The optimization and shock waves in evolution dynamics

David B. Saakian\textsuperscript{1,2} and José F. Fontanari\textsuperscript{1}
\textsuperscript{1}Instituto de Física de São Carlos, Universidade de São Paulo, Caixa Postal 369, 13560-970 São Carlos, São Paulo, Brazil and
\textsuperscript{2}Yerevan Physics Institute, Alikhanian Brothers St. 2, Yerevan 375036, Armenia

(Dated: August 17, 2009)

We consider the optimal dynamics in the infinite population evolution models with general symmetric fitness landscape. The search of optimal evolution trajectories are complicated due to sharp transitions (like shock waves) in evolution dynamics with smooth fitness landscapes, which exist even in case of popular quadratic fitness. We found exact analytical solutions for discontinuous dynamics at the large genome length limit. We found the optimal mutation rates for the fixed fitness landscape. The single peak fitness landscape gives the fastest dynamics to send the vast majority of the population from the initial sequence to the neighborhood of the final sequence.

PACS numbers: 87.23.Kg, 64.60.De

I. INTRODUCTION

The search of optimization in evolutionary processes is a rather popular idea in evolution research \cite{1, 2, 3, 4, 5, 6, 7}. Here we should distinguish the optimization via mutation rate \cite{2} and via fitness landscapes \cite{3}. The first is rather relevant for the real biology. According to Darwinian view to evolution, the force driving evolution is the natural selection, not the creation of genetic variants, because the mutations are random. Nevertheless there have been experimental results which suggest that mutation rates can vary, e.g. increasing during certain stresses \cite{1}. This phenomenon has been called "adaptive mutation", which means that the mutation rate is under the selective pressure \cite{2}.

We will give the theory of optimal mutation rates in case of infinite populations. The realistic case, of cause, is connected with the finite population, and our results could be considered just as a first step in that direction.

From the early days of Darwin-Wallace evolution theory \cite{8} there has been a hope that there is some optimization of the fitness during the evolution process. Such picture really was confirmed in the case of proteins \cite{9, 10, 11}. In connection with \cite{3} has been considered a mathematical problem. What has been examined was a direct parallelism with the famous Brachistochrone problem suggested in 1696 by Johann Bernoulli. Given two mutants, A and B, separated by \textit{n} mutational steps, what is the evolutionary trajectory which allows a homogeneous infinite population of A to reach B in the shortest time? In \cite{3} has been considered an approximate solution of the mathematical problem in the case of finite population, considering an optimization via fitness landscape. To find an optimized evolution trajectory, one should have, first of all, exact solutions of evolution dynamics. Such solutions have been found only recently in the case of a single-peak fitness landscape for the Crow-Kimura \cite{3, 12, 13} in \cite{15} and for the Eigen model \cite{13, 14} in \cite{12}. In \cite{16} has been solved the evolution dynamics (the manner of change of the mean number of mutations in population) for the general symmetric fitness landscape case, derived using the Hamilton-Jacobi equation (HJE) method \cite{17, 18}. The optimization problem is highly complicated due to discontinuous effects in the dynamics of a mean number of mutations, as has been found in \cite{16} (see also \cite{19, 20}). The phenomenon exists even in smooth fitness landscape. In Fig. 2 there is an example of such discontinuity. The overlap \(x^*\) (mean number of mutations is defined as \(1 - 2x^*/N\), \(N\) being the genome length) is first a smooth function of time, then its value jumps from the low branch of the \(S\) like loop to the upper one, and again is a smooth function of time. As evolution equations are exactly mapped into HJE equations, one can introduce Hamiltonians and corresponding potentials. In \cite{16} has been suggested a receipt to identify a class of discontinuities: when the evolution potential has two local maximums. It has been observed also that the discontinuous dynamics could occur even for the case of a single maximum in evolution potential, when the fitness function is steep enough. The phenomenon is rather involved and in \cite{19} neither the "enough steepness" could be identified nor the position of sharp transitions for any case of discontinuities. We will give an analytical theory for some cases of discontinuous dynamics, and exact results for the optimization via mutation rate. We found discontinuities even in the quadratic fitness landscapes, missed in \cite{16}.

II. THE MUTATION OPTIMIZATION

A. Crow-Kimura model with asymmetric mutations

Consider the case of model with different forward and back mutation rates as in \cite{3}. For symmetric-fitness landscapes this model \cite{11} assumes that the relative probabilities \(p_l, l = 0, 1, ..., N\) (\(N\) being the genome length),
where we have the following expression for $F$:
\[
F(\gamma, x^*, \xi) = \left[ f(x^*) + \frac{1 + \xi}{2} + \gamma_b \frac{1 - \xi}{2} - f(\xi) \right]^2 - \gamma_f \gamma_b (1 - \xi^2)
\] (6)

For the small $x_0$ there is another expression:
\[
\begin{align*}
t^* &= \frac{1}{2} \int_{x_0}^{x_1} d\xi \left[ F(\gamma, x^*, \xi) \right]^{-1/2} \\
&+ \frac{1}{2} \int_{x^*}^{x_1} d\xi \left[ F(\gamma, x^*, \xi) \right]^{-1/2}
\end{align*}
\] (7)

and $x_1$ is the solution of
\[
F(\gamma, x^*, x_1) = 0.
\] (8)

In [16] has been considered the symmetric mutation scheme $\gamma_f = \gamma_b = \gamma$ with $F_s$ instead of $F$:
\[
F_s(\gamma, x^*, \xi) = [f(x^*) + \gamma - f(\xi)]^2 - \gamma^2 (1 - \xi^2)
\] (9)

For the quadratic fitness function
\[
f(x) = \frac{c}{2} x^2
\] (10)

Eqs. (5),(7) have real solutions provided that $x^* < 1 - \gamma/c$. This upper bound determines the asymptotic value of the overlap with the reference sequence. Of course, in the case $\gamma/c > 1$ the selective phase is lost and the dynamics drifts in the sequence space so that the asymptotic regime is characterized by a zero overlap with the reference sequence. To decide which equation to use we need to calculate $t_h$:
\[
t_h = \frac{1}{2} \int_{x_h}^{x_0} d\xi \left[ F_s(\gamma, x_h, \xi) \right]^{-1/2}
\] (11)

where $x_h$ is a root of $F_s(\gamma, x_h, x_0) = 0$. This equation has a solution provided that $f(x_h) \leq f(x_0)$, which in the case of monotonically increasing fitness implies $x_h \leq x_0$. Thus for a given $x_0$ and $t^*$ we calculate $x_h$ and then $t_h$. If $t^* < t_h$ we use Eq. (5), otherwise we use Eq. (8), to obtain $x^* = x^* (t^*)$.

### B. Discontinuous dynamics in case of quadratic fitness function

In [16] there have been derived analytical formulas Eqs.(5),(7) with $F = F_s$. The [16] failed to describe the discontinuities of $x^* (t)$ analytically. The mean fitness is defined as a minimum of $U(x)$. When this function has two maxima at $1 > x > 0$, there is a discontinuity in the dynamics, [16]. The point is that there can be singularities in the dynamics, even for the fitness function:

\[
\frac{du}{dt} = p_l [N f (m_l) - (\gamma_f - \gamma_b) l + \gamma_b N] + \gamma_b (N - l + 1) p_{l-1} + \gamma_f (l + 1) p_{l+1},
\] (1)
by Eq. (7) for the symmetric case $\gamma_f = \gamma_b = \gamma$ and (top to bottom at $c^* = 2$) $\gamma/c = 0.05, 0.1, \ldots , 0.7, 0.75$. The initial population has overlap $x_0 = 0.01$ with the reference sequence. For $t^* \rightarrow \infty$ we find $x^* = 1 - \gamma/c$.

with a single maximum at $x > 0$, when the fitness is too steep. We performed a numerics for symmetric mutations ($\gamma_f = \gamma_b = \gamma$) to clarify the character of discontinuous dynamics, see Fig.1-Fig.3. In the selective phase $c > \gamma$, the potential $U(x)$ has a single maximum at $1 > x > 0$. Nevertheless, sometimes the function $x^*(t^*)$ has jumps.

Figure 4 illustrates the time evolution of $x^*$ for $x_0 = 0.01$. For not too small $\gamma/c$ the $x^*(t^*)$ is a monotonic function, and the direct numerics of the system of equations for Crow-Kimura model supports well the theoretical formulas for $x^*(t^*)$.

For small values of $\gamma/c$ the S-shaped curves indicate the existence of a discontinuity in the position of the maximum of the overlap probability distribution. This threshold phenomenon was overlooked in a previous analysis of this problem which considered a single parameter setting, $c = 2$ and $\gamma = 1$ [16].

The unusual time dependence of $x^*$ exhibited in Fig. 1 is quite counter-intuitive since it implies that for, say, $\gamma/c = 0.05$ there is an entire range of overlap values which are never reached by the evolutionary dynamics. To check that finding and to gather information on the stability of the solutions in the multi-solution regime, we present in Fig. 2 the results of the numerical solution of the ODE system (1) for different values of sequence lengths. These results not only confirm the theoretical predictions but complement them by showing that the solution corresponding to the lower branch of the S-shape is the stable one. This information allows us to obtain the value $t^* = t^*_d$ at which the discontinuity takes place as well as the size of the discontinuity $\Delta x^*$. This can be done by locating the lower value of $x^*$ for which $dt^*/dx^* = 0$ in Eq. (7).

Our conclusion, deduced from the analysis of Fig. 2 that the jump in the dynamics occurs at the point where $dx^*/dt^* = 0$, is a rather general one. We checked that it is valid in other cases with discontinuous dynamics as well, see Fig. 4.

C. Optimal mutation rates in case of fixed overlap value in original population

Here we explore another important result exhibited in Fig. 1 namely, that there is an optimal value of the scaled mutation rate $\gamma/c$ that minimizes the evolutionary time to go from $x_0$ to $x^* > x_0$. To assess this point in more detail, we note first the obvious fact that this evolutionary trajectory is possible only for $\gamma/c < 1 - x^*$. With this fact in mind, we can see from Fig. 1 that to reach the end point, say, $x^* = 0.2$ it is a bad strategy to choose
either small or large values of $\gamma/c$. In fact, there is an optimal value of the mutation rate, which for the parameter setting of this example ($x_0 = 0.01$ and $x^* = 0.2$) is $\gamma_{opt}/c = 0.3632$. This interesting analytical finding substantiates the empirical strategy of fine tuning the mutation rate in Genetic Algorithms [23].

Figure 5 neatly illustrates the existence of an optimal mutation rate for the fixed initial condition $x_0 = 0.01$. To draw one of the curves in this figure we keep the end point $x^*$ fixed and measure the evolution time as a function of the scaled mutation rate. The existence of an optimal mutation rate that corresponds to the fastest evolutionary trajectory (i.e., minimum $t^*$) for the particular fitness choice, Eq. (10), is patent from this figure.

To find the exact location of the minima exhibited in Fig. 5 we put the condition $\frac{d^2t}{dx^2} = 0$, and get

$$-\frac{1}{4} \int_{x_0}^{x^*} \frac{d\xi}{F_s^{1/2}} \frac{dF_s(\gamma, x^*, \xi)}{d\gamma} - \frac{1}{4} \int_{x^*}^{\infty} \frac{d\xi}{F_s^{1/2}} \frac{dF_s(\gamma, x^*, \xi)}{d\gamma} = \frac{1}{\epsilon} \frac{dF_s(\gamma, x^*, \xi)}{d\gamma} = \frac{dF_s(\gamma, x^*, \xi)}{d\gamma}$$

where $F_s$ and $x_1$ are defined by Eqs. (9) and (8), respectively. As pointed out in Ref. [16], the initial overlap distribution has a peak at $x = 0$, which yields the maximum of the overlap distribution for $t < t_0$ where

$$c_t = \frac{\cos^{-1}(1 - \gamma/c^{1/2})}{\gamma/c^{(1 - \gamma/c)^{1/2}}}.$$ (15)

Note that $c_t \rightarrow 1$ for $\gamma/c \rightarrow 0$, and $c_t \approx \sqrt{2} (1 - \gamma/c)^{-1/2}$ for $\gamma/c \rightarrow 1$. We turn now to the case where the initial population is uniformly distributed among the $2^N$ configurations.

Figure 6 shows the time evolution of $x^*$ for the flat initial distribution. The results are in stark contrast with those of the peaked initial distribution (see Fig. 1): the odd S-shaped curves that produced the interesting dynamic behavior discussed before are absent in this case. In addition, the curves for different values of $\gamma/c$ never cross which indicates that the fastest trajectory to reach any point $x^*$ is given by a vanishingly small mutation rate.

Let us calculate the optimal period to have a peak of population with the overlap $x^*$ at the moment of time $t^*$. We should find the $x^*(t^*)$ looking the maximum of the

$$-\frac{1}{2} + \frac{\ln(1 + x^*)}{2} - \frac{1}{2} + \frac{\ln(1 - x^*)}{2} + t f(x^*)$$

$$-\frac{1}{2} + \frac{\ln(1 + x^*)}{2} - \frac{1}{2} + \frac{\ln(1 - x^*)}{2} + t f(x^*)$$

and

$$t^* = \frac{1}{2} \int_{x^*}^{x^*} d\xi \left[ F_s(\gamma, x^*, \xi) \right]^{-1/2}$$ (14)

III. FITNESS OPTIMIZATION

Although the selection of a fitness function that minimizes the evolution time between any two points $x_0$ and $x^*$, which correspond to the maximum of the overlap distribution in two distinct times, is not as biologically significant as the selection of the optimal mutation rate, it
has a considerable aesthetical appeal as the problem is somewhat akin to the Brachistochrone problem of physics. In [3] has been assumed that the fastest evolution dynamics between two sequences is given by a single peak fitness. The point is that one should accurately formulate the optimization task. The first possibility - we look the arrival of some fraction of population to the master peak. The second version: we look the arrival of a vast majority of population to the small (the Hamming distance is miserable compared with N) neighborhood of the master sequence. The situation is highly non-trivial. If we took the first version with some small fraction, then the linear fitness could give better results than the single-peak fitness, see Figure 7.

If we take the second version of optimization, then the single-peak fitness looks like as the fastest one. For the considered case (from sequence to sequence) we can just give the expression of the minimal time following to the considered case (from sequence to sequence) we can just add the optimization to the solution of [15]:

\[ t = \frac{\phi(x, t_1) - J t_1}{J - \gamma} \]

\[ \frac{1 + x}{2} \tanh(\gamma t_1) + \frac{1 - x}{2 \tanh(\gamma t_1)} - \frac{J}{\gamma} = 0 \]

\[ \phi(x, t) = \left[ \frac{1 + x}{2} \ln \cosh(\gamma t) + \frac{1 - x}{2} \ln \sinh(\gamma t) \right] \]

\[ \frac{\partial \phi}{\partial \gamma} = 0 \quad (17) \]

We have done some numerics, see Figure 7, supporting the choice of single-peak fitness as an optimal fitness for the fastest relaxation, and t by Eq. (17) as a minimal time period.

Consider now the fitness optimization problem in case of overlap distributions (to send the population from the original overlap with \( m = x_0 \) to the eventual one with \( m = x^* \)) and symmetric fitness landscape. We are looking the optimization problem for the special fitness with

\[ f(m) = 0, x < x^* \]

\[ f(x^*) = J \quad (18) \]

Eq. (8) gives \( x_1 = x^* \), then Eq. (7) is simplified: the first term disappears. For the fitness by Eq. (18) we have

\[ t^* = \frac{1}{2} \int_{x_0}^{x^*} \frac{d\xi}{\sqrt{(J + \gamma)^2 - \gamma^2(1 - \xi^2)}} \quad (19) \]

It is easy to check that the minimal time is given by the fitness of Eq. (18). As

\[ \sqrt{(J + \gamma)^2 - \gamma^2(1 - \xi^2)} > \sqrt{(J + \gamma - f(\xi))^2 - \gamma^2(1 - \xi^2)} \quad (20) \]

\[ f(x) = 2N x^a \quad \text{for} \quad a = 1, 2, 4 \quad \text{(show in the figure)} \]

\[ f(x) = 0 \quad \text{for} \quad x < 1 \quad \text{and} \quad f(1) = 2N. \]

\[ \text{FIG. 7: Location These are the results of the simulations for} \quad N = 20, \text{symmetric mutation rate} \quad \gamma = 1. \text{Fitness} \quad f(x) = 2N x^a \quad \text{for} \quad a = 1, 2, 4 \quad \text{(show in the figure)} \quad \text{SP} \quad f(x) = 0 \quad \text{for} \quad x < 1 \quad \text{and} \quad f(1) = 2N. \]

\[ \text{FIG. 8: Location} \quad x^* \text{of the maximum of the overlap distribution as function of time} \quad t^* \text{for directed mutation case with} \quad x_0 = 0, \text{left to right} \quad \gamma_f/c = 0.1, 0.05 \text{and} \quad 0.01. \text{The numerical solution of the system} \quad (1) \text{is given by the dashed vertical lines for} \quad \text{left to right} \quad N = 1000, 5000 \text{and} \quad 10000. \]

The time given by Eq.(19) is less than the time given by Eq.(7) for any \( f(m) > 0 \).

\[ \text{IV. DIRECTED MUTATION CASE} \]

Consider the case of asymmetric mutations [3]. We have original distribution at some \( x_0 \), and our goal is to send the population to the overlap \( x^* \). Now there is a single characteristic, therefore, contrary to the symmetric mutation case, all the properties are defined via the behavior of the fitness function in the considered interval \([x_0, x^*]\). Eqs.(4),(5) give the following equation

\[ t^* = \frac{1}{2} \int_{x_0}^{x^*} \frac{dx}{f(x^*) + \gamma \frac{dx}{dt^*} - f(x)} \quad (21) \]

We see that the optimization via mutation is trivial: raising the mutation rate we can send the population to the point \( x^* \) immediately. The optimization via fitness is also trivial: the fastest trajectory is via the fitness \( f(m) = 0, m < m^* \) and \( f(1) = J_0 \).

We have done a numerics for quadratic fitness case, see Figure 8. We see that the results again support the conjecture that the jumps are at the point with \( dx^*/dt^* = 0. \)
V. DISCUSSION

We considered the problem of optimization in evolution in case of infinite population, symmetric fitness landscape and large genome length and found exact solutions. We found that the optimization (optimal control, see [24]) is a highly non-trivial problem, as sharp, discontinuous transitions are typical for the evolution dynamics even with smooth fitness landscapes. We investigated these discontinuities and gave an analytical description of such sharp transitions for symmetric smooth landscape. We could succeed doing numerics for a larger values of N than those in [10]. We found dynamical discontinuities even in case of directed mutations. The sharp transitions in evolution are important regarding the punctual evolution phenomenon (see [25] and the review [26]).

The optimization via mutation rate is most intriguing from the point of view of adaptive mutations. We calculated the minimal time to send the population from original sequence with small overlap (with the master sequence) and low fitness to the some final one (with a higher fitness). The solution of the optimization problem is nontrivial, and there is some optimal mutation rate. It is interesting that the optimal rate of mutation to send the population from the overlap $x_0$ to $x^*$ is defined with the behavior of the fitness outside the interval $[x_0, x^*]$. The numerics confirm our analytical results. On the contrary, when we need to send the population from the high fitness configurations with the fixed original overlap to the final one with lower overlap, the mutation’s optimization is a trivial task: just increase the mutation rate. Similar is the situation in case of directed mutation: one can send the population in a fastest way just increasing the mutation rate.

If we consider the evolution from originally flat distribution (all sequences have the same probability), then the optimal mutation rate is zero.

The optimization via fitness landscape (to send the population from the original sequence to the final sequence) should be carefully defined as a mathematical problem. When we are interested to send some small fraction of the population to the master sequence, the linear fitness can give better results than the single-peak one. When we are looking how to send the vast majority of population to the some infinitesimal neighborhood of the master sequence, then the optimum is given by a single-peak fitness landscape. Such hypothesis has been assumed first in [23]. We could not prove it rigorously, but we gave just an exact expression for this optimal time period, as well as performed numerics illustrating the optimization. If we are looking how to send the population with the initial overlap $x_0$ to the final overlap $x^*$, then, as we proved rigorously, the minimal time is given by the single-peak like fitness Eq. (18).

We looked only at the infinite population problem. Our consideration could be a first step in consideration to the real biological situation.

The work at Yerevan was supported in part by the VolkswagenStiftung grant “Quantum Thermodynamics”. The research at São Carlos was supported in part by CNPq and FAPESP, Project No. 04/06156-3. D.B.S. thanks to the hospitality of the Instituto de Física de São Carlos, Universidade de São Paulo, and the FAPESP travel grant No. 08/10420-9 for the support to his visit to São Carlos.

[1] P. L. Foster Annu Rev Genet 33:57(1999).
[2] P. L. Foster BioEssays 22:1067(2000).
[3] A. Traulsen, Y. Iwasa Y., M.A. Nowak, J. Theor. Biol. 249:617(2007).
[4] D. T. Kysela, P. E. Turner J. Theor. Biology 249:411(2007).
[5] S. Lenhart, J. T. Workman Optimal Control Applied to Biological Models CRC Mathematical and Computational Biology, Chapman and Hall (2007).
[6] P. Schuster Nonlinear Dynamics from Physics to Biology Complexity 12:9(2007).
[7] R. Chakrabarti, H. Rabitz, G. L. McLendon, Arxiv. quant. bio, 0806:233
[8] A. R. Wallace (1858) Proc. Linn. Soc. London 3, 53.
[9] J. F. Crow, M. Kimura (1970) An Introduction to Population Genetics Theory (Harper Row, NY).
[10] E. Baake, M. Baake, H. Wagner, Phys. Rev. Lett. 78:559(1997).
[11] E. Baake, H. Wagner, Genet. Res. 78:93(2001).
[12] D. B. Saakian, C. K. Hu Phys. Rev. E 69:046121(2004).
[13] M. Eigen M 58:465(1971).
[14] M. Eigen M, J. J. McCaskill, P. Schuster Adv. Chem. Phys. 75:149(1989).
[15] D. B. Saakian, C. K. Hu Phys. Rev. E 69:021913(2004).
[16] D. B. Saakian, O. Rozanova, A. Akmetzhanov Phys. Rev. E 78:041908(2008).
[17] D. B. Saakian Journal of Stat. Physics, 128:781(2007).
[18] K. Sato, K. Kaneko Phys. Rev. E 75:061909(2007).
[19] J. Hermisson, H. Wagner, and M. Baake J. Stat Phys 102:315(2001).
[20] F. G. Carvalhaes, C. Goldman Physica A 379:111(2007).
[21] A. Melikyan Generalized Characteristics of First Order PDEs, Birkhäuser, Boston(1998).
[22] L. C. Evans Partial Differential Equations, AMS(2002).
[23] M. Mitchell An Introduction to Genetic Algorithms (MIT Press, Cambridge, MA(1996))
[24] W. H. Fleming, R. W. Rishel Deterministic and Stochastic Optimal Control, Springer-Verlag (1975).
[25] S. J. Gould, N. Eldredge, Punctuated equilibrium comes of age, Nature, 366:223(1993).
[26] B. Drossel, Biological evolution and statistical physics. Advances in Physics 50:209(2001).