A solvable model of the evolutionary loop

L. Peliti(*)

Laboratoire de Physico-Chimie Théorique, CNRS URA 1382, ESPCI
10, rue Vauquelin, F-75231 Paris Cedex 05, France
Dipartimento di Fisica and Unità INFM, Università “Federico II”
Mostra d’Oltremare, Pad. 19, I-80125 Napoli, Italy(**)

(received 22 June 1998; accepted in final form 5 October 1998)

PACS. 02.50Ey – Stochastic processes.
PACS. 05.40+j – Fluctuation phenomena, random processes, and Brownian motion.
PACS. 87.10+e – General, theoretical and mathematical biophysics (including logic of biosystems, quantum biology, and relevant aspects of thermodynamics, information theory, cybernetics, and bionics).

Abstract. – A model for the evolution of a finite population in a rugged fitness landscape is introduced and solved. The population is trapped in an evolutionary loop, alternating periods of stasis to periods in which it performs adaptive walks. The dependence of the average rarity of the population (a quantity related to the fitness of the most adapted individual) and of the duration of stases on population size and mutation rate is calculated.

The simplest conceivable evolutionary situation is a population of asexually reproducing individuals set in a fixed environment. The reproductive power of an individual is measured by its fitness, i.e. by a quantity proportional to the expected number of its offspring [1,2]. In model building, one often assumes that the fitness is determined by the genotype, and that the genotype itself is transmitted identically from parent to offspring, apart from mutations.

The role of mutations is favorable if the overall fitness of the members of the population is low, because they allow the population to find genotypes with higher fitness, i.e. to adapt. This can be represented, following S. Wright [3], by saying that the population approaches a fitness peak. On the other hand, mutations become pernicious when the population is located on such a peak, since they may let the population lose contact with it. In fact, the two effects have different relevance depending on population size: if the population size is large, and the fitness small, adaptation dominates; but if the population is small, and the fitness peak, no matter how lofty, is narrow, mutations have a negative effect.

This situation has been described by two classes of models:

1. In the quasispecies model [4] one takes the infinite population size limit from the outset, obtaining an equation (akin to a Master Equation) for the genotype distribution in the
population. It is interesting that, if the fitness peaks are narrow enough, this equation exhibits a transition (the \textit{error threshold}) between an adaptive regime, and a regime in which adaptation is irrelevant. Nevertheless, the description of the non-adaptive regime is not satisfactory within this class of models.

2. The adaptation process has been described as a special kind of random walk, the \textit{adaptive walk}, by Kauffman and Levine [5] and others. In this model, the fitness can only increase, and mutations only have positive effects. An “annealed” version of this model has been exactly solved by Flyvbjerg and Lautrup [6].

The \textit{stochastic escape} of a finite population from a narrow fitness peak has been discussed by Higgs and Woodcock [7]. They find that, in the same limit in which the error threshold appears in its fullest glory in the quasispecies model, a finite population eventually loses contact with the adaptation peak. Building on this observation and on numerical simulations, Woodcock and Higgs [8] have described the behavior of a population evolving in a rugged fitness landscape (i.e., in a situation where even slight changes of the genotype lead to arbitrarily large changes in the fitness). This behavior can be characterized as an \textit{evolutionary loop} [9]:

1. If the fitness of the population is low, favorable mutations get fixed in the population, which thus performs an adaptive walk, reaching a local fitness peak.

2. The population can be evicted from the adaptation peak by stochastic escape, and start a new adaptive walk from a random, usually low, fitness value.

In this letter, I introduce a solvable model that exhibits such a behavior. The model is a slight generalization of the Annealed Adaptive Walk Model introduced and solved by Flyvbjerg and Lautrup [6], and allows for stochastic escape. It depends on only two parameters, namely population size and mutation rate. I argue that it should describe any mutation-selection model in the strong selection limit, i.e., when the fitness distribution is broad, provided that the correct variables are identified and the correct scaling of the parameters is performed. This conclusion is borne out by simulations of a slightly more realistic model which I report at the end of the letter.

I consider a population of $M$ individuals ($M$ is fixed) evolving in a rugged fitness landscape. At each generation, for each member $\alpha$ of the new population, its parent $\alpha'$ is chosen among the old population. The probability $W_\gamma$ that the individual $\gamma$ is chosen to reproduce is given by

$$W_\gamma = \frac{F_\gamma}{\sum_{\beta} F_\beta},$$

where $F_\gamma$ is the fitness of the individual $\gamma$. The genotype of $\alpha$ is taken to be equal to that of its parent $\alpha'$ apart from mutations. I denote by $u$ the probability that the offspring undergoes at least one mutation.

I make the following simplifications:

\textit{Rugged fitness landscape:} The fitnesses $F$ of different genotypes are independent random variables, identically distributed according to some distribution $\rho(F)$.

\textit{Infinite genome limit:} On each mutation, a wholly new genotype appears in the population.

\textit{Strong selection limit:} At each generation, only the fittest individuals are allowed to reproduce.
Given a fitness distribution $\rho(F)$, one can define the \textit{rarity} $h$ of a fitness value $F$ as the probability that, picking a new fitness at random with the distribution $\rho(F)$, one obtains a higher fitness value [8]:

$$h(F) = \int_F^\infty \rho(F')\,dF'.$$

(2)

Note that higher fitness corresponds to smaller rarity. Within our hypotheses, it is easy to see that the genetic properties of the whole population are summarized by the rarity of its fittest individual, which we shall simply call the rarity of the population. Consider the population at generation $t$, and let $h(t)$ be its rarity. For each individual of the new generation, decide (with probability $u$) if it mutates. If it does, assign to it a rarity $h_\alpha$ with uniform probability between 0 and 1. Otherwise, assign to it a rarity $h_\alpha$ equal to $h$. The rarity of the population is then $h(t+1) = \min_\alpha h_\alpha$. Therefore, the evolution of an ensemble of populations is described by the probability distribution function $P(h,t)$ of their rarity.

In the following I derive the evolution equation for $P(h,t)$ and solve for its asymptotic form in the limit of large, but finite populations.

Let us denote by $\pi^M_\nu$ the probability that, at any one generation, exactly $\nu$ individuals mutate:

$$\pi^M_\nu = \binom{M}{\nu} u^\nu (1-u)^{M-\nu},$$

(3)

and by $\phi_\nu(h)$ the probability that, picking up $\nu$ genotypes at random, one obtains rarities all larger than $h$:

$$\phi_\nu(h) = (1-h)^\nu.$$

(4)

It is useful to introduce the notation

$$\psi_\nu(h) = -\frac{d\phi_\nu}{dh} = \nu h (1-h)^{\nu-1} \geq 0.$$

(5)

It is then easy to see that $P(h,t)$ satisfies the following equation:

$$P(h,t+1) = \pi^M_0 P(h,t) + \pi^M_M \psi_M(h) +$$

$$+ \sum_{\nu=1}^{M-1} \pi^M_\nu \left[ \phi_\nu(h) P(h,t) + \psi_\nu(h) \int_h^1 \frac{dh'}{h'} P(h',t) \right].$$

(6)

The first term represents the case in which there are no mutations, and the second one the case in which all individuals mutate, and the rarity of the new population is equal to $h$. The sum represents the case in which some individuals mutate, and some do not: the first term in square brackets describes the case where the rarity of all mutated individuals exceeds $h$, and the second one the case in which the rarity of at least one mutated individual is equal to $h$ and smaller than the preceding rarity of the population. Introducing the notations

$$\Phi(h,t) = \int_h^1 \frac{dh'}{h'} P(h',t),$$

(7)

$$f(h) = \sum_{\nu=0}^{M-1} \pi^M_\nu \phi_\nu(h) = (1-u)M - u^M (1-h)^M,$$

(8)

$$g(h) = \pi^M_M \psi_M(h) = u^M M(1-h)^{M-1},$$

(9)
eq. (6) can be written
\[ \frac{\partial \Phi(h, t + 1)}{\partial h} = f(h) \frac{\partial \Phi(h, t)}{\partial h} + \frac{df(h)}{dh} \Phi(h, t) - g(h) = \frac{\partial}{\partial h} [f(h)\Phi(h, t)] - g(h). \] (10)

The solution of this equation is
\[ \Phi(h, t) = (f(h))^t \Phi(h, 0) + \frac{1 - (f(h))^t}{1 - f(h)} \int_h^1 dh' g(h'). \] (11)

Let us consider large values of \( M \) and set
\[ h = \frac{k}{M}, \quad 1 - u = \frac{w}{M}. \] (12)

In this limit, one has
\[ f(h) \simeq e^{-k} - e^{-(k+w)}, \] (13)
\[ \int_h^1 dh' g(h') \simeq e^{-(k+w)}. \] (14)

We obtain therefore
\[ \Psi(k, t) \equiv \lim_{M \to \infty} \Phi(k/M, t) = e^{-kt}(1 - e^{-w})^t \Psi(k, 0) + \frac{1 - e^{-kt}(1 - e^{-w})^t}{1 - e^{-k} + e^{-(k+w)}} e^{-(k+w)}. \] (15)

Therefore, the \( t \to \infty \) limit of \( \Psi(k, t) \), denoted by \( \Psi_\infty(k) \), is given by
\[ \Psi_\infty(k) = \frac{1}{e^w(e^k - 1) + 1}. \] (16)

One has
\[ \Psi_\infty(0) = 1, \quad \Psi_\infty(k) \sim e^{-k}, \text{ for } k \to \infty. \] (17)

It can be checked that the average value of \( k \) is given by
\[ \langle k \rangle = -\int_0^\infty dk' \Psi_\infty(k')k' = \frac{w}{e^w - 1}. \] (18)
and varies from $\langle k \rangle = 1$ to $\langle k \rangle = 0$ as $w$ varies between 0 and infinity.

Let us define stasis the regime in which the rarity $h$ of the population remains constant or decreases, and stochastic escape the event by which it increases, since a harmful mutation gets fixed in the population. We can then compute the distribution of stasis duration as follows. Denote by $K(k, t)$ the conditional probability that, if the minimal rarity was equal to $k/M$ at generation $t = 0$, it has never decreased up to generation $t$. This function obeys the following equation:

$$K(k, t + 1) = \left[1 - \pi^M_M + \pi^M_M \phi_M(k/M)\right] K(k, t) \simeq \left[1 - e^{-(k+w)}\right] K(k, t),$$

from which we deduce

$$K(k, t) = \left[1 - e^{-(k+w)}\right]^t.$$

The average duration of a stasis is therefore

$$\langle t \rangle = e^{k+w} - 1.$$  

If we take as a “typical” value of $k$ that for which $\Psi_\infty(k) = \frac{1}{2}$, we obtain $\langle t \rangle = e^w$.

I now consider a population in which the probability $W_\alpha$ that an individual $\alpha$ reproduces is given by eq. (1). For the strong selection limit to hold, the probability that individuals with less than the maximum fitness reproduce should be negligible. This implies in turn that the fitness distribution function $\rho(F)$ should be very broad. I have therefore assumed that the fitnesses are extracted from a Lévy distribution $\rho(F) = sF^{-s-1}$ for $1 \leq F < \infty$, which, for $0 < s < 1$, has an infinite second moment. The curves of $\langle k \rangle$ vs. $w$ should be independent of $s$. The results of the simulation for this model are shown in fig. 1. One notices that the points tend to lie above the theoretical curve for larger values of $w$. In fact, the deviations from the strong selection limit become significant in this regime.

Indeed, the probability that the ratio of the largest to the second largest fitness value, extracted from a Lévy distribution of parameter $s$, exceeds $\lambda$, is given by $\lambda^{-s}$, independently of the number of extracted values. The strong selection limit holds, therefore, only if among the individuals that reproduce without mutations (on average $w = (1 - u)M$ at each generation), the chance that the second fittest one reproduces is negligible. This happens if the probability that this ratio is smaller than $w$ is itself small, say of order $\epsilon$. This implies in turn $w^{-s} > 1 - \epsilon$, or, for small values of $s$, $w < e^{1/s}$. It may easily be checked that this is indeed the case.

I am afraid that it would be difficult to observe stochastic escape in all but the smallest populations, although the analogous effect in smooth fitness landscapes (namely Muller’s ratchet [10]) has been observed during repeated genetic bottleneck transfers of monoclonal antibody-resistant mutants of vesicular stomatitis virus, or of mutants of an RNA bacteriophage [11, 12]. I hope nevertheless that this approach provides at least a better grasp of the evolutionary behavior of a finite population in a rugged fitness landscape, and may be used as a starting point for the study of more realistic situations.

***

I thank M. MÉZARD and J.-B. FOURNIER for useful suggestions. I also thank A. AJDARI and G. PARISI for their interest in this work. I acknowledge the support of a Chaire Joliot de l’ESPCI.
REFERENCES

[1] The concept of fitness is nicely discussed in Maynard Smith J., Evolutionary Genetics (Oxford University Press, Oxford) 1989.
[2] An introduction to the statistical point of view in evolutionary theory and a recent bibliography can be found in Peliti L., cond-mat/9712027.
[3] Wright S., Genetics, 16 (1931) 97.
[4] A comprehensive review of quasispecies models is contained in Eigen M., Mc Caskill J. and Schuster P., Adv. Chem. Phys., 75 (1989) 149.
[5] Kauffman S. A. and Levine S., J. Theor. Biol., 128 (1987) 11.
[6] Flyvbjerg H. and Lautrup B., Phys. Rev. A, 46 (1992) 6714.
[7] Higgs P. G. and Woodcock G., J. Math. Biol., 33 (1995) 677.
[8] Woodcock G. and Higgs P. G., J. Theor. Biol., 179 (1996) 61.
[9] Woodcock G. and Higgs P. G., unpublished.
[10] Muller H. J., Mutat. Res., 1 (1964) 2.
[11] Chao L., in The Evolutionary Biology of Viruses edited by S. S. Morse (Raven, New York) 1994, p. 233.
[12] Duarte E. A., Clarke D., Moya A., Domingo E. and Holland J., Proc. Natl. Acad. Sci. USA, 89 (1992) 6015; Duarte E. A., Clarke D., Elena S. F., Moya A., Domingo E. and Holland J., J. Virol., 67 (1993) 3620.