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LETTER TO THE EDITOR

**Diffusion on a hypercubic lattice with pinning potential:  
exact results for the error-catastrophe problem in  
biological evolution**

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**Abstract.** In the theoretical biology framework one fundamental problem is the so-called *error catastrophe* in Darwinian evolution models. We re-examine Eigen's fundamental equations by mapping them into a polymer depinning transition problem in a 'genotype' space represented by a unitary hypercubic lattice  $\{0, 1\}^d$ . The exact solution of the model shows that error catastrophe arises as a direct consequence of the equations involved and confirms some previous qualitative results.

An important question in the context of Darwinian 'natural' selection theory is: how could complex life evolve and finally reach the structure we can see nowadays by selecting the fittest species among the huge number of different allowed choices? Could we explain the mechanism of self-organization (guided evolution) to complex life from basic principles or is it necessary to consider some other 'external' organizing parameter? The number  $N$  of different realizations of a given virus DNA chain, made of a very long random sequence of basic units (chemical bases), is typically given by  $N \approx 10^{1000}$ . Hence the time needed by random evolution to 'explore' all possible choices before reaching the optimum sequence (i.e. complex life) is really enormous.

Here we consider a simplified model, that is evolution in a genotype space of dimension  $d$  with a unique *master sequence* (MS) being the favoured one, i.e. the one corresponding to individuals with highest *fitness*. All other sequences are supposed to have the same lower fitness, which, for sake of simplicity, we will take as unity. The *quasi-species* [1] can 'diffuse' in this genotype space with a mutation rate per base  $\mu$ , generally assumed to be very small. A so-called *error catastrophe* arises since increasing the chain length  $d$ , even though the master sequence  $I_m$  has highest fitness, it can hardly survive evolution. In other words, we need extremely large fitness for  $I_m$  or, equivalently, exceedingly small mutation rate to keep the MS in a population.

The first investigation of this simple model was achieved by Eigen and co-workers [1]. The aim of the present work is to solve the problem exactly and particular attention will be devoted to the conditions for the occurrence of the error catastrophe.

Natural selection, in Eigen's model, is described by a simple prototype evolution equation. The space of configurations, i.e. the genotype space, is constructed from a set  $\mathcal{I}$  of sequences of uniform length comprising  $d$  monomeric units of which  $k$  classes (chemical bases) can exist. The number of different sequences is the cardinality of the set  $\mathcal{I}$ , and

obviously given by  $N = |\mathcal{I}| = k^d$ . In the simplest case (the one we will consider in the following)  $k = 2$  and then sequences are made of binary units:  $I_i = a_i\{a_i = \{0, 1\}, \forall i = 1, \dots, d\}$ .

One can then introduce a continuous-time master equation for the concentration of individuals  $x_i$  [1]. The main result is that the target of selection is a species defined by the dominant, that is the most probable, sequence  $I_m$  (MS) [2–4], which is reached after finite time in a self-organized way, i.e. without any external fine tuning. Some heuristic arguments show that if the *excess production rate*† of the master sequence  $A_m$  is too small, when compared with those of the mutants  $A_{k \neq m}$ , then *error catastrophe* arises [5]: no convergence to the  $I_m$  sequence takes place and the dynamics is dominated by a random creation and annihilation of all possible individuals in the set  $\mathcal{I}$ .

Our main goal in this letter is the following. We solve the evolution equations exactly, by means of a mapping to a polymer localization problem, and prove that *error catastrophe* always occurs in Eigen’s model: the ratio  $a = A_m/A_{k \neq m}$  necessary to self-organize the process to the master sequence is exponentially big in the sequence length  $d$ .

We first define our system and the space of configurations. Let us consider a  $d$ -dimensional hypercubic unitary lattice  $\Omega = \{0, 1\}^d$ , mimicking a genotype space. Each side is made of only two points representing binary units. Each point of  $\Omega$  has a one-to-one correspondence with a sequence  $I_i$  ( $i = 1, |\mathcal{I}|$ ) since the cardinality of  $\mathcal{I}$  is equal to the number of points of  $\Omega$  (we take  $k = 2$ ).

The discretized time version of the rate equation, in the polymer context, describes a depinning transition [6]. A polymer, directed along the time axis, moves in a  $(d + 1)$ -dimensional space,  $\Omega \times N$ , subjected to a contact energy term with energy gain  $-u < 0$  per step of the interface located at the wall. At finite temperatures  $T > 0$  the polymer fluctuates in order to increase its configurational entropy but large fluctuations are unlikely [7].

The polymer is completely specified by the Hamiltonian

$$\mathcal{H}_L(\{\mathbf{h}\}^{(i)}) = \sum_{i=1}^L (J|\mathbf{h}^{(i)} - \mathbf{h}^{(i-1)}| - u\delta_{\mathbf{h}^{(i)}, \mathbf{0}}) \quad (1)$$

and the partition function [7]

$$\mathcal{Z}_L(\mathbf{x}) = \sum_{\{\mathbf{h}\}} \exp\{-\mathcal{H}_L(\{\mathbf{h}\}^{(i)})/T\} \quad (2)$$

where  $\mathbf{h}^{(i)}$  is the position of the polymer in  $\Omega$  at time  $i$ . Overhangs are forbidden and the RSOS condition is imposed, that is  $|\mathbf{h}^{(i)} - \mathbf{h}^{(i-1)}|$  can be zero or one. This condition means that in one time step ( $i \rightarrow i + 1$ ) mutations are possible only between species with Hamming distance equal to one.

Let us consider the transfer matrix (see also [8])

$$\mathcal{Z}_{L+1}(\mathbf{x}) = (1 - (a - 1)\delta_{\mathbf{x}, \mathbf{0}}) \left( \sum_{i=1}^d t \mathcal{Z}_L(\mathbf{x} + \mathbf{e}^{(i)}) + (1 - dt)\mathcal{Z}_L(\mathbf{x}) \right) \quad (3)$$

where we have introduced the unitary vectors  $\mathbf{e}^{(i)} = (0, \dots, 1, \dots, 0)$  as those having a ‘1’ bit in the  $i$ th position. Moreover, we have defined the parameters  $a = \exp(u/T)$  and  $t = \exp(-J/T)$ .

Actually we should say that equation (3) defines a transfer matrix which is equivalent to that associated with Hamiltonian (1) apart from a multiplicative constant which does not

† The excess production rate  $A_i$  of the sequence (or species)  $I_i$  describes autocatalytic amplification during reproduction (see also [5]).

affect our final result. The reason why we use this form is that it is the discretized-time version of Eigen's original rate equation (in the hypothesis of vanishing average of deaths per unit time and of unitary excess production rates for all sequences except the master one:  $A_{k \neq m} = 1$ ,  $A_m = a$ ; see also [5]). In fact, in this scheme the *hopping constant*  $t \in [0, 1]$  is the probability that, given a pair of neighbouring sites, a 'jump' occurs between them in one time step. As a consequence  $dt$  represents the probability that a mutation of a given individual takes place, while  $1 - dt$  is the probability of exact replication. In the usual notation the last quantity is given by  $q^d$  since  $q$  is defined as the probability of exact replication of one base in the DNA chain.

Our goal is to find the spectrum of the matrix defined by (3), or, at least, its spectral radius (i.e. the maximum eigenvalue) since it gives the only significant contribution to the free energy density (per unit length)  $f$  in the thermodynamic limit  $L \rightarrow \infty$ .

The knowledge of the spectral radius as a function of the free parameters  $\{a, d, t\}$  of the system is then what we need to show the appearance of the error catastrophe in Eigen's model. The argument is straightforward. One can prove that if the polymer is in the localized phase, then the spectral radius  $\varepsilon$  is bigger than one, while it attains unity in the unbounded state [9]. This result can be easily mapped into the biological framework. In fact, 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 species preferentially to (apart from) the master sequence. Therefore the error-catastrophe problem is reduced to the search for the critical pinning  $a$  necessary to localize the polymer for fixed values of  $d$  and  $t$ .

In this simplified model we allow, of course, only one mutation in a single time step. This hypothesis is indeed not an approximation nor a limit of our approach. One can simply prove that allowing more than one mutation per time step corresponds to taking higher powers  $n$  of the matrix (3). With a simple redefinition of the time units this new linear operator will take into account multiple jumps between points of  $\Omega$  in one step. However, in what follows, we will show that our result can be well associated with the set of eigenvectors of our transfer matrix (3), which does not depend, as is obvious, on the power  $n$ .

We now introduce a dual space representation to have periodic boundary conditions in all directions:

$$\mathcal{Z}_L(\mathbf{x}) = \sum_{\mathbf{k}=\{0,1\}^d} (-1)^{\mathbf{x} \cdot \mathbf{k}} \mathcal{Z}_L(\mathbf{k}) \quad \mathcal{Z}_L(\mathbf{k}) = 1/2^d \sum_{\mathbf{x}=\{0,1\}^d} (-1)^{\mathbf{x} \cdot \mathbf{k}} \mathcal{Z}_L(\mathbf{x}).$$

The summation is over the  $2^d$  possible binary realizations of  $\mathbf{k}$  and  $\mathbf{x}$ . In the dual space equation (3) takes the form

$$\mathcal{Z}_{L+1}(\mathbf{k}) = s(\mathbf{k}) \mathcal{Z}_L(\mathbf{k}) + \frac{a+1}{2^d} \sum_{\mathbf{q}=\{0,1\}^d} s(\mathbf{q}) \mathcal{Z}_L(\mathbf{q}) \quad (4)$$

with  $s(\mathbf{q}) = t \sum_{i=1}^d (-1)^{q_i} + 1 - dt$ . Our goal is then to solve a  $2^d$ -dimensional eigenvalue for the dual transfer matrix  $\mathcal{M}$  acting on the right-hand side of equation (4). After some algebraic manipulation one can show that the spectrum of the matrix is given by the  $2^d$  solutions of the following equation (in the thermodynamic limit we focus our attention only on the largest eigenvalue of the spectrum):

$$\frac{a-1}{2^d} \sum_{\mathbf{k}=\{0,1\}^d} \frac{s(\mathbf{k})}{\varepsilon - s(\mathbf{k})} = 1. \quad (5)$$

We will list below, without proof, a series of exact results; all mathematical details will be given elsewhere [9]. The maximum eigenvalue of the transfer matrix  $\mathcal{M}$  is always *non-degenerate*, as a consequence of the Frobenius–Perron theorem, and has a corresponding positive right eigenvector. We can use  $\mathcal{M}$  to calculate, as a first approximation, the bounds for the spectral radius  $\rho(\mathcal{M}) = \varepsilon$  by means of some theorems on positive matrices [10].

We note that, strictly speaking, one could have a phase transition for polymer localization only in the limit  $d \rightarrow \infty$ . For finite  $d$  the situation is less clear. At any finite dimension  $d$  the total number of accessible sites is finite and equal to  $2^d$ . As a consequence our polymer never wanders at infinity even in the thermodynamic limit  $t \rightarrow \infty$ . However, 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  $\ell$  within which the polymer is confined to the origin is independent of the linear size  $L$  and is always finite (even at  $d \rightarrow \infty$ ). The two different behaviours take place at a given characteristic value  $u_{\text{crit}}$  of the pinning potential which will be our definition of criticality. The following statements are equivalent: in the unbounded state one has  $\varepsilon \rightarrow 1^+$ , vanishing free energy per unit length  $f$ , and constant components  $Z(i)$  of the positive eigenvector associated with  $\varepsilon$ . The opposite applies in the localized phase.

Now we can turn our attention to equation (5). The idea is to transform it into a simpler formula for  $\varepsilon$  by means of a Feynman integral representation. The result is that the maximum eigenvalue is given by the only real solution of the following implicit equation:

$$\frac{a}{a-1} = \varepsilon \int_0^\infty e^{-(\varepsilon-1+dt)u} (\cosh(ut))^d du = {}_2F_1\left(-d; 1; \frac{\varepsilon-1}{2t} + 1; \frac{1}{2}\right). \quad (6)$$

We note that the integral diverges iff  $\varepsilon = 1$ . Therefore if the attractive potential at the origin is omitted ( $a = 1$ ), the maximum eigenvalue must be unitary, too. Then the free energy  $f$  vanishes and we attain a delocalized phase, as expected. In the above formula  ${}_2F_1(-a; b; c; d)$  is the usual hypergeometric series of negative argument  $-a$  [11].

We define  $I(d; \varepsilon, t)$  the integral in (6). The basic results are: (i)  $\varepsilon(a)$  is a convex non-decreasing function of  $a$ , and (ii) for large  $a$ , the function  $\varepsilon(a; d, t)$  is linear in  $a$ :  $\varepsilon \simeq (1-dt)a$ , ( $a \gg 1$ ). The shape of  $\varepsilon I(d; \varepsilon, t)$  is shown in figure 2 as a function of  $d$ . Parameters  $\{t, \varepsilon\}$  are fixed in the physical range.

A detailed analysis of the asymptotic development for  $I(d; \varepsilon, t)$  at large  $d$  needs particular attention, since we should properly take into account the condition  $dt \leq 1$ . This means that both the limits  $d \rightarrow \infty$  and  $t \rightarrow 0$  must be performed *simultaneously* in the development in such a way that  $\alpha = dt$  is constant. The result of the calculation is

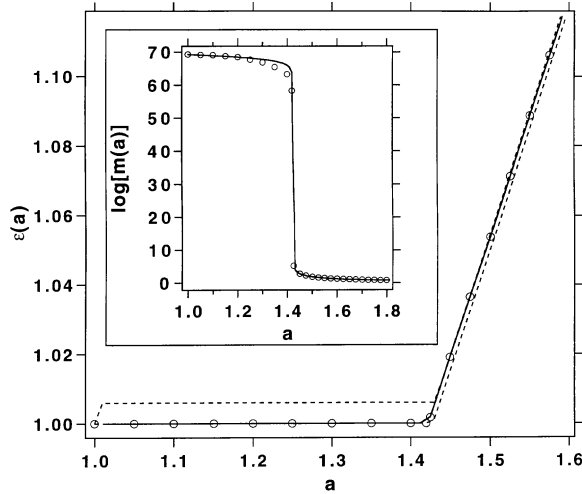
$$\frac{a}{a-1} = \frac{\varepsilon}{\varepsilon-1+dt} + \frac{(dt)^2\varepsilon}{d(\varepsilon-1+dt)^3} + \frac{3(dt)^4\varepsilon}{d^2(\varepsilon-1+dt)^5} + O\left(\frac{1}{d^3}\right). \quad (7)$$

This implicit algebraic equation can be solved for the maximum  $\varepsilon$  and the result is compared with the exact calculation performed by numerically finding the spectral radius of  $\mathcal{M}$  for a given set of parameters  $\{d, t, a\}$  (see figure 1).

The shape of the eigenvector corresponding to  $\varepsilon$  is relevant from the point of view of the depinning transition. It is represented by the sum of its components  $m(d; a, \varepsilon, t) = \sum_i Z(i)$ . One can prove that

$$m(d; a, \varepsilon, t) = \frac{\varepsilon}{\varepsilon-1} \frac{a-1}{a} = \frac{1}{\varepsilon-1} I(d; \varepsilon, t)^{-1}. \quad (8)$$

As a direct consequence we have that (see equation (9) below)  $\lim_{a \rightarrow 1^+} m = 2^d$  and  $\lim_{a \rightarrow \infty} m = 1$ . Figure 1 shows the shape of  $m$  comparing the numerical result obtained



**Figure 1.** Main figure: maximum eigenvalue of the transfer matrix  $\mathcal{M}$  plotted against the pinning strength  $a$ . Numerical data, full line; analytical result (up to order  $O(1/d^3)$ ), circles. The dashed lines are the bounds for  $\varepsilon$  obtained from the transfer matrix. Inset:  $\log[m(a)]$  plotted against  $a$ . In all cases  $d = 100$ ,  $t = 0.003$ . Numerical data, full line; analytical result, circles.

by the transfer matrix and the analytical one from the asymptotic development truncated at order  $O(1/d^3)$ . The coincidence is very good. Our depinning transition can be easily studied in terms of  $\mu = \log(m)$ . In the unbounded state the polymer wanders in all the accessible space of  $\Omega$  and then  $m$  reaches its maximum value, while if  $a$  is very high  $\mu$  converges towards zero.

If one asks for the critical pinning  $a_c$  necessary to localize the polymer on the origin, we should fix the parameters  $d$  and  $t$ , with the constraint  $dt \leq 1$ , necessary to preserve the probabilistic interpretation, and search for the maximum allowed  $a$  associated with an eigenvalue  $\varepsilon$  ‘sufficiently’ close to one. We specify this statement by considering as values close to one those which differ from unity for a vanishing quantity in the limit  $d \rightarrow \infty$ .

This definition can be justified, and made rigorous, by noting that for  $a \rightarrow 1^+$  equation (5) is dominated by only one term in the sum and one gets the result (here  $\varepsilon$  stands for the maximum eigenvalue of  $\mathcal{M}$ )

$$\frac{a}{a-1} \underset{a \rightarrow 1^+}{\simeq} \frac{1}{2^d} \frac{\varepsilon}{\varepsilon-1} \quad \text{or} \quad \varepsilon \simeq 1 + \frac{a-1}{1+a(2^d-1)} = 1 + \delta_d. \quad (9)$$

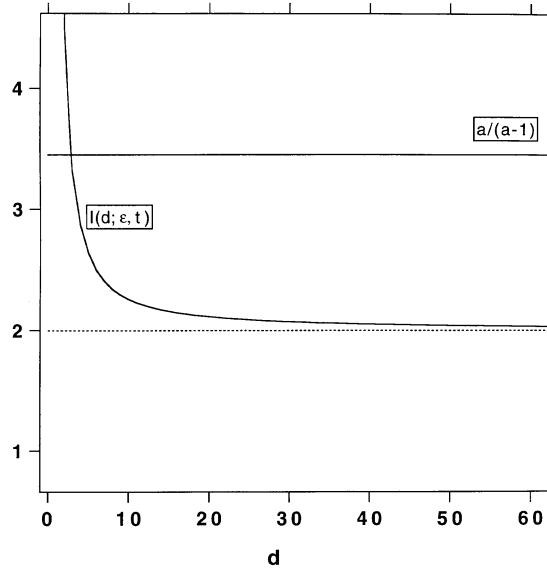
Then we can properly define  $a_c = \sup_{a \in (1, \infty)} \{a | \varepsilon \leq 1 + \delta_d\}$ .

The conclusion is that, if  $a$  is below  $a_c$ ,  $\varepsilon$  converges exponentially to  $1^+$  in the limit  $d \rightarrow \infty$ . Now we will prove the main physical result of this article, namely that the threshold is the critical pinning  $a_c$  necessary to localize the polymer and that we have, at criticality,  $\forall d$

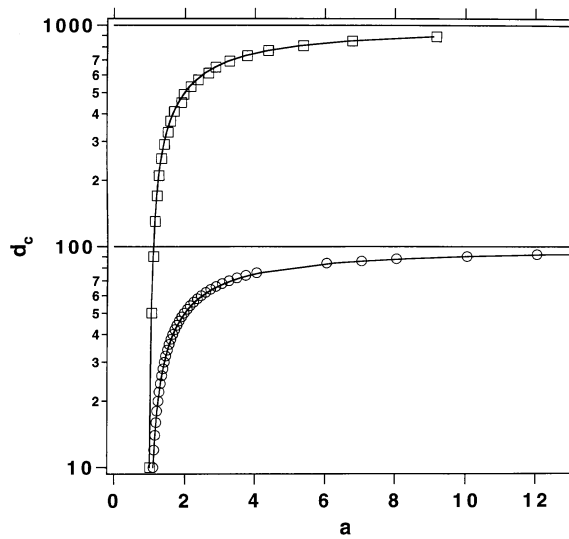
$$a_c = \frac{1 + \delta_d}{1 - dt} \iff d_c \simeq -\frac{\log a}{\log q} \quad (10)$$

where  $\delta_d$  is a function tending to zero as  $O(2^{-d})$ , (see equation (9)).

The proof is rather simple if we look at the graphical interpretation of equation (6), see also figure 2. For a given set  $\{d, t, a\}$  in the physical range, the non-degenerate  $\varepsilon$  is found by intersecting the curve  $\zeta = \varepsilon I(d; a, t)$  with the horizontal line  $a/(a-1) = A = \text{constant}$ .



**Figure 2.** Shape of  $I(d; \varepsilon, t)$  and of  $a/(a-1)$  plotted against  $d$  (see text). The dashed line gives the asymptotic limit of  $I$  for large dimensions  $d$  at  $\varepsilon \rightarrow 1^+$ .



**Figure 3.** Critical dimension  $d_c$  plotted against pinning strength  $a$  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 the numerical data from the transfer matrix.

As we showed above,  $\zeta$  asymptotically converges to  $K = \varepsilon/(\varepsilon - 1 + dt)$  for large  $d$  and then to  $1/dt$  in the extreme situation  $\varepsilon \rightarrow 1^+$ . If  $a$  is too big, namely  $A < K$ , for a fixed  $\varepsilon$ , then no solutions can be found since  $A$  is below  $\zeta$ . In that case a solution always exists but for a bigger  $\varepsilon$ , necessary to lower  $K$  below  $A$ . As a consequence, the critical  $a_c$  following our

definition, can be found by asking for the maximum allowed  $a$  compatible with a solution of the form  $\varepsilon = 1 + \delta_d$ . The answer is now obvious and it is given by equation (10).

Figure 3 shows the critical dimension  $d_c$  as a function of the pinning  $a$  for two values of  $t$ . The coincidence between formula (10) and the numerical results is remarkable.

In conclusion, in this letter we have re-examined the evolution equations introduced by Eigen and co-workers in order to mimic Darwinian natural selection in biological evolution. A particle diffusing on the  $\Omega$  space and subjected to an attractive wall localized at the origin can be viewed, in the biological context, as a reproduction process in the genotype space. The mutation rate  $t$  and the excess production rate  $A_i$  for a given DNA sequence are easily mapped into other physical quantities for the polymer localization problem. We have proved that the so-called error-catastrophe problem naturally arises as a consequence of the model introduced: in other words, for given copying fidelity  $q$  and fitness  $a$ , equation (10) represents an upper limit for the genome length.

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## References

- [1] Eigen M 1971 *Naturwissenschaften* **58** 465–526
- [2] Eigen M and Schuster P 1979 *The Hypercycle—a Principle of Natural Selforganization* (Berlin: Springer)
- [3] Eigen M 1986 *Chem. Scr.* B **26** 13–26
- [4] Schuster P 1986 *Chem. Scr.* B **26** 27–41
- [5] Eigen M, McCaskill J and Schuster P 1988 *J. Phys. Chem.* **92** 6881–91
- [6] Chui S T and Weeks J D 1981 *Phys. Rev. B* **23** 2438  
Burkhardt T 1981 *J. Phys. A: Math. Gen.* **14** 263  
van Leeuwen J M J and Hilhorst H J 1981 *Physica A* **107** 319
- [7] Forgacs G, Lipowsky R and Nieuwenhuizen Th M 1991 *Phase Transitions and Critical Phenomena* vol 14 ed C Domb and J L Lebowitz (New York: Academic)
- [8] Nechaev S and Zhang Y-C 1995 *Phys. Rev. Lett.* **74** 1815
- [9] Galluccio S and Graber R in preparation
- [10] Lancaster P and Tismenetsky M 1985 *The Theory of Matrices* 2nd edn (New York: Academic)
- [11] Abramowitz M and Stegun I A (ed) 1965 *Handbook of Mathematical Functions* (New York: Dover)