overset{N\gg 1}{\sim} \frac{1}{\tau}(\widetilde{T}_{ij} - \delta_{ij}) x_i(N\tau). \tag{9}$$

Usually τ is simply related to the inverse of the transition probability per unit time in the continuous equation. The above relation shows that, apart from the identity operator δ_{ij}, the dynamics on the discrete time can be described by the repeated application of a $2^d \times 2^d$ *transfer matrix* $\widetilde{T}_{ij}$ with $i,j = 1,2,\ldots,2^d$. (5) In general, one should take into account multiple one-basis mutations per time step τ. This is contained in the original Eigen model as the rate matrix W_{ij} has all nonzero off-diagonal entries. Nevertheless, we will formulate the hypothesis that the transfer matrix $\widetilde{T}_{ij}$ can be reduced to another matrix T_{ij}, which allows only single-basis mutation per time step. The reason is that T_{ij} has a much simpler structure than $\widetilde{T}_{ij}$, since almost all off-diagonal elements are zero. We will prove below that using the one-jump formulation of the system does not modify the physical picture that emerges from the model. In fact, allowing more than one mutation per time step corresponds to taking higher powers of T_{ij}, as one can easily see. All our results can be associated, however (see below), to the behavior of the set of eigenvectors of the transfer matrix, which does not depend on the power of T_{ij} we actually take into account.

We finally note that, without loss of generality, one can take $b = 1$, apart from unimportant multiplicative factors.

V. THE MODEL

Let us consider a d-dimensional hypercubic unitary lattice $\Omega = \{0,1\}^d$, representing the configuration space. For mathematical convenience, we will assume to have periodic boundary conditions in all directions, even though this hypothesis is not essential to the physics of the problem. Each side of Ω is made of only two points representing binary units. Each point of Ω has a one-to-one correspondence to a sequence I_i $(i = 1,|\mathcal{I}|)$ since the cardinality of $\mathcal{I}$ is equal to the number of points of Ω. We formulate the implicit hypothesis that all individuals of the population have the same sequence length d.

On each site $\mathbf{x} \in \Omega$ we have a variable $\mathcal{Z}(\mathbf{x})$ corresponding to the relative concentration of individuals of wild-type $I_{\mathbf{x}}$. Equivalently, we can interpret $\mathcal{Z}(\mathbf{x})$ as the probability to find the sequence $I_{\mathbf{x}}$ in the total of the population. At each time step a fraction $t \in [0,1]$ of the population of the same wild-type reproduces incorrectly and their sequences change one basis among d and transform itself into a new set of individuals $I_{\mathbf{y}}$. In our usual probabilistic interpretation, t gives the probability that the MS $I_{\mathbf{x}}$ transforms into $I_{\mathbf{y}}$.

Since there are d bases for each sequence, the probability that a mutation takes place is td while $1-td$ is the probability of exact replication. In other words, $1-td$ is the fraction of the population $\mathcal{Z}(\mathbf{x})$ that survives evolution. We need to consider pairs (d,t) such that $td < 1$. This is not a limitation of our approach, in fact, even though d is usually very large, we only study conditions in which the reproduction fidelity is very high, i.e., $t \ll 1$.

All sequences have the same fitness $b = 1$, apart from the origin $\mathbf{0} = (0,0,\ldots,0)$ having selective advantage $a > 1$.

It is then simple to write down a recursive relation for the relative concentrations $\mathcal{Z}_N(\mathbf{x})$ at time N on the basis of the above arguments:

$$\mathcal{Z}_{N+1}(\mathbf{x}) = [1 + (a-1)\delta_{\mathbf{x},\vec{0}}]\left(\sum_{i=1}^{d} t\mathcal{Z}_N(\mathbf{x} + \mathbf{e}^{(i)}) + (1-td)\mathcal{Z}_N(\mathbf{x}) \right), \tag{10}$$

where we have introduced the unitary vectors $\mathbf{e}^{(i)}$ as those having a ''1'' bit as ith element if $\mathbf{x}$ has a ''0'' in the same position and vice versa. The above equation uniquely defines the transfer matrix T_{ij} as $\mathcal{Z}_{N+1}(\mathbf{x}) = \mathbf{T}\mathcal{Z}_N(\mathbf{x}')$.

The interpretation of the above relation is simple. At time $N+1$, the fraction of individuals with sequence $I_{\mathbf{x}}$ is equal to $(1-td)$ times the original concentration $\mathcal{Z}_N(\mathbf{x})$ (this corresponds to the individuals who have not experienced any mutation), plus the fraction of individuals with Hamming distance equal to 1 respect to $\mathbf{x}$ who, after reproduction, have mutated to $I_{\mathbf{x}}$. This fraction is given by $t\mathcal{Z}_N(\mathbf{x} + \mathbf{e}^{(i)})$. Moreover, we have chosen the origin as a favored sequence, that is, the population in $\mathbf{x} = \mathbf{0}$ is amplified by a factor $a > 1$ with respect to all others. This hypothesis is nothing but a simple mathematical way to impose that a *single* MS $I_{\mathbf{0}}$ exists.

In this framework, the existence of a quasispecies characterized by a unique MS corresponding to $(0,0,\ldots,0)$ depends on its selective advantage with respect to other sequences, i.e., on the value of a. We thus expect to find quasispecies formation around $I_{\mathbf{0}}$ if a is larger than a threshold a_c.

Roughly speaking, this transition can be equally interpreted in a different context. Let us indeed consider a directed elastic polymer (a line) wandering in Ω, directed along the ''time'' axis N, and subjected to an attractive potential located at the origin $\mathbf{0}$. If the potential is uniform in N, the energy gain per time step located at the wall is $-U$. If we introduce a vector $\mathbf{h}^{(i)} \in \Omega$, we can use it to identify the position of the polymer at each time step i. The elasticity of the polymer, in a discrete geometry, is usually described by restricting the one-step polymer fluctuations to be smaller than a fixed threshold. In the literature this constraint is usually called restricted solid-on-solid condition, and means that $|\mathbf{h}^{(i)} - \mathbf{h}^{(i-1)}|$ can be 0 or 1 [13].

In a continuous formulation, the polymer statistics is associated to a restricted (i.e., with fixed extremes) partition function (here ''s'' is the continuous analog of N)

$$\mathcal{Z}(\mathbf{h},s) = \int_{\mathbf{h}(0)=\mathbf{0}}^{\mathbf{h}(s)=\mathbf{h}} \mathcal{D}[\mathbf{h}'] \exp\left\{ -\beta \int_0^s ds' \left[\frac{\nu}{2}[\partial_{s'}\mathbf{h}'(s')]^2 + V(\mathbf{h}', s') \right] \right\}. \tag{11}$$

In general, $V(\mathbf{h},s)$ is a random potential distributed accord-

ing to a given density (DPRM problem). In the discrete formulation, we introduce a Hamiltonian with short-range uniform interaction

$$\mathcal{H}_N(\{\mathbf{h}\}^{(i)})=\sum_{i=1}^{N}\left(J\left|\mathbf{h}^{(i)}-\mathbf{h}^{(i-1)}\right|-U\delta_{\mathbf{h}^{(i)},\mathbf{0}}\right), \qquad (12)$$

as our potential is localized at the origin and is attractive, that is, $V(\mathbf{h}^{(i)},i)=-U\delta_{\mathbf{h}^{(i)},\mathbf{0}}$. The continuous partition function then becomes a sum over all possible realizations of the restricted polymer between 0 and N [12]

$$\mathcal{Z}_N(\mathbf{x})=\sum_{\{\mathbf{h}\}}\exp\{-\mathcal{H}_N(\{\mathbf{h}\}^{(i)})/T\}. \qquad (13)$$

The above sum completely specifies the state of the polymer at a given temperature T, or equivalently, at a given potential strength U. By general considerations, we know that in the thermodynamic limit the polymer has a phase transition from a localized into a delocalized state, depending on T, or, equivalently, on U [13]. As we will discuss below, this transition is perfectly defined only at $d\to\infty$, as the cardinality of Ω is finite for every finite d and thermodynamic limit does not hold.

There exists an interesting mapping between Eigen's model and the statistical mechanics of a directed polymer. For instance, in our case, a simple look at the partition function (13) shows that it is mathematically equivalent to the concentration $\mathcal{Z}_N(\mathbf{x})$, which identically satisfies the recursive relation (10), once we have introduced the definitions $a=\exp(U/T)$ and $t=\exp(-J/T)$. That is why we implicitly used the same notation for the concentration of individuals and the polymer partition function.

As an example, let us suppose that for a given set $\{a,d,t\}$ the polymer is in the localized (delocalized) phase: this can be equivalently expressed by saying that evolution brings sequences preferentially close to (apart from) the master sequence $I_{\mathbf{0}}$. Therefore the error threshold transition in the self-reproductive model is reduced to a search for the critical pinning a necessary to localize the directed polymer for fixed values of d and t. The error catastrophe transition will then be perfectly understood in the general context of thermodynamic phase transitions. Even though we will concentrate our study on the simplest case of a single peaked fitness, it is worth mentioning that the same formalism applies in more realistic situations, for which we are forced to consider a quenched bulk potential, as in Eq. (11). Generally speaking, studying the dynamics of the quasispecies model turns out to be not a simpler problem than DPRM.

VI. THE EFFECTIVE MATRIX

In order to calculate the partition sum (13), we must first solve a $2^d\times 2^d$ eigenvalue problem associated to the transfer matrix $\mathbf{T}$, $\mathcal{Z}_{N+1}(\mathbf{x})=\mathbf{T}\mathcal{Z}_N(\mathbf{x}')$.

As we are interested in the stationary state at $N\to\infty$, we do not need to find the whole spectrum of $\mathbf{T}$ but its spectral radius (i.e., the maximum eigenvalue) ε as a function of the free parameters $\{a,d,t\}$, only. ε is the only significant contribution to the free energy density (per unit length) $f=\lim_{N\to\infty}-\ln(\mathcal{H}-TS)/\beta N$. At large times N, the action of $\mathbf{T}$ is dominated by the spectral radius ε, that is, $\mathcal{Z}_{N+1}(\mathbf{x})\sim\varepsilon\mathcal{Z}_N(\mathbf{x})$.

It is worth considering some simple mathematical preliminaries that will be useful in the future. A straight investigation of the transfer matrix shows that it is definite positive and irreducible, and then, as a consequence, the Perron-Frobenius theorem on finite matrices applies [14]: the spectral radius is positive and nondegenerate, and corresponds to a positive, unique, eigenvector.

Due to the high dimensionality of the system (recall that typically $d\sim 10^{3,4}$ in a virus sequence), it is not convenient to use this form of the matrix for numerical investigation.

To this aim, we observe that the system has a symmetry with respect to any change of ''1'' and ''0'' bits in a given sequence. In other words, if two points $\mathbf{x}$ and $\mathbf{y}$ of Ω have the same Hamming distance from the MS $(0,0,\ldots,0)$ they are completely equivalent. The transfer matrix is in fact completely invariant in this case under permutation of the two points.

Therefore the partition function must be invariant under rotations in Ω and we can restrict ourselves to study its radial dependence only, i.e., $\mathcal{Z}(\mathbf{x})=\mathcal{Z}(|\mathbf{x}|)=\mathcal{Z}(\nu)$ where we have defined $\nu=D_H(\mathbf{x},\mathbf{0})$. It is a simple combinatorial result that the number of points of Ω with the same Hamming distance ν from the origin is given by $M=d!/[(d-\nu)!\,\nu!]$.

If we define a new vector as $P_N(\nu)=\Sigma_{|\mathbf{x}|=\nu}\mathcal{Z}_N(\mathbf{x})$ we can equally study our eigenvalue problem in terms of a new transfer matrix $\mathbf{S}$ defined as $P_{N+1}(\nu)=\mathbf{S}P_N(\nu)$. It can be found by observing that

$$P_N(\nu)=[1+(a-1)\delta_{\mathbf{x},\vec{0}}]+\left(\sum_{|\mathbf{x}|=\nu}\sum_{i=1}^{d}t\mathcal{Z}_N(\mathbf{x}+\mathbf{e}^{(i)})+(1-td)\sum_{|\mathbf{x}|=\nu}\mathcal{Z}_N(\mathbf{x})\right), \qquad (14)$$

where the last term in parentheses is simply given by $(1-td)P_N(\nu)$. By definition, $\mathcal{Z}_N(\mathbf{x}+\mathbf{e}^{(i)})$ is of the form $\mathcal{Z}_N(\mathbf{x})$ with $|\mathbf{x}|=\nu+1$ or $|\mathbf{x}|=\nu-1$. Hence, after some algebra, we find that

$$\sum_{|\mathbf{x}|=\nu}\mathcal{Z}_N(\mathbf{x}+\mathbf{e}^{(i)})=(\nu+1)\sum_{|\mathbf{x}|=\nu+1}\mathcal{Z}_N(\mathbf{x}+\mathbf{e}^{(i)})+(d-\nu+1)\sum_{|\mathbf{x}|=\nu-1}\mathcal{Z}_N(\mathbf{x}+\mathbf{e}^{(i)}). \qquad (15)$$

By using this identity we can show that the recursion relation for $P_N(\nu)$ reads

$$P_{N+1}(\nu)=[1+(a-1)\delta_{\mathbf{x},\vec{0}}][(1-td)P_N(\nu)+t(\nu+1)P_N(\nu+1)+(d-\nu+1)P_N(\nu-1)],$$

with

$$P_N(\nu)=0 \quad \text{for } \nu>d. \qquad (16)$$

We can then study the system by means of an *effective* $(d+1)\times(d+1)$ matrix $\mathbf{S}$ defined as

$$\mathbf{S}=\begin{pmatrix} a(1-td) & at & & 0 & \\ td & (1-td) & 2t & & \\ & \ddots & \ddots & \ddots & \\ & & 2t & (1-td) & td \\ & 0 & & t & (1-td) \end{pmatrix}. \tag{17}$$

It is easy to see that **S** and **T** are completely equivalent to our problem, since they have same spectral radius, as it turns out from very general results in group theory [15]. As an advantage, **S** is certainly more suitable for numerical diagonalization respect to **T**.

What is more important, however, is that we can use the effective matrix to calculate some accurate upper and lower bounds for ε. This is a consequence of a theorem on positive, irreducible matrices: it states that the spectral radius $\varepsilon(A)$ of a positive matrix $A=a_{ij}$ satisfies the inequalities

$$\min_i \sum_j a_{ij} \leqslant \varepsilon(A) \leqslant \max_i \sum_j a_{ij},$$

$$\min_j \sum_i a_{ij} \leqslant \varepsilon(A) \leqslant \max_j \sum_i a_{ij}.$$

In summary, we find that

$$\varepsilon(\mathbf{S}) \geqslant \begin{cases} 1 & a \leqslant (1-td)^{-1} \\ a(1-td) & a \geqslant (1-td)^{-1}, \end{cases} \tag{18}$$

while the upper bound is estimated as

$$\varepsilon(\mathbf{S}) \leqslant \begin{cases} cca(1-td)+td & a \leqslant \dfrac{1-(d-2)t}{1-td} \\ 1+2t & a \in \left(\dfrac{1-(d-2)t}{1-td}, \dfrac{1+2t}{1-(d-1)t} \right] \\ a(1-td+t) & a \in \left(\dfrac{1+2t}{1-(d-1)t}, d \right] \\ a(1-td)+td & a > d. \end{cases} \tag{19}$$

The result is shown in Fig. 1 where the two curves corresponding to the upper $\varepsilon_+(\mathbf{S})$ and lower bound $\varepsilon_-(\mathbf{S})$ are plotted (dashed lines). From the above inequalities we immediately find some interesting results concerning our system.

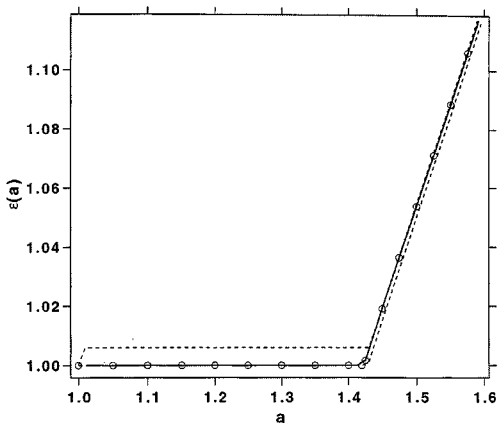

FIG. 1. The maximum eigenvalue of the transfer matrix **T** plotted vs the selective advantage a for $d=100$, $t=0.003$. The full line has been obtained by numerical diagonalization of the transfer matrix. Circles represent the analytical result [up to order $O(1/d^3)$, see Eq. (41)]. The dashed lines are the upper and lower bounds for ε obtained from the transfer matrix (see text).

In fact we deduce that, $\forall d$ finite, $\varepsilon > 1$ and that in the limit $d \to \infty$ the spectral radius is bounded between two values, converging to

$$\varepsilon(\mathbf{S}) \to 1^+ \quad \text{if } a < \frac{1}{1-td},$$

$$\varepsilon(\mathbf{S}) \to a(1-td) \quad \text{if } a > \frac{1}{1-td}. \tag{20}$$

This result indicates that $a=a_c=1/(1-td)$ is the critical value of the pinning we need to localize the polymer at the origin for any fixed set of parameters (T,J). It is intuitively clear that, rigorously speaking, we cannot have a phase transition at finite d, since finite is the cardinality of Ω too. Only in the limit $d \to \infty$ do the polymers have a finite probability to completely delocalize from the defect; at any finite dimension it can wander up to a distance of the order of d even at $N \to \infty$. Naively speaking, we can say that, at large (finite) dimensions, and if the pinning strength is not big enough, the polymer is ''rough'' in the sense that it can visit *all* accessible configuration space up to the maximum size allowed for that fixed d. On the other hand, in the ''pinned'' phase, the transversal localization length ℓ within which the polymer is confined to the origin is independent on the linear size N and is always finite (even at $d \to \infty$). The two different behaviors take place at a given characteristic value U_c (or equivalently a_c) of the pinning potential. Later on we will further discuss this problem and its implications in the biological context.

It is worth noting that, from simple inspection of the effective matrix, one can also get some information about the distribution (or concentration) of individuals in the configuration space. This can be easily achieved by the knowledge of the eigenvector associated to the spectral radius $\varepsilon(\mathbf{S})$. We consider the sum of its components $m_N=\Sigma_{\nu=0}^{d} P_N(\nu)$, and from the above iterative relation for $P_N(\nu)$ have

$$m_{N+1}=\sum_{\nu=0}^{d}[(a-1)\delta_{\nu,0}+1][(1-td)P_N(\nu)+t(\nu+1)P_N(\nu+1)+t(d-\nu+1)P_N(\nu-1)]$$

$$=(a-1)[(1-td)P_N(0)+tP_N(1)]+(1-td)\sum_{\nu=0}^{d}P_N(\nu)+t\sum_{\nu=0}^{d}(\nu+1)P_N(\nu+1)$$

$$-t\sum_{\nu=0}^{d}(\nu-1)P_N(\nu-1)+td\sum_{\nu=0}^{d}P_N(\nu-1)$$

$$=(a-1)[(1-td)P_N(0)+tP_N(1)]+\sum_{\nu=0}^{d}P_N(\nu). \tag{21}$$

Apart from a constant multiplicative (normalization) factor, we find, in the thermodynamic limit $N\to\infty$, that

$$m=\frac{\varepsilon}{\varepsilon-1}\frac{a-1}{a}. \tag{22}$$

It is easy to prove that the inverse of m gives (apart from a constant factor) the fraction of the population at the origin [that is with MS equal to $(0,0,\ldots,0)$). In fact a simple calculation shows that $m^{-1}\propto P(0)/\Sigma_\nu P(\nu)$.

The dependence of m on the pinning strength a is depicted in Fig. 2 in a semilogarithmic scale. We see that $m\sim 2^d$ for $a<a_c$, i.e., the fraction of individuals with MS equal to $\mathbf{0}$ is 2^{-d}. In other words, the origin is not, in this situation, a privileged site, as all individuals are equally likely to be found in Ω. In the opposite situation, at $a>a_c$, we see that m is approximately given by 1. This means that almost all of the population shares the same sequence, the quasispecies is well defined, and evolution has reached a stationary state around the master sequence $(0,0,\ldots,0)$. Remarkably, the transition appears again to occur at $a_c=(1-td)^{-1}$.

VII. DUAL SPACE APPROACH

The direct investigation of the effective transfer matrix has given some insight into the physics of the problem, in particular with respect to the origin of the phase transition. The simplicity of our model fortunately allows an exact solution, which is, however, nontrivial, due to the high dimensionality of the system.

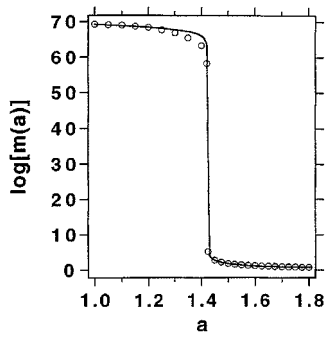

FIG. 2. $\ln[m(a)]$ is plotted vs the selective advantage a for $d=100$, $t=0.003$. At $a_c=(1-td)^{-1}$ the sharp jump indicates the presence of a depinning transition (which is well defined only at $d\to\infty$, as explained in the text). Numerical diagonalization: full line. Analytical result: circles.

To this aim we first need to simplify the transfer matrix $\mathbf{T}$ by means of an appropriate transformation. As the system is defined on $\Omega=\{0,1\}^d$, we use a discretized transformation to achieve the result. We then introduce the following dual space representation of the partition sum $\mathcal{Z}(\mathbf{x})$:

$$\mathcal{Z}_N(\mathbf{x})=\sum_{\mathbf{k}=\{0,1\}^d}(-1)^{\mathbf{x}\cdot\mathbf{k}}\mathcal{Z}_N(\mathbf{k}), \tag{23}$$

and its inverse

$$\mathcal{Z}_N(\mathbf{k})=\frac{1}{2^d}\sum_{\mathbf{x}=\{0,1\}^d}(-1)^{\mathbf{x}\cdot\mathbf{k}}\mathcal{Z}_N(\mathbf{x}). \tag{24}$$

The dual space is obviously identical to Ω and the Kronecker delta is defined as $2^d\delta_{\mathbf{x},\mathbf{0}}=\Sigma_{\mathbf{k}\in\Omega}(-1)^{\mathbf{x}\cdot\mathbf{k}}$.

A rapid inspection shows that this representation implicitly contains periodic boundary conditions in all directions. In the dual space the transfer matrix $\mathbf{T}$ reads

$$\mathcal{Z}_{N+1}(\mathbf{k})=s(\mathbf{k})\mathcal{Z}_N(\mathbf{k})+\frac{a-1}{2^d}\sum_{\mathbf{q}=\{0,1\}^d}s(\mathbf{q})\mathcal{Z}_N(\mathbf{q}), \tag{25}$$

with $s(\mathbf{q})=t\Sigma_{i=1}^{d}(-1)^{q_i}+1-td$.

Our goal is then to solve a 2^d-dimensional eigenvalue problem for the dual transfer matrix $\mathbf{T}$ acting on the right-hand side of the last equation. In the limit $N\to\infty$ the system reaches a stationary state and in this regime $\mathbf{T}$ is dominated by its spectral radius ε. We can then write that in the thermodynamic limit $\mathcal{Z}_{N+1}(\mathbf{k})=\varepsilon\mathcal{Z}_N(\mathbf{k})=\varepsilon\mathcal{Z}(\mathbf{k})$, and

$$\mathcal{Z}(\mathbf{k})=\frac{a-1}{2^d}\frac{1}{\varepsilon-s(\mathbf{k})}\sum_{\mathbf{q}}\mathcal{Z}(\mathbf{q})s(\mathbf{q}). \tag{26}$$

Let us focus, for the moment, on the computation of ε, and define a new constant $Q=\Sigma_{\mathbf{k}\in\Omega}s(\mathbf{k})\mathcal{Z}(\mathbf{k})$. By multiplying both sides by $s(\mathbf{k})$, and summing over $\mathbf{k}$, we finally arrive at the equation for ε:

$$\frac{a-1}{2^d}\sum_{\mathbf{k}=\{0,1\}^d}\frac{s(\mathbf{k})}{\varepsilon-s(\mathbf{k})} \tag{27}$$

or

$$\frac{a}{a-1}=\frac{1}{2^d}\sum_{\mathbf{k}=\{0,1\}^d}\frac{\varepsilon}{\varepsilon-s(\mathbf{k})}. \tag{28}$$

It is clear that any attempt to directly calculate the sum appearing in the above formula is a very hard task, and we are forced to rely on different approaches. First of all we note that, since $s(\mathbf{k})$ can take values of kind $1-2nt$ (with $n=1,2,\ldots,d$) in $d!/[n!(d-n)!]$ different ways, we can recast the sum as follows:

$$\frac{a}{a-1}=\frac{1}{2^d}\sum_{n=0}^{d}\binom{d}{n}\frac{\varepsilon}{\varepsilon-1+2nt}. \tag{29}$$

Despite the simplification, the last expression is still too difficult to solve exactly, nevertheless it can be used to study the structure of the eigenvalues of the transfer matrix. In fact, the rhs of the above equation has $d+1$ singular points in $\varepsilon=1-2nt$, the largest of which is located at $\varepsilon=1$. For each interval between any two singular points, Eq. (29) behaves as a continuous function of ε and it is monotonically decreasing, and then invertible. The solutions to the above equation are given by the intersections of this function with the horizontal line $a/(a-1)$. There are $d+1$ intersections, each of them corresponding to one eigenvalue of the transfer matrix. As the largest singular point is located at $\varepsilon=1$, we have a unique eigenvalue larger than 1, and it corresponds to the spectral radius of **T**. We then concentrate, in what follows, on the solution of Eq. (27) with the restriction $\varepsilon>1$, disregarding all other roots. It is worth noting that in one simple case the sum can be explicitly performed. In fact if we take $\varepsilon=1+2t$, the sum reads

$$\sum_{n=0}^{d}\binom{d}{n}\frac{1}{1+n}=\frac{2^{d+1}-1}{d+1}, \tag{30}$$

and Eq. (29) can be solved for a giving

$$a=1+\frac{2t(d+1)}{(1+2t)(2-2^{-d})-2t(d+1)}. \tag{31}$$

Above we have anticipated that no sharp phase transition can occur at any finite d. In performing the limit $d\to\infty$ we must be sure that t goes to 0 at least linearly in $1/d$ in order to preserve the probabilistic interpretation of the system (recall that $td\in[0,1]$). If, for instance, we approach the critical state on the manifold $\varepsilon=1+2t$, that is, $\varepsilon\to1$ linearly in t, we have, from Eq. (31), that $a\to a_c=1/(1-td)$. This again proves that, at least on the above manifold, $(1-td)^{-1}$ is the critical selective advantage separating the two phases.

VIII. THE EXACT SOLUTION

Let us consider the eigenvalue equation (28). The idea is to introduce a new representation to simplify the formula. The final result must be expressed in implicit integral form.

By using a Feynman-like representation, we have

$$\sum_{\mathbf{k}=\{0,1\}^d}\frac{\varepsilon}{\varepsilon-s(\mathbf{k})}=\frac{1}{A}\sum_{\mathbf{k}\in\Omega}\left(1-\frac{1}{A\varepsilon}t\sum_{i=1}^{d}(-1)^{k_i}\right)^{-1}$$
$$=\frac{1}{A}\int_0^\infty du F(u,t,\varepsilon,A), \tag{32}$$

with $A=(\varepsilon-1+td)/\varepsilon$, and

$$F(u,t,\varepsilon,A)=\sum_{\mathbf{k}\in\Omega}\exp\left[u\left(\frac{1}{A\varepsilon}t\sum_{i=1}^{d}(-1)^{k_i}-1\right)\right]. \tag{33}$$

By noting that the sum in the exponent easily factorizes, we get

$$\sum_{\mathbf{k}\in\Omega}\exp\left(\frac{u}{A\varepsilon}t\sum_{i=1}^{d}(-1)^{k_i}\right)=\left[2\cosh\left(\frac{ut}{A\varepsilon}\right)\right]^d, \tag{34}$$

and therefore, after a change of variable in the integral, the eigenvalue equation takes the form

$$\frac{a}{a-1}=\varepsilon\int_0^\infty e^{-(\varepsilon-1+td)u}[\cosh(ut)]^d du. \tag{35}$$

A few remarks are important at this point on the meaning and validity of the above expression. It represents, for each fixed set of parameters (T,J,d), an integral implicit relation between ε and a. Nevertheless, it is not equivalent to the original series solution (28) of the spectrum of **T** since in the above procedure we have implicitly assumed that the integral representation was mathematically well defined. In order to do this, we must require that the integral (32) converges. This is indeed the case if and only if $\Sigma_{i=1}^{t}d(-1)^{k_i}<A\varepsilon$, or equivalently, if $\varepsilon>1$. If $\varepsilon\leqslant1$ the integral diverges and no real solutions to the above equation can be found. As a consequence, we can use Eq. (35) to calculate the spectrum of **T** corresponding to eigenvalues >1. From the previous argument, we know that there exists a unique eigenvalue larger than 1, and it corresponds to the spectral radius. In conclusion, the unique real solution in ε of Eq. (35) is the spectral radius of the transfer matrix. Moreover, since the integral diverges at $\varepsilon=1$, when the attractive potential at the origin is omitted (i.e., $a=1$), the maximum eigenvalue must be unitary too. Then the free energy density f vanishes and we attain a delocalized phase, as expected.

The implicit integral can be expressed in terms of known mathematical functions. After successive integrations by parts we have that [here $\delta=(\varepsilon-1)/t$]

$$\frac{1}{\varepsilon}\frac{a}{a-1}=\frac{1}{t\delta}\left(1-\frac{d}{\delta+2}\left\{1-\frac{d-1}{\delta+4}\left[1-\cdots-\frac{2}{\delta+2d-2}\right.\right.\right.$$
$$\left.\left.\left.\times\left(1-\frac{1}{\delta+2d}\right)\cdots\right]\right\}\right), \tag{36}$$

and recalling the definition of the hypergeometric series of negative argument [16]

$$F(-m,b;c,z)=\sum_{n=0}^{m}\frac{(-m)_n(b)_n}{(c)_n}\frac{z^n}{n!}, \tag{37}$$

with $(a)_n=a(a+1)\cdots(a+n-1)$, we finally arrive at the result that

$$\frac{a}{a-1}\frac{\varepsilon-1}{\varepsilon}=F\left(-d,1;\frac{\varepsilon-1}{2t}+1,\frac{1}{2}\right). \tag{38}$$

We immediately deduce that [recall definition (22)] $m^{-1}=F(-d,1;(\varepsilon-1)/2t+1,1/2)$.

Let us define $I(d;\varepsilon,t)$ the integral in Eq. (35). $I(d;\varepsilon,t)$ is a monotonic decreasing function of d. This result can be easily proved by using the integral representation of the hypergeometric series. Physically we are interested in the behavior of the system at large dimensions, and in this regime we can use a Laplace saddle-point approximation of the integral solution. A detailed analysis of the asymptotic development of $I(d;\varepsilon,t)$ at large d needs, however, particular attention, since we should properly take into account the condition $td\leqslant 1$. This means that both the limits $d\to\infty$ and $t\to 0$ must be performed *simultaneously* in such a way that $\alpha=td$ is constant. We are implicitly assuming that t goes to 0 linearly in $1/d$, but we would obtain the same final result if $td\to 0$ for $d\to\infty$.

Let α be equal to td, a quantity that must be kept finite during the calculation. We see that $I(d;\varepsilon,t)$ can be written as $\int_0^\infty du g(u)\exp[df(u)]$, with

$$f(u)=\ln[\cosh(u)]-\frac{\varepsilon-1+\alpha}{\alpha}u,$$
$$g(u)=\frac{d}{\alpha}. \tag{39}$$

Since for $\varepsilon>1$ the maximum of $g(u)$ is located at the extreme of integration $u=0$, the integral can be well approximated, at large d, by expanding in a McLaurin series the integrand. At first order in $1/d$ it reads

$$I\sim\int_0^\infty du g(0)\exp[d(f(0)+f'(0)u)]=\frac{1}{\varepsilon-1+\alpha}. \tag{40}$$

More precisely, if we take into account higher powers and the relative error, after some more algebra we arrive at the approximate result:

$$\frac{1}{\varepsilon}\frac{a}{a-1}=\frac{1}{\varepsilon-1+td}+\frac{(td)^2}{d(\varepsilon-1+td)^3}+\frac{3(td)^4}{d^2(\varepsilon-1+td)^5}+\frac{1}{d^3}\left[\frac{15(td)^6}{(\varepsilon-1+td)^7}-\frac{2(td)^4}{(\varepsilon-1+td)^5}\right]+O\left(\frac{1}{d^4}\right). \tag{41}$$

If we are interested in the unique real solution of the above algebraic equation, Eq. (41) can be inverted for the maximum ε. The final solution, up to order $O(1/d^3)$ reads, for $a\in[1,\infty)$

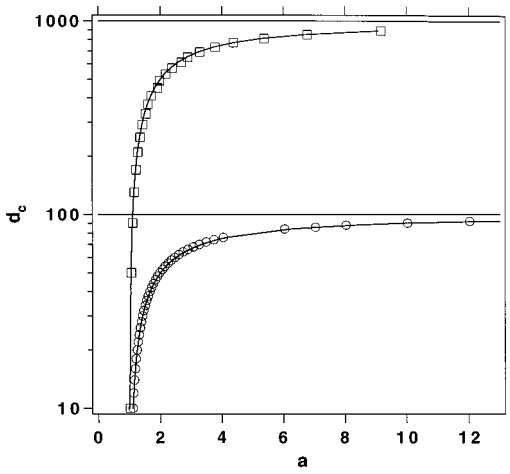

FIG. 3. The critical dimension d_c plotted vs a for two distinct values of t. Lower curve: $t=10^{-2}$; upper curve: $t=10^{-3}$. Full lines represent the function $d_c=t^{-1}(1-1/a)$ (see text). Circles and squares: numerical data from the transfer matrix.

$$\varepsilon=\max\left\{1,a(1-td)+\frac{1}{d}\frac{a(td)^2}{(a-1)(1-td)}+\frac{1}{d^2}\frac{a(2-a)(td)^4}{(a-1)^3[1-(td)^3]}+O\left(\frac{1}{d^3}\right)\right\}, \tag{42}$$

since we know from the above arguments (from the effective matrix) that the spectral radius cannot be less than 1 if $a>1$. This result can be finally compared with the exact calculation performed by numerically finding the spectral radius of **T** for a given set of parameters $\{d,t,a\}$, and the two curves are plotted in Fig. 1.

In the limit $d\to\infty$ we have

$$\varepsilon^{(\infty)}=\max\{1,a(1-td)\}, \tag{43}$$

a result that coincides with that obtained from the analysis we performed on the effective matrix **S**. Hence the critical selective advantage for the MS (0,0, . . . ,0) to create a stable quasispecies around it is $a_c=(1-td)^{-1}$. In other words, as we will clarify below, a_c defines the error threshold for quasispecies formation. Alternatively, one can arrive at the same result on the basis of the convexity property of I as a function of d, as shown in [17]. Figure 3 shows the critical dimension d_c as a function of the pinning a for two values of t. The coincidence between Eq. (43) and the numerical result is remarkable.

IX. THE STATIONARY "GROUND STATE" EIGENVECTOR

In order to have a full solution of our system, we still need to calculate the partition sum (13), or more precisely, the eigenvector corresponding to the maximum eigenvalue we have studied in the previous paragraph. Therefore, let us go back to the recursion relation (25) in the dual space. Disregarding, for the moment, the normalization condition, we have $\mathcal{Z}(\mathbf{k})=Q(a-1)2^{-d}/(\varepsilon-s(\mathbf{k}))$. In the direct space, it reads

$$\mathcal{Z}(\mathbf{x}) = Q\frac{a-1}{2^d}\sum_{\mathbf{k}\in\Omega}(-1)^{\mathbf{x}\cdot\mathbf{k}}\frac{1}{\varepsilon - s(\mathbf{k})}. \tag{44}$$

The summation of the series appearing in the above formula can be done following the same general procedure as before, that is, at $\varepsilon > 1$ we have

$$\sum_{\mathbf{k}=\{0,1\}^d}\frac{(-1)^{\mathbf{x}\cdot\mathbf{k}}}{\varepsilon - s(\mathbf{k})} = \sum_{\mathbf{k}\in\Omega}\left(1 - \frac{t}{B}\sum_{i=1}^{d}(-1)^{k_i}\right)^{-1} = \frac{1}{B}\int_0^\infty du\, G(u,x,t,B), \tag{45}$$

with $B = \varepsilon - 1 + td$ and

$$G(u,x,t,B) = \sum_{\mathbf{k}\in\Omega}(-1)^{\mathbf{x}\cdot\mathbf{k}}\exp\left[u\left(\frac{t}{B}\sum_{i=1}^{d}(-1)^{k_i} - 1\right)\right]. \tag{46}$$

With respect to the above case, we now have an additional term in the sum over $\mathbf{k}\in\Omega$. After factorization, we find that

$$\sum_{\mathbf{k}\in\Omega}(-1)^{\mathbf{x}\cdot\mathbf{k}}\exp\left(\frac{ut}{B}\sum_{i=1}^{d}(-1)^{k_i}\right) = \prod_{i=1}^{d}\sum_{k=0,1}(-1)^{kx_i}\exp\left((-1)^k\frac{ut}{B}\right). \tag{47}$$

In this form the formula is still too hard to allow a simple summation, but a rapid inspection shows how to simplify the problem by taking into account the symmetries of the system. In fact we know that the partition sum must be the same for any two points with equal Hamming distance from the origin. Therefore we can concentrate on studying only the ''radial'' function $P(\nu)$ where ν is the Hamming distance from $(0,0,\ldots,0)$. In practice this observation allows us to neglect the order in which bits ''1'' and ''0'' appear in Eq. (47). What is physically important is the number of bits of each kind that are contained in a given sequence of total length d. If there are ν bits of kind ''1,'' that is, if the Hamming distance of the respective sequence is ν, in the product on the rhs of Eq. (47) will be present ν factors of kind $\exp(ut/B) - \exp(-ut/B) = 2\sinh(ut/B)$ and $d-\nu$ of kind $\exp(ut/B) + \exp(-ut/B) = 2\cosh(ut/B)$. Finally, as the number of ways we can arrange ν bits ''1'' in the total of d bits in $d!/[(d-\nu)!\,\nu!]$, we can write that

$$P(\nu) = Q(a-1)\binom{d}{\nu}\int_0^\infty du e^{-(\varepsilon-1+td)u} \times [\sinh(ut)]^\nu[\cosh(ut)]^{d-\nu}. \tag{48}$$

The constant Q can be fixed by normalization, that is, if we impose that $\mathcal{Z}(\mathbf{x})$ be summable, we must require that $\Sigma_{\nu=0}^{d}P(\nu) = 1$. The last calculation is easy to perform, in fact, $\Sigma_{\nu=0}^{d}\binom{d}{\nu}[\sinh(ut)]^\nu[\cosh(ut)]^{d-\nu} = \exp(utd)$ and thus, after integration, we get the result that $\Sigma_{\nu=0}^{d}P(\nu) = Q(a-1)/(\varepsilon-1)$. The normalized solution reads

$$P(\nu) = (\varepsilon-1)\binom{d}{\nu} \times \int_0^\infty du e^{-(\varepsilon-1+td)u}[\cosh(ut)]^d[\tanh(ut)]^\nu. \tag{49}$$

At generic d it is not possible to perform the above integral, which is convergent $\forall\,\varepsilon > 1$, but we can restrict ourselves to study the form of the solution at large dimensions.

Since one may equally characterize the depinning phase transition in terms of U or a, we can study its order by considering the discontinuities of the partition sum in a. At $d\to\infty$ the maximum eigenvalue is defined by Eq. (43). By inserting this expression into $P(\nu)$ we simply find that the partition sum is a $\mathcal{C}^0$ function in a, that is, the phase transition is of first order. This is also clear if one looks at the shape of $\ln(m)$, which can be considered a sort of ''order parameter,'' near the critical point a_c (see Fig. 2). Moreover, from very general arguments [13], we expect that the typical length $\xi_\perp$ within which the polymer is confined around the potential, diverges at the critical point as $\xi_\perp \sim |a - a_c|^{-\nu_\perp}$ with a given characteristic exponent. In a sense, the variable ν appearing in Eq. (49) can be considered a sort of external control parameter for the system described by Eq. (44) at equilibrium.

In order to calculate the critical exponent $\nu_\perp$ we can introduce the generating function $G(\lambda)$ associated to $P(\nu)$, as

$$G(\lambda) = \langle e^{\lambda\nu}\rangle = \sum_{\nu=0}^{d}P(\nu)e^{\lambda\nu}. \tag{50}$$

The various momenta $\zeta_m = \langle\nu^m\rangle$ can be calculated from $G(\lambda)$ in the usual way: $\zeta_m = \partial_\lambda^{(m)}G(\lambda)|_{\lambda=0}$. In order to study the behavior of $\xi_\perp$ we need the knowledge of the fluctuations of the polymer around the origin, and therefore we need the second cumulant $\mu_2 = \zeta_2 - \zeta_1^2$. We thus calculate the connected generating function $\Gamma(\lambda) = \ln G(\lambda)$, since $\mu_m = \partial_\lambda^{(m)}\Gamma(\lambda)|_{\lambda=0}$.

From the above exact formula, we can write that

$$G(\lambda)=(\varepsilon-1)\int_0^\infty du\exp(-(\varepsilon-1+td)u+d\ln\{\cosh(ut)[1+K\tanh(ut)]\})$$

$$=(\varepsilon-1)\frac{d}{\alpha}\int_0^\infty dx\exp\left\{d\left[\ln\{\cosh(x)[1+K\tanh(x)]\}-\frac{\varepsilon-1+td}{\alpha}x\right]\right\}, \tag{51}$$

where $K=e^\lambda$ and $x=ut$. If we are interested in the large d behavior, the integral can be estimated by saddle-point methods. The function at the exponent is maximum in $x=0$ if $\varepsilon>1$, and then

$$G(\lambda)\simeq(\varepsilon-1)\frac{d}{\alpha}\int_0^\infty dx\exp\left\{d\left[\left(K-\frac{\varepsilon-1+td}{\alpha}\right)+\frac{1-K^2}{2}x^2\right]\right\}\simeq(\varepsilon-1)\left[\frac{1}{\varepsilon-1+\alpha(1-K)}+\frac{(1-K^2)\alpha^2}{[(\varepsilon-1+\alpha)/\alpha-K]^3}\frac{1}{d}\right]. \tag{52}$$

Corrections to the previous formula are of the order $O(1/d^2)$. By applying the definition of $\Gamma(\lambda)$, we finally find that

$$\mu_1=\frac{td}{\varepsilon-1}-\frac{2(td)^5}{(\varepsilon-1)^2}\frac{1}{d}+O\left(\frac{1}{d^2}\right),$$

$$\mu_2=\frac{(td)^2}{(\varepsilon-1)^2}-\frac{2(td)^5(\varepsilon-1+4td)}{(\varepsilon-1)^3}\frac{1}{d}+O\left(\frac{1}{d^2}\right). \tag{53}$$

As expected, the fluctuations around the average have a power-law divergence at the critical point $\varepsilon=1$. Since ε goes to 1 linearly with $a\to a_c$, we deduce that the critical exponent is $\nu_\perp=1$ at $d\to\infty$.

It is also interesting to look at the shape of the partition function in ν. From the biological point of view, it tells us how mutants of a given MS are distributed around it to form a quasispecies. If we restrict ourselves, for simplicity, to the leading term in $1/d$ in Eq. (52), we must inverse transform it to get the real space solution at first order. To simplify the calculation, we assume that $\lambda=i\eta$ is a complex number, and this allows us to write

$$P^{(1)}(\nu)=(\varepsilon-1)\int_{-\infty}^{\infty}d\eta e^{-i\eta\nu}\frac{1}{\varepsilon-1+td(1-e^{i\eta})}. \tag{54}$$

By analytic continuation in the complex plane, $\eta=z$ becomes a complex variable and the resulting integral can be calculated by means of the residue theorem. The integrand has a simple pole at $z^*=-i\ln[1+(\varepsilon-1)/(td)]$ and to apply Cauchy's lemma we must close the integration path in the semiplane $\mathrm{Im}\{z\}<0$. After having calculated the residue in z^*, we find that $\mathrm{Res}(z^*)=-i\alpha[1+(\varepsilon-1)/\alpha]^{-\nu-1}$. Hence,

$$P^{(1)}(\nu)=\mathcal{N}\frac{2\pi}{td}(\varepsilon-1)\left(1+\frac{\varepsilon-1}{td}\right)^{-(\nu+1)}$$

$$=\mathcal{N}\frac{2\pi(\varepsilon-1)}{\varepsilon-1+td}\exp\left[-\nu\ln\left(1+\frac{\varepsilon-1}{td}\right)\right], \tag{55}$$

where $\mathcal{N}$ is a normalization factor. It can be easily calculated by noting that the sum involves a truncated geometric series:

$$\sum_{\nu=0}^{d}P^{(1)}(\nu)=2\pi\frac{\varepsilon-1}{\varepsilon-1+td}\frac{(1-a^{d+1})}{1-a},$$

$$a^{-1}=\left(1+\frac{\varepsilon-1}{td}\right). \tag{56}$$

The partition function shows an exponential decay as a function of ν. The *mass gap* [13] is therefore given by $\ln[1+(\varepsilon-1)/\alpha]\simeq(\varepsilon-1)/\alpha$, close to the phase transition. Since the transversal correlation length is usually defined as the inverse of the mass gap, we again recover the result that, at the critical point, $\nu_\perp=1$.

A more refined expression of the partition function at large d can be obtained by directly considering a saddle point approximation of Eq. (49). Without entering into mathematical details (similar to those employed in previous calculations), we see that the integral in Eq. (49) is dominated by the region close to $u^*=0$. By expanding the integrand around u^* and integrating term by term, we finally find

$$P(\nu)=(\varepsilon-1)\binom{d}{\nu}\left(\frac{\alpha}{d(\varepsilon-1+\alpha)}\right)^\nu\left[\frac{1}{\varepsilon-1+\alpha}\Gamma(\nu+1)\right.$$

$$\left.+\frac{\alpha^2}{2d(\varepsilon-1+\alpha)^3}\Gamma(\nu+3)\frac{1}{d}+O\left(\frac{1}{d^2}\right)\right]. \tag{57}$$

In Fig. 4 we compare this approximate result (by only retain-

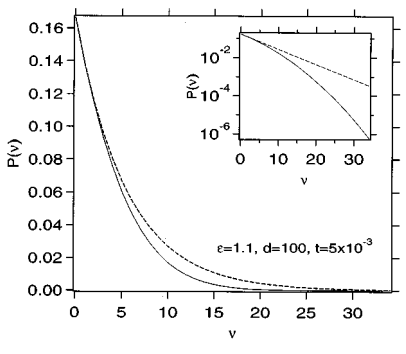

FIG. 4. Comparison between the two real-space forms of the solution $P(\nu)$ at the first significant order in $1/d$. The dashed and the full lines correspond to Eqs. (55) and (58), respectively.

ing the first term in parentheses) with $P^{(1)}(\nu)$ given by Eq. (55). The coincidence of the two curves is good up to $d\sim\nu$, i.e., in the physical range (recall that by definition $\nu\leqslant d$). In fact it is possible to show that Eq. (57) is a monotonically increasing function of ν for $\nu\gg d$, while the exact function is always decreasing. The minimum of the approximating function is found indeed for $\nu\sim d$. More precisely, if we only take the first term in Eq. (57), a rapid inspection shows that it can be rewritten as

$$P^{(1)}(\nu)=(\varepsilon-1)\frac{d!}{(d-\nu)!}\frac{\alpha}{d(\varepsilon-1+\alpha)}\left(\frac{\alpha}{d(\varepsilon-1+\alpha)}\right)^{\nu}$$

$$\sim\mathcal{N}'\frac{(\varepsilon-1)}{\varepsilon-1+\alpha}\left(1+\frac{\varepsilon-1}{\alpha}\right)^{-\nu}, \tag{58}$$

the last approximation being valid if $\nu\ll d$. We then see that, apart from inessential factors, Eqs. (55) and (58) give the same result only if $\nu\ll d$. At larger ν, Eq. (58) shows the presence of power-law corrections in the exponential decay of the partition sum.

X. COMPARISON WITH PREVIOUS RESULTS AND CONCLUSIONS

We are now in a position to compare our result with the general approach by coming back to the usual ''quasispecies'' notation. The copying fidelity in a given reproduction process has been defined in our model by $1-td$, while in the original work [6] it was indicated by q^d [see also Eq. (7)]. Therefore, the first result of our work has been to show that the critical threshold for quasispecies formation is given by

$$a_c=\frac{1}{1-td}=q^{-d},\quad d_c=-\frac{\ln a}{\ln q}, \tag{59}$$

which coincides with Eq. (8).

Let us now discuss similarities and differences between our mapping and the previous approaches. In the above cited work, Leuthäusser introduced a mapping of Eigen's model to a system at equilibrium. Briefly, we describe the mapping as follows. Let us consider again Eq. (4) with discretized time k, representing ''generations''of macromolecules. If we define the vector $\mathbf{X}(k)=(x_1(k),x_2(k),\ldots,x_{2^d}(k))$, representing the set of the relative concentrations of the macromolecules at time k, Eigen's model can be easily rewritten as

$$\mathbf{X}(k)=\mathbf{W}^k\mathbf{X}(0). \tag{60}$$

As in our case, the problem is then reduced to a linear system associated to $\mathbf{W}$. This matrix, actually, can be thought of as a transfer matrix of an equilibrium system. In fact, if one considers only binary sequences I_j made, for instance, of d Ising spins $(\sigma_1,\sigma_2,\ldots,\sigma_d)$, the evolution of the system can be represented in a square lattice geometry. One side of the lattice (that composed of different rows) has a length equal to that (d) of the sequences, while the other one is semi-infinite in one direction, as each column can be associated to the state of the system at time k. The final state, in this geometry, is therefore associated to the properties of the lattice edge, which indeed represents the state of the system after N generations. If each site along the binary chain is exactly copied with probability q, independently from other sites, the replication matrix takes the form

$$W_{ij}=A_j q^d\left(\frac{1-q}{q}\right)^{(d-\sum_{k=1}^{d}\sigma_k^i\sigma_k^j)/2}. \tag{61}$$

This represents a transfer matrix of a two-dimensional Ising-like system with nearest neighbors interactions along the ''time direction.'' The Hamiltonian corresponding to Eq. (61) has, however, a very complicated mathematical form

$$-\beta\mathcal{H}=-\sum_{i=0}^{N-1}\left[\beta\sum_{j=1}^{d}\sigma_j^i\sigma_j^{i+1}+\ln A(I_i)\right]+\frac{Nd}{2}\ln[q(1-q)], \tag{62}$$

Tarazona [10] numerically solved the system for various fitness landscapes A_j, and discussed the results with respect to the original quasispecies model.

Apart from the intrinsic difficulty in solving problems described by Hamiltonians of the kind (62), there is a subtle problem contained in this formulation. The actual state of the system after N generations depends *only* on the structure of the layer at the edge of the square lattice, that is, on the spin configurations at the Nth column. Therefore, as one may expect, the error threshold transition cannot be fully understood in terms of the bulk properties on the square lattice, as already pointed out in [10]. We thus need the complete knowledge of the structure of the lattice surface, and not of the bulk, to solve the original Eigen's model. With the Leuthäusser mapping, there is no hope of accomplishing that goal, in general. The fact that the critical properties of the quasispecies model are associated to surface structures is, in a sense, conserved in our mapping, as we have also associated the error threshold problem to the statistical mechanics properties of an interfacelike object. On the other hand, our mapping to the directed polymers' statistical mechanics seems to be more natural and able to better clarify the delicate mechanisms involved in the error-threshold transition.

In conclusion, we have analyzed Eigen's model in the simplest situation characterized by a single-peaked fitness. The main issues of our exact solution can be summarized in three main points. First, we have proved that, in the limit of infinite sequence lengths d, the error threshold phenomenon is associated to a first-order critical phase transition. Moreover, the typical amplitude of the quasispecies around the MS diverges with exponent $\nu_\perp=1$ at criticality. Numerical simulations [10], seem, however, to indicate that this picture no longer holds for more general situations. It would be ex-

tremely interesting to use our mapping to investigate these other cases as well. Finally, we have proved that the critical selective advantage for quasispecies formation depends exponentially on the sequence length d.

We believe that, even in more realistic situations, in which the fitness landscape is characterized by rough fluctuations from point to point, and with the help of the directed polymers theory, the present study can be extended.

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