Relationship between Measures of Fitness and Time Scale in Evolution

E. M. Rauch,[1,2] H. Sayama,[1] and Y. Bar-Yam[1,3]

[1]*New England Complex Systems Institute, 24 Mt. Auburn Street, Cambridge, Massachusetts 02138*
[2]*MIT Artificial Intelligence Laboratory, 200 Technology Square, Cambridge, Massachusetts 02139*
[3]*Harvard University, Department of Molecular and Cellular Biology, Bio Labs, 16 Divinity Avenue, Cambridge, Massachusetts 02138*

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The notion of fitness is central in evolutionary biology. We use a simple spatially extended predator-prey or host-pathogen model to show a generic case where the average number of offspring of an individual as a measure of fitness fails to characterize the evolutionary dynamics. Mutants with high initial reproduction ratios have lineages that eventually go extinct due to local overexploitation. We propose general quantitative measures of fitness that reflect the importance of time scale in evolutionary processes.

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The work of Fisher, Haldane, and Wright [1] established the generation-to-generation change in frequency of genotypes as a measure of fitness characterizing the role of natural selection in evolution. The centrality of this characterization [2] has not been diminished by recognized observational difficulties due to sampling error, the intricacies of the genotype-phenotype relationship, and the possibility of environmental changes. The measure most often used to quantify fitness of a type is the net reproduction ratio R, the expected number of surviving offspring per organism over its lifetime (in an environment with other individuals and species present), or its differential analog, the "Malthusian parameter" r. The concept of invasibility is another approach to the question of what types will come to dominate a population. One considers a population dominated by a type p and asks whether a mutant type p' can invade. An evolutionarily stable strategy [3] is one for which no mutant can invade. Under the assumptions normally used, the evolutionarily stable strategy is the one that maximizes R [4]. The assumption that populations that have reached a stationary state will be composed mainly of types with the highest number of offspring applies only to systems where the instantaneous change in frequency is sufficient to determine the long-term composition of the population. Conditions such as frequency-[5] and density-dependent [6] selection provide contexts in which this measure does not predict the fate of a type before equilibrium has been reached. In this paper, we use a simple spatially extended predator-prey or host-pathogen model [7–10] to show a more direct departure from this characterization. We first reproduce the results obtained by others using similar models and then extend these results by studying the time-dependent fitness of strains. We then present our conclusions, which have been qualitatively anticipated, but are first quantified here. In the model, the evolutionarily stable type is out-competed in the short term by seemingly fitter mutants. These mutants enjoy high reproduction ratios for many generations, but go extinct in the long term (e.g., after 200 generations). The rapidly reproducing types modify their local environment in a way that is detrimental to their survival, but this environmental modification and its feedback to population growth requires many generations. The distinct fates of the different types are made possible by self-organized spatial segregation. We will define a more general measure of invasion fitness that acknowledges that descendents may have different reproductive success than their ancestors of the same type. This measure indicates the evolutionarily stable type in such cases, and it can be used to quantify the time scale at which selection acts against the mutants with short-term advantage.

As an example of a system with different short-term and long-term fitness, we use a simple spatially extended model of a parasite or pathogen spreading through a host population [8,9]. The model can also be thought of as a predator-prey system, with the pathogens being predators and the hosts prey [10,11]. Such systems exhibit interesting spatial dynamics which are not present in the mean-field approximation; hence, space is fundamental to their dynamics, a property believed to be shared by many real biological systems [12,13]. The model is a probabilistic cellular automaton, with possible states 0 (empty), H (susceptible host), and I_τ (host infected with pathogen of transmissibility τ). It has three parameters. At each time step, susceptible hosts reproduce into each neighboring cell with probability g if that cell is not yet occupied; the probability of reproduction is independent for each neighbor. An infected host dies with probability υ (virulence). Finally, an infected host I_τ causes a neighboring uninfected host to become infected with probability τ. In predator-prey language, g is the prey reproduction rate, ν describes the rate of predation, and τ describes the rate of migration or dispersal to neighboring sites. The subscript τ allows more than one type to be present on the lattice. The state transition probabilities are

$$\begin{aligned} P(0 \to S) &= 1 - (1 - g)^n, \\ P(I_\tau \to 0) &= \upsilon, \\ P(S \to I_\tau) &= 1 - (1 - \tau)^{m_\tau}, \end{aligned} \tag{1}$$

where n is the number of uninfected host neighbors, and m_τ is the number of infected neighbors of transmissibility

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τ. The lattice is updated synchronously, as the dynamics are not significantly different when updating asynchronously [8]. When all pathogen individuals are of the same type, the model reduces to the predator-prey model studied in [10] except that the probabilities of any two neighbors of a site sending offspring to that site are independent of each other (and if more than one neighbor sends offspring to the site, the parent is chosen at random), rather than being linear in the number of neighbors. However, this difference does not significantly affect the dynamics. The model differs more fundamentally from the forest fire model [14] and other models of excitable media [15]: growth of susceptible hosts occurs locally rather than uniformly in space.

In a mean-field approximation [8], the growth rate of a type monotonically increases with τ. Thus, in homogeneous systems with competing strains, higher-τ strains dominate [16]. The mean-field approximation does not capture interesting aspects of the spatial variation in this model. The densities of host and pathogen fluctuate locally [10]. The system as a whole can have one of the following outcomes: the pathogen dies out but the host survives, host and pathogen coexist, or the pathogen drives the host to extinction. Parasite-driven extinction occurs above a threshold of τ which depends on the values of the other parameters [17].

In order to investigate the evolutionary dynamics more fully, we introduce mutation into the dynamics of the model, as has recently been done in similar models [9,18,19]. The transmissibility becomes a quantitative trait of an individual pathogen. When a pathogen of transmissibility τ reproduces, its offspring has probability μ of having transmissibility $\tau \pm \epsilon$:

$$P(S \to I_\tau) = \left[1 - \prod_{\tau'} (1 - \tau')^{m_{\tau'}}\right]\left[\frac{\frac{\mu}{2} p_{\tau-\varepsilon} + \frac{\mu}{2} p_{\tau+\varepsilon} + (1-\mu) p_\tau}{\sum_{\tau''} (\frac{\mu}{2} p_{\tau''-\varepsilon} + \frac{\mu}{2} p_{\tau''+\varepsilon} + (1-\mu) p_{\tau''})}\right], \quad (2)$$

where $p_\tau = 1 - 1 - \tau^{m_\tau}$ and m_τ is the number of infected neighbors of transmissibility τ. For suitably large lattice sizes, the system evolves to an evolutionarily stable average value of τ [9]. When high values of τ lead to extinction, τ does not increase to the point of extinction; rather, the system reaches an evolutionarily stable value which is lower than the extinction limit. This is the case for the entire region of parameter space where parasites and hosts coexist.

The distribution of τ during evolution has significant features that have not yet been noted. Figure 1 is a density plot showing the distribution of τ over time. In this figure, it is apparent that strains of pathogens continue to evolve higher τ, but these strains go extinct. A population of pathogens above the evolutionarily stable value, but able to coexist with the host, evolves to a lower transmissibility.

To shed light on the evolutionary dynamics of the system, we will begin by examining the reproduction ratio for pathogens of different types when mutations are to a random transmissibility rather than being a fixed increment. Figure 2a shows the net reproduction ratio $R(\tau)$ for mutants when they first arise; it increases monotonically with τ. However, Fig. 2b shows $R(\tau)$ for all pathogens, averaged over time. It peaks at the evolutionarily stable value. Thus, selection favors high-τ mutants initially, consistent with the spatially homogeneous case. The difference between these two plots shows that selection against high-τ mutants acts only on longer time scales; evolutionary dynamics are different at different time scales.

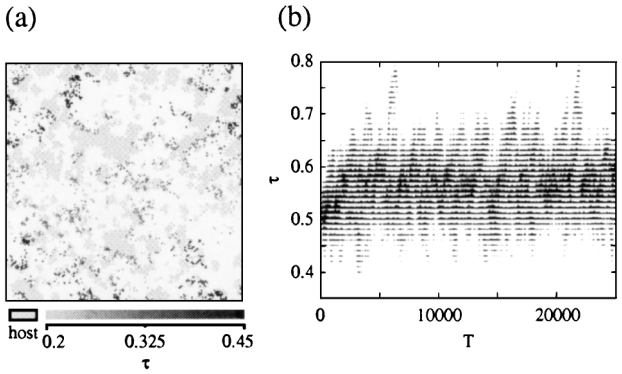

FIG. 1. (a) Snapshot of the lattice for the evolving pathogen-host model. The pattern changes over time due to host reproduction, infection, mutation of pathogens, and infected host death. Susceptible hosts are shown as light gray and infected hosts are darker shades of gray depending on their value of transmissibility τ, as shown in the legend. Empty sites are white. (b) Time series of the distribution of τ. Each vertical slice represents the distribution of τ at a particular moment in time. Strains of individuals exceed the evolutionarily stable value of 0.57 (most notably at $T = 6000$ and $T = 22\,000$) but then go extinct. The virulence ν is 0.5 and the host reproduction rate g is 0.1. In this and all subsequent figures, the system has settled to a stable value of τ.

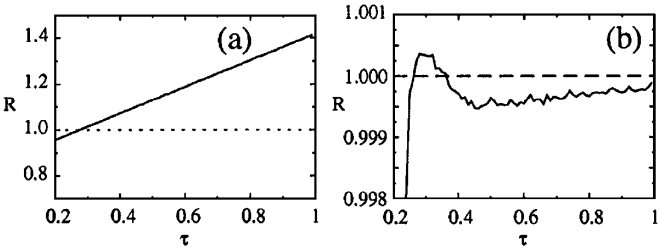

FIG. 2. (a) R (the net reproduction ratio) as a function of τ for mutants, showing the expected number of offspring of a mutant one generation after it arises. The dominant phenotype has reached its evolutionarily stable value of $\tau = 0.3$. (b) As above, but for all pathogens, averaged over time; R peaks at the evolutionarily stable value of 0.3 and is below one when τ is significantly greater or less than the evolutionarily stable value. In order to collect data for all τ, mutants' transmissibility is set to a random value between 0.2 and 1 rather than being a small increment. The virulence ν is 0.5, host reproduction rate g is 0.05, mutation rate μ is 0.15, mutation increment ε is 0.005, and the lattice size L is 175. These parameters will be used in subsequent figures unless otherwise noted.

In order to explicitly contrast the fitness at different time scales, we must consider the reproductive success not only of the mutant, but also of its descendants, which can vary as a function of time since the beginning of the strain. For a general evolving system, we define the *time-dependent invasion fitness* $F_i(T, p)$ to be the expected number of descendants at time $t_0 + T$ of a mutant of type p introduced at time t_0. T can be measured as time or in generations; here we use the number of generations. Note that $F_i(1, p)$ is the net reproduction ratio R for mutants. In general, F_i should include environmental factors in its arguments. When, however, the local environment of type p is shaped by p itself, as in the model [20], one may write it as a function of only time and type. In order to make a more explicit comparison with the reproduction ratio R, one can calculate the normalized reproduction ratio as a function of time $R(T, p) = F_i(T, p)^{1/T}$. The evolutionarily stable types p_{es} are given by p such that $\lim_{T\to\infty} F_i(T, p) > 0$. No other value of p can successfully invade in the long term.

In our model, the type p of the evolving species corresponds to the transmissibility τ. Figure 3 shows $F_i(T, \tau)$, obtained numerically for the host-pathogen model. Strains where τ is less than the evolutionarily stable value τ_{es} have both a short-term and long-term disadvantage, and decline immediately. Strains with $\tau > \tau_{es}$, by contrast, initially grow much more quickly than those of the evolutionarily stable type, but begin declining after an average of about 30 generations. Nevertheless, they remain more successful than the evolutionarily stable type for a large number of generations. Selection begins to act against strains of a given non-evolutionarily stable type when its curve drops below that of the evolutionarily stable type.

Using time-dependent fitness, one can determine which types dominate at each time scale. For a given time scale T, the most successful type for that time scale $p_{\text{opt}}(T)$ is the value of p such that $R(T, p)$ is maximized [$p_{\text{opt}}(T) = \arg\max_p (R(T, p))$]. Systems for which $p_{es} = p_{\text{opt}}$ (1) have the same short- and long-term fitness. Figure 5a shows that, for the model, one type dominates for short time scales, and another dominates for long time scales, with a sharp transition between the two scales. This curve determines the meaning of "short term" and "long term" as we have been using them.

Since selection acts differently on a given type at different time scales, one can determine the relevant time scales for a particular type. For all $p \neq p_{es}$ we can define the time scale $T_s(p)$ at which selection acts against p as $T_s(p) = \min\{T \mid \forall\, t > T, F_i(t, p) < F_i(t, p_{es})\}$. Thus for some $T_s(p)$, mutants of phenotype p have more descendants than those of p_{es}. The time scale at which the evolutionarily stable type begins to dominate is given by $T_L = \min\{T \mid p_{\text{opt}}(T) = p_{es}\}$. For the host-pathogen system ($p = \tau$), Fig. 5b shows $T_s(\tau)$. For $\tau < \tau_{es}$, $T_s(\tau) = 0$ since these low-transmissibility types have a disadvantage on all time scales. For $\tau > \tau_{es}$, $T_s(\tau)$ approaches a constant number of generations (about 200 for the parameters used in Fig. 5b) but is larger when τ is close to τ_{es}. Thus, for $\tau > \tau_{es}$, on time scales significantly shorter than T_s, the dynamics of the relative frequencies of different types can be determined from their values of the net reproduction ratio R; on longer time scales, other mechanisms are essential to the dynamics, such as the feedback between the population and the environment. In general, when a type has a short-term advantage [$R(p) < (p_{es})$], $T_s(p)$ is a quantitative measure of the time scale in which instantaneous change in frequency dominates the evolutionary dynamics for that type.

Because some of the individuals in the population can be of rapidly reproducing types that have high short- but low long-term fitness, the long-term composition of types in the population cannot necessarily be given by the types with high long-term fitness plus mutation-selection balance. Instead, the distribution $P(p)$ of types, $p \neq p_{es}$, is given for low mutation rates by:

$$P(p) = \frac{n(p) \int_{T=0}^{\infty} F_i(T, p)}{n_{es} + \sum_{p' \neq p_{es}} n(p') [\int_{T=0}^{\infty} F_i(T, p')]} \qquad (3)$$

where $n(p)$ is the rate at which mutants of type p arise, and n_{es} is the average number of individuals of the evolutionarily stable type. $P(\tau)$ for the model measured

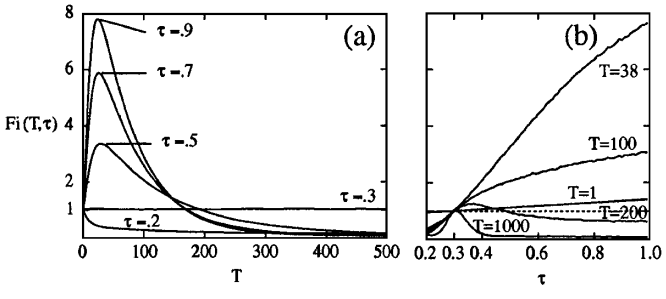

FIG. 3. The time-dependent invasion fitness $F_i(T, \tau)$ for the host-pathogen system. (a) As a function of time T, with curves for various transmissibilities τ. (b) The same data as a function of τ, with curves for various time scales T. The lattice size L is 250.

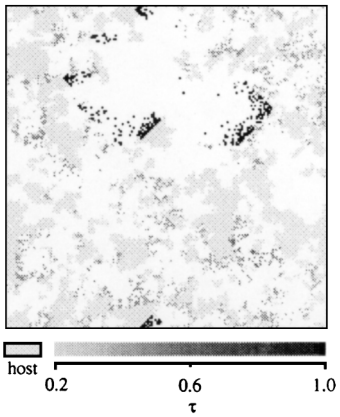

FIG. 4. A mutant strain. In this snapshot of the lattice, black indicates a high-transmissibility mutant strain that arose 50 generations ago. Because of the wider range of τ, a different color scale is used from that of Fig. 1a.

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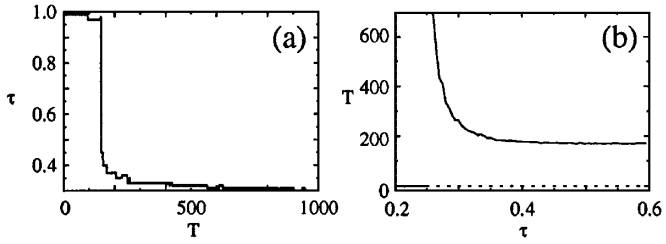

FIG. 5. Time scale of selection. (a) The most successful type $\tau_{\mathrm{opt}}(T)$ as a function of time since the beginning of the strain. Types of high transmissibility (those with high values of R in Fig. 2a) dominate for time scales shorter than about $T = 175$, while types close to the evolutionarily stable type (those with high values of time-averaged R in Fig. 2b) dominating on time scales longer than $T = 250$. (b) The time scale $T_s(\tau)$ at which selection acts against strains of pathogens with transmissibility τ. $T_s(\tau)$ is 0 for $\tau < \tau_{es}$, indicating that selection acts instantaneously. For $\tau > \tau_{es}$, the time scale is very long for values close to τ_{es}, converging on $T_s \approx 180$ for high τ.

numerically agrees with the above (except for types which are within 0.1 of the evolutionarily stable type, since these strains take a long time to decline and were not tracked longer than 1000 generations).

The tendency to spatial segregation of different strains can be seen in Fig. 4. Although different strains are always coming in contact, pathogens tend to be surrounded by those of a similar type. This results from local reproduction and local extinction of higher-R strains. Mutation causes individuals of a range of types to arise for selection to act on; since these types are segregated spatially, selection can be viewed as acting on clusters of organisms associated by spatial proximity.

A connection has been made between spatially inhomogeneous models and group selection and/or "altruism." Such a connection can be loosely justified; however, while strict individual selection is a restrictive limit of evolving systems, the dichotomy of group and individual selection also does not capture the richness of spatial populations. Typically, in our model, neither the spatial groups nor the genetically related groups nor structures of spatial patterns (e.g., spiral waves in Ref. [21]) are clearly determinable. Rather than focusing on the distinction or balance between group and individual selection, we have focused on the multigenerational fitness of strains as a dynamic property of organisms in spatially inhomogeneous environments.

Since organisms often greatly affect their own environment, the feedback between the environmental change caused by the organism and selection may be substantial [5]. The model demonstrates one possible mechanism for this feedback: the local depletion of the resource by organisms is ultimately detrimental to their survival. The contrast between long-term and short-term fitness may characterize other systems which have the general property that a population depends on, and can deplete, a resource that grows locally, and where reproduction is local. If mutations are frequent, such a system observed in nature may contain a significantly different distribution of organism types than would be expected if selection acts only at one time scale. It is more appropriate to view the composition of types in such systems as a mixture of types, each of which is adapted to a particular time scale.

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