

Bacterial evolution and the Bak-Sneppen model

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Abstract

Recently, Lenski et al [1, 2, 3] have carried out several experiments on bacterial evolution. Their findings support the theory of punctuated equilibrium in biological evolution. They have further quantified the relative contributions of adaptation, chance and history to bacterial evolution. In this paper, we show that a modified M -trait Bak-Sneppen model can explain many of the experimental results in a qualitative manner.

Keywords : Bacterial evolution, punctuated equilibrium, Bak-Sneppen model, mutations

Recently, a set of experiments has been carried out on bacterial evolution which are part of a new sub-discipline in the area of evolutionary biology, namely, experimental evolution [1, 2, 3, 4]. This implies the study, in the laboratory, of the fundamental processes of evolutionary change, namely, spontaneous mutation and adaptation by natural selection. Experiments on evolutionary dynamics require passage through thousands of generations which is an impossibility for most living species. Microorganisms like bacteria, yeast or viruses, however, have very short generation times (bacteria like *E.coli* have about seven generations everyday in sugar solution). The short generation times make it possible to observe population dynamics over thousands of generations and thereby address a wide range of evolutionary questions. Darwin laid the foundation of evolutionary biology by setting forth the principle of adaptation by species through natural selection [5]. It is now known that spontaneous mutation plays an important role in generating differences among individual organisms. A mutation involves a change

in the base sequence of a DNA and can occur with a certain probability during cell division. Mutations are random events and may be harmful, neutral or beneficial as regards their effect on an organism. According to the modern version of Darwin's theory, random mutations give rise to heritable differences among organisms whereas natural selection tends to increase the number of fitter variants. The processes of reproduction, mutation and natural selection are responsible for evolution of species or that of a single population.

The experiments on the evolutionary dynamics of the bacterial population *E.coli* have been carried out by Lenski and co-workers [1, 2, 3]. As pointed out by them [6], a large population size of *E.coli* ensures that a large number of mutations occur in every generation so that the origin and the fate of genetic variation can be well studied. It is possible to store bacteria in suspended animation at low temperatures. One can then measure the relative fitness (RF) of descendant and ancestral populations by placing them in direct competition. The RF is expressed as the ratio of the realized growth rates of the two populations. One can also measure a morphological quantity like the average cell size which is preserved in fossil records. Finally, the populations are easy to handle and propagate so that intensive replication of experiments is possible allowing subtle effects to be measured. Bak and Sneppen (BS)[7, 8] have proposed a model of evolution at the level of the global ecosystem of interacting species (macroevolution). The model self-organises into a critical steady state characterised by power-laws of various types. The major focus of the BS model is on self-organised-criticality (SOC) and its various aspects. In this paper, we apply the BS model to evolution at the level of a single population of reproducing bacteria (microevolution) and show that the evolutionary dynamics of the BS model can describe many of the experimental results of Lenski et al in a qualitative manner.

In the first experiment [1, 2], Lenski and co-workers studied an evolving bacterial population for approximately 10,000 generations. The bacterial population was allowed to expand to 5×10^8 cells in low sugar solution. At the end of the growth period (one day), 1/100 th of the population was siphoned into a fresh flask of food to allow the population to evolve. Since there was a 100-fold expansion of the bacterial population in a day, $6.6 (= \log_2 100)$ generations of binary fission occurred during this time. Every fifteen days, a sample of the population was frozen for later analysis giving rise to a 'frozen fossil record'. Since the population originated from a single cell, mutations,

about 10^6 everyday, provided the sole source of genetic variation. Four years later, Lenski et al had data for the evolving bacterial population over 10,000 generations. They measured two quantities, the average cell size and the RF. They found that the average cell size and the RF grow in a punctuated manner, i.e., in steps, as a function of time (number of generations) when the data are plotted every 100 generations (inset of Fig.1). At a larger interval of 500 generations, the changes appear to be gradual (inset of Fig.2). A major debate in evolutionary biology revolves around the question of whether evolution is best described as a gradual change or occurs in bursts. In the latter case, short periods of evolutionary activity are punctuated by long periods of stasis. This is the theory of punctuated equilibrium (PE). Lenski et al's data seem to support this theory though their interpretation is open to controversy [9]. The experiment, however, clearly demonstrates that both the average cell size and the RF of the evolving population grow over a certain time interval. In the first 2000 generations or so, there is a rapid growth followed by a period of slower growth till the growth is imperceptible. The bacteria, being in low sugar solution, have to compete for the food. Natural selection favours the mutations that confer some competitive advantage in exploiting the experimental environment. This leads to adaptation of the bacterial population to the environment through the emergence of larger and fitter variants.

In the second experiment [2], twelve populations of E.coli were evolved over 10,000 generations in identical environments. Each population was founded by a single cell from an asexual clone to eliminate genetic variation within and between populations. It was found that the replicate populations, after 10,000 generations, differ considerably from one another in both the average cell size and the RF (inset of Fig.3), even though the populations evolved in identical environments. In the third experiment [3], the relative contributions of adaptation, chance (mutations) and history to evolution were investigated. Twelve replicate populations were founded from a single clone of E.coli and serially propagated for 2000 generations in glucose-limited medium. The 12 populations had similar fitness values when evolving in glucose medium but when put into a maltose-limited medium showed large differences in fitness values. Some populations thrived while some others were found to languish. Ancestral fitness values of the populations in maltose were thus very heterogeneous (inset of Fig.4). One genotype from each of the 12 replicate populations was cloned and from this 3 new replicate populations

were founded. The 36 populations were then evolved under ancestral conditions in the maltose medium. The inset in Fig.4 shows the derived fitness in maltose versus the ancestral fitness in maltose for 36 populations.

Boettcher and Paczuski [10] have generalised the BS model to the M -trait BS model in which each species is characterised by M traits rather than one as in the original BS model. The rules of evolutionary dynamics are, however, the same. We now show that the M -trait ($M = 2$) BS model with a minor variation in the rules, can reproduce some of the experimental observations of Lenski et al. The model is applied to a single, evolving population of *E.coli*, rather than to many species. The BS model gives a coarse-grained representation of real evolution but contains the essential elements to capture the course of evolution. In our modified $M = 2$ BS model, the bacterial population is divided into N categories. Each category contains bacteria of similar characteristics. The N categories correspond to the N sites of a one-dimensional (1D) lattice with periodic boundary conditions. In the original BS model, each site represents a species. Two traits, namely, cell size and fitness are associated with the population at each site $i, i = 1, 2, \dots, N$. One assigns a number (between 0 and 1) to each of the traits at all the N sites. At each time step, the two sites with the minimum values for each of the two traits are identified. Mutations occur to bring about changes in the traits. The minimum random numbers are replaced by new random numbers. This takes into account the fact that the weakest species are the most liable to mutate. In the original $M = 2$ BS model, the minimum value, amongst all the $2N$ values of the two traits, is replaced by a new random number. The random numbers associated with any one of the traits of the neighbouring sites are also replaced by new random numbers. This is to take into account the linkage of neighbouring populations in food chain. The bacteria, evolving in low sugar solution, have to compete for food and one assumes that the neighbouring sub-populations affect each other the most in the evolution of traits. The last two steps are repeated and averages are taken for both the traits locally (over 40 sites) and globally (over 2000 sites). The minor change in the evolutionary rules from those of the $M = 2$ BS model gives a better agreement with the experimental results. In fact, other minor variations of the rules (like changing the random number interval from (0-1) to a smaller range of values) may provide an improved agreement. The essential ingredients of the BS model are, however, retained. Unlike in the original BS model, we calculate quantities from the very beginning

and not after the SOC state is reached. The SOC state corresponds to the region in which evolutionary growth is imperceptible and fluctuates around an average value. Our major focus is on the evolutionary dynamics leading to the critical state as this dynamics has been probed experimentally. Fig.1 shows the variation of the RF versus time. The inset shows the experimental data [1, 2]. The averages are taken over 40 sites and every 100 time steps. The local averaging gives rise to an improved quality of data points. Fig. 2 shows the corresponding variation with averages taken every 500 time steps and over the whole lattice. For a very large lattice one needs to take only global averages. The RF is defined to be the ratio of the current fitness and the initial fitness at time $t = 0$. In the actual experiment, fitness is related to the growth rate of the bacterial population via replication. The RF increases rapidly during the first 2000 generations. After that the growth becomes slower till it becomes imperceptible. The rapid growths can be fit by an hyperbolic model

$$y = x_0 + \frac{ax}{b+x} \quad (1)$$

for both the experimental and simulation data. During the periods of punctuation the beneficial mutations have no significant effect. When such mutations occur in quick succession, rapid evolutionary growth is observed. Recent research findings [11] have highlighted the importance of large beneficial mutations in the initial stages of evolutionary growth. Organisms must adapt to the new conditions fairly quickly in order to survive. Later, mutations with smaller effect fine-tune the adaptation. Fig.2 shows this clearly with a rapid evolutionary growth in the first 2000 generations brought about by beneficial mutations of large effect. The growths are imperceptible when the bacterial population gets adapted to its environment. The average cell size as a function of time has similar variations as in the case of the RF (Figs. 1 and 2).

Fig.3 shows a comparison of the simulation data for the RF with the data (inset) of the second experiment of Lenski et al [2]. The plots show that the independent populations diverge significantly from one another. In the simulation, the initial random number seed was chosen to be different for the six populations. The average fitness at time $t = 0$ does not vary noticeably from one population to another. Fig.4 shows the simulation results for the third experiment [3] with 2×4 populations rather than the 3×12

populations in the actual experiment. In the experiment, the populations growing in glucose-limited medium were transferred after 2000 generations to maltose-limited medium. In the latter medium, the average fitness values of the populations showed large differences. Thus, in the simulation for the maltose medium, one starts with widely different average fitness values for the populations. The populations are evolved for 1000 time steps. One finds, in agreement with the experimental results, that after 1000 generations, the average fitness values have similar magnitudes. This shows that adaptation and chance (effect of mutation) have eliminated the initial heterogeneity in average fitness values to a great extent. The effect of history (initial heterogeneity) is reduced after several generations of evolution. The effect of adaptation is pronounced (shown by the evolution of the data points above the isocline). The effect of chance is seen in the small dispersion in the average fitness values of the two populations corresponding to each genotype.

Lenski et al [12, 13, 14, 15] have developed theories based on standard population-genetics approaches to explain some of their experimental results. Such theories provide a microscopic picture of evolution but require detailed information about various parameters. These include the Malthusian parameter m_i of a strain ($m_i = \ln[N_i(1)/N_i(0)]$ per day, where $N_i(0)$ and $N_i(1)$ are the densities of the population at the beginning and the end of the day), the fitness w_{ij} of one strain relative to another ($w_{ij} = m_i/m_j$), the selection coefficient S_{ij} ($S_{ij} = w_{ij} - 1$) and the selection rate constant r_{ij} ($= m_i - m_j = m_j S_{ij}$). When a mutation occurs for the first time, the frequency of the mutant genotype, $P(0)$, is equal to $1/N$, where N is the population size. If the new mutation is not lost by drift, the rate of change in the frequency of the allele (genetic variant) is governed by the equation [12]

$$\frac{dP}{dt} = r_{ij}P(1 - P) \quad (2)$$

where r_{ij} , the selection-rate constant, is the difference in the Malthusian parameters of the favourable mutant and its progenitor. Mean fitness in the population, $W_{av}(t)$, depends on the frequency of the favoured mutant according to

$$W_{av} = 1 + S_{ij}P(t) \cong 1 + r_{ij}P(t)/m_{av} \quad (3)$$

where m_{av} is the average Malthusian parameter. Solving Eqs. (2) and (3)

for appropriate values of the parameters, Lenski et al could reproduce the step-like trajectory for relative fitness versus time, observed in experiments (inset of Fig. 1). The beneficial mutation takes many generations to reach a frequency which has appreciable effect on relative fitness and hence the plateau in the trajectory. Population genetics approaches certainly give a more detailed and accurate picture of biological evolution. Such approaches, however, require detailed assumptions and considerable computational effort. The $M = 2$ BS model, on the other hand, is an oversimplified model which incorporates the essential features of real evolution in the form of a set of rules. In this paper, we have shown that the minimal model gives a satisfactory description of the experimental data on bacterial evolution. Both simulation and experiments show evidence of PE on a short time scale (data points taken every 100 generations). Over a longer time scale, both show a hyperbolic growth in relative fitness. This is also true for the average cell size. Recent exhaustive studies of fossil beds lend support to the theory of PE [16]. The simulation further shows that chance (mutations) gives rise to parallel evolution of replicate populations. The relative contributions of adaptation, chance and history to average fitness before and after 1000 generations in maltose are correctly highlighted in the simulation data. Thus a BS-type model can explain the major experimental observations on bacterial evolution in a qualitative manner.

The BS model is well-known for its characterization of the self-organised critical state in the ecosystem of interacting species. Such self-organization can also occur in an evolving population. In the case of E.coli, the critical state is obtained when evolutionary growth becomes imperceptible and fluctuates around a steady value. With appropriate designing of experiments, the phenomenon of SOC in an evolving bacterial population can be studied experimentally. Experiments have recently been performed on the growth of RNA virus fitness [17]. The adaptive evolutionary capacity in this case is overwhelming. The gain in fitness is nearly 5000 after 50 passages. In that time, the gain in E.coli fitness changes can be explained by an hyperbolic model whereas RNA virus evolution follows exponential kinetics. Again, a simple model has been proposed to explain the experimental observations. The several experiments on the evolutionary dynamics of microorganisms open up the possibility of a rich interplay between theory and experiments. Simple models like the BS model capture the significant features of evolutionary dynamics of single populations. It is, however, desirable to explore the

connection between such models and the more comprehensive population-genetics approaches.

Acknowledgement

We are grateful to R.E.Lenski for sending us his publications on bacterial evolution. We also acknowledge the help from the Distributed Informatics Centre, Bose Institute, in preparing the manuscript.

Figure Captions

Fig.1 Relative fitness versus time in experiment [2] and simulation. A local average is taken over 40 sites in simulation. The experimental data points are taken every 100 generations.

Fig.2 Relative fitness versus time in simulation and experiment (inset) [2]. The data points are taken every 500 generations and the average is over the 2000 sites of the lattice.

Fig.3 Trajectories for relative fitness in six replicate populations of bacteria during 10,000 generations (simulation) and the same for twelve replicate populations (experiment). The data points are taken at an interval of 500 generations.

Fig.4 Evolution of fitness during 1000 generations in maltose. Derived versus ancestral values for relative fitness in 8 populations (simulation) and the same for 36 populations (experiment). The different symbols indicate the different progenitor genotypes.

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