Clonal interference and Muller’s ratchet in spatial habitats

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Abstract

Competition between independently arising beneficial mutations is enhanced in spatial populations due to the linear rather than exponential growth of clones. Recent theoretical studies have pointed out that the resulting fitness dynamics is analogous to a surface growth process, where new layers nucleate and spread stochastically, leading to the build up of scale-invariant roughness. This scenario differs qualitatively from the standard view of adaptation in that the speed of adaptation becomes independent of population size while the fitness variance does not. Here we exploit recent progress in the understanding of surface growth processes to obtain precise predictions for the universal, non-Gaussian shape of the fitness distribution for one-dimensional habitats, which are verified by simulations. When the mutations are deleterious rather than beneficial the problem becomes a spatial version of Muller’s ratchet. In contrast to the case of well-mixed populations, the rate of fitness decline remains finite even in the limit of an infinite habitat, provided the ratio \( U_d/s^2 \) between the deleterious mutation rate and the square of the (negative) selection coefficient is sufficiently large. Using, again, an analogy to surface growth models we show that the transition between the stationary and the moving state of the ratchet is governed by directed percolation.

Keywords: population genetics, KPZ, non-equilibrium wetting, surface growth, evolution

(Some figures may appear in colour only in the online journal)

1. Introduction

The appearance of a mutation in a population and its fixation or loss is the most basic process of adaptation. This process determines the rate of evolution, or how quickly populations adapt to new environments. One approach in quantitative models of adaptation is to assume that non-neutral mutations are rare. In this regime, generally referred to as periodic selection [1, 2], the population has no genetic variation except for brief periods when a mutation sweeps through and fixates, and therefore the rate of fixation is mutation limited. Adaptation in the regime of periodic selection and strong selection, dubbed strong selection weak mutation has been studied extensively in the context of extreme value theory [3]. Notably, these models assumed populations were well-mixed, with no spatial structure.

When mutations are more common due to higher rates or larger population sizes, genetic variation builds up. Clonal interference is the competition between these mutations to reach high frequency, when there is little or no recombination. This is especially relevant in the case of beneficial mutations in microbial populations, since recent experiments suggest they are more common than previously thought [4–6]. Microbial evolution experiments have observed reduced rates of evolution due to the competition between beneficial mutations [7, 8]. Fisher’s fundamental theorem equates the rate of evolution with the variance of the fitness distribution [9], which can be approximated analytically in simplified population genetic models. These recent theoretical analyses have found the rate of evolution in large populations of asexuals is not proportional to the total supply rate of
beneficial mutations, but depends much more weakly (logarithmically) on population size and mutation rate \[10–15\].

Deleterious mutations are more common than beneficial ones, but their chance of fixation is much smaller and vanishes for infinite populations. However, in finite populations and in the absence of beneficial mutations and recombination, deleterious mutations will eventually fix by genetic drift, leading to a fitness decline known as Muller’s ratchet \[16, 17\]. Determining the rate of the ratchet as a function of population size, mutation rate and selection strength is a long-standing problem that continues to attract considerable interest \[11, 18–25\]. Recombination can prevent Muller’s ratchet and also mitigates the slowdown in the rate of evolution from clonal interference, which is why Muller’s ratchet and clonal interference are often argued as reasons for an evolutionary advantage of sex \[26–28\].

Previous analyses of clonal interference and Muller’s ratchet were largely limited to well-mixed populations, where each individual competes with the whole population, such as microbes in liquid culture. However, many populations are not well-mixed, but are confined in space such that they only compete with a limited neighborhood population on time-scales of a generation. Spatially structured population genetics have been studied with finitely subdivided, and continuous populations \[29–34\]. In a spatially structured population individuals compete only within a limited spatial neighborhood, reducing the effective population size. However, when mutations are rare a single beneficial mutation can compete with the whole population, and the fixation probability is the same in well-mixed and spatially structured populations \[35, 36\]. Recently, models incorporating large amounts of beneficial mutations and one or two dimensional spatial structure have found the rate of evolution to be even slower than in well-mixed populations, as the slower than exponential growth of clones increases the likelihood of competition \[37–42\]. In fact, the rate of evolution becomes independent of system size, while the variance (in the steady state) scales as a power of population size, violating Fisher’s theorem \[39, 40\]. This also implies that there is a long transient regime during which the stationary variance builds up, while the speed of adaptation is constant.

Here, we study the transient regime of Wright–Fisher models of evolution on a one-dimensional lattice for both adaptation with beneficial mutations, and Muller’s ratchet. In the former case the fitness variance grows as a power law in time, and saturates at a value determined by the system size (also as a power law) \[39, 40\]. The fitness may be pictured as a surface in space, which advances over time. This behavior is analogous to surface growth models in physics, where particles are deposited on an initially flat surface, which develops roughness over time \[43, 44\]. Specifically, the accumulation of beneficial mutations was found to be analogous to poly-nuclear growth (PNG) in \[40\]. In the next section we introduce the model for adaptation on a one dimensional lattice, and review previous results. In section 3, we use extensive simulations to show the model of adaptation belongs to a class of surface growth models called the Kardar–Parisi–Zhang (KPZ) universality class \[45–48\]. By exploiting the equivalence to models of surface growth, the dynamics can be described in great detail, including in particular the non-Gaussian shape of the fitness distribution. In section 4, we modify the model to study Muller’s ratchet. We find that for certain parameters the rate of fitness decline does not go to zero as the population size becomes large, and we characterize the transition between fitness decline and no decline. The model with deleterious mutations is similar to a different class of models in surface growth physics, and we use this analogy to find other asymptotic properties.

2. Model

The spatial constraints are realized as a one dimensional lattice of size \(L\) with periodic boundary conditions, where each point represents a single organism that occupies a space \[39\]. The evolution follows standard haploid asexual Wright–Fisher dynamics in discrete generations, where the next fitness of each site is chosen randomly from one of the parents in the neighborhood, weighted according to their fitness. The smallest possible neighborhood in one dimension is such that the child in the next generation inherits its genotype and fitness from only two possible parents, that is, the fitness \(f_{i}(t + 1)\) of site \(i\) at generation \(t + 1\) is chosen from either \(f_{i}(t)\) or \(f_{i+1}(t)\). In other words, \(f_{i}(t + 1) = f_{i}(t)\) with probability \(f_{i}(t)/(f_{i}(t) + f_{i+1}(t))\), and \(f_{i}(t + 1) = f_{i+1}(t)\) with probability \(f_{i+1}(t)/(f_{i}(t) + f_{i+1}(t))\). Simulations were written in C and parallelized with parallel \[49\] (code available upon request).

In the case of a homogeneous system of fitness 1, where a single mutant appears with fitness \(1 + s\), the fixation probability for a beneficial mutation is the same as in the well-mixed case, \(\pi = 2s\) for \(s \ll 1\) \[35, 36\]. Intuitively, the fixation probability is unaffected because a single mutation has ample time to compete with the entire system, regardless of spatial structure. Since the fixation probability is the same, the speed of evolution in the periodic selection regime is the same as in the well-mixed case. What is different is the timescale of fixation. The boundary between two domains with different fitnesses is a biased random walker, and the speed of this walker is the expected value of its displacement after one time step, \(c = s/2\) for small \(s\). In the continuum limit, this model corresponds to a special case of the more general stochastic Fisher equation (or SFKPP equation) \[50–52\], where it is possible to have traveling waves with speed \(c \sim s\) in the strong noise regime, or \(c \sim \sqrt{s}\) in the weak noise regime. However, the dependence of the wave speed on \(s\) does not change the essential features. Importantly, the time for fixation may be much longer in the presence of spatial structure compared to well-mixed populations. A wave spreading with finite speed \(c\) will take time \(t_{\text{fix}} \sim L/c\) to cover the whole system (and total population size \(N \sim L\), as opposed to a well-mixed population where \(t_{\text{fix}} \sim \log(N)\). The slow spread of mutations makes it more likely that many clones exist simultaneously in large systems. A site may also contain more than one organism, in which case \(c\) is different, but it does not
change the overall results [40] (unless interference happens within one site.)

Since we are interested in the rate of evolution during competition, a steady rate of beneficial mutations is supplied, akin to a population adapting to a new environment. Beneficial mutations appear randomly at rate $U_b$ per site per generation (deleterious mutations are studied in section 4.) We assume that mutations have independent effects, with no epistasis, and therefore increase the fitness according to $\log f' = \log f + s$, where $s$ is a constant with $|s| \ll 1$.

An important quantity is the rate of fitness change $V = \lim_{t \to \infty} \langle \log f \rangle / t$, where the average is over the population. When the time between mutations to appear and become established, $t_{\text{mut}} = (\pi U_b L)^{-1}$, is much longer than $t_{\text{fix}}$, $V$ is mutation limited: $V = s \pi U_b L = 2s^2 U_b L$. However, when $t_{\text{mut}} \approx t_{\text{fix}}$, multiple unfixed mutations in the population compete with each other, slowing down $V$. In well mixed populations the condition for mutation limited adaptation is that there should be less than one new beneficial mutation per generation. In contrast, with spatial structure $t_{\text{mut}} \sim t_{\text{fix}}$ defines a characteristic interference length scale $L_c \approx (c/\beta U_b)^{1/2}$, above which mutation competition sets in. In this competitive regime, the rate of evolution no longer depends on the supply of beneficial mutations, but $V$ becomes independent of $L$ for $L > L_c$ [39, 40]. Using this observation and dimensional analysis, one may deduce that this maximum speed grows as $U_b^{1/2}$ in one dimension, and $U_b^{3/2}$ in two dimensions.

3. Adaptation with many beneficial mutations

3.1. Analogy to surface growth

The rough spatial profile of the fitness resembles a typical surface seen in surface growth models [39, 43]. In surface growth, particles are deposited on an initially smooth surface randomly, and they may diffuse or stick to each other, gradually forming a rough surface. Many simple models of surface growth were studied by statistical physicists interested in non-equilibrium systems [43, 44]. They discovered that a surface seen in surface growth models [39, 43]. In surface growth were studied by statistical physicists interested in non-equilibrium systems [43, 44]. They discovered that a surface roughens due to multiple simultaneous nucleation events (corresponding to clonal interference) [53, 54]. In the rough regime the PNG model belongs to the universality class of growth processes described on large length and time scales by the KPZ equation, a nonlinear stochastic partial differential equation [45, 55, 56]. While in PNG the spreading is fast and deterministic, in the evolutionary model it is stochastic, and the new layer may even disappear [54]. The boundaries may collide with each other, and they either annihilate or stack up creating differences in log fitness greater than $s$. From the point of view of surface growth it is natural to hypothesize that the universal features of the PNG model are robust with respect to these differences, but this has to be verified by explicit simulations. The test of the universality hypothesis proceeds in two steps. First, one estimates the scaling exponents governing the power law dependence of the standard deviation of the surface height (or log fitness) distribution on time and system size. Second, the shape of the full distribution of height fluctuations is considered. In surface growth, starting from flat initial conditions, the standard deviation of the surface height fluctuation grows in time as $\sigma(t) \sim t^\beta$, where $\beta$ is the growth exponent, then reaches a steady state when the correlation length reaches the size of the system [43, 57]. In the steady state, $\sigma(t \to \infty) \sim L^\alpha$ where $\alpha$ is the saturation exponent. Figure 1(a) confirms this scenario for the evolution model. The crossover time is where saturation sets in (the elbow), and it scales as $L^{\alpha/\beta}$. One may try to measure the exponents from the simulations, but based on the similarity to the PNG model one expects that the scaling exponents are those of the one-dimensional KPZ-equation, $\alpha = 1/2$, $\beta = 1/3$ and $\alpha/\beta = 3/2$. Figure 1(b) shows that the data indeed collapses when plotted as $\sigma^2/L$ versus $t/L^{3/2}$. In the evolutionary context the saturation time scale $\sim L^{3/2}$ is proportional to the fixation time of beneficial mutations [40]. Note that these values of the exponents characterize the asymptotic, long time and large scale behavior of the model, and the behavior in the pre-asymptotic regime may be somewhat different [39].

3.2. Transient fitness distributions

Over the past decade, a much more refined characterization of the KPZ universality class has been developed that extends beyond the values of the scaling exponents $\alpha$ and $\beta$ to the full probability distribution of surface height fluctuations [46–48]. The essence of this refined universality hypothesis is that the log fitnesses (or surface heights) can be written as

$$\log f(t) = Vt + (\Gamma t)^{1/2} \chi,$$  \hspace{1cm} (1)

where $\chi$ is a random variable from one of the Tracy–Widom (TW) distributions, $V$ is the long-time growth rate, and $\Gamma$ is a constant related to the parameters of the KPZ equation [46]. From equation (1) we find the width of the distribution

$$\sigma^2(t) = \text{var}\{\log f(t)\} = (\Gamma t)^{1/2} \text{var}(\chi).$$ \hspace{1cm} (2)

The TW distributions were first discovered in fluctuations of the largest eigenvalues of random matrices [58]. The relation to the PNG model was established by mapping the PNG surface height to the length of the longest increasing subsequence of random permutations [56, 59], and subsequently TW
universality was derived directly from the KPZ equation [48, 60]. Remarkably, the distributions were found to be geometry dependent, with the flat (monomorphic) initial condition leading to the TW distribution characteristic of random matrices from the Gaussian orthogonal ensemble (GOE).

Here we show numerically that, despite the additional randomness of the stochastic spreading, the distribution of fitnesses in the non-stationary regime of the spatial evolution model is a TW distribution characteristic of the KPZ universality class. One signature of the TW distributions can be seen by measuring higher moments, such as skewness, \( \langle \log f - \langle \log f \rangle \rangle \) and excess kurtosis, \( \langle \left( \log f - \langle \log f \rangle \right)^4 \rangle - 3 \), which do not depend on the parameters \( V \) and \( \Gamma \). Figure 2 shows that the skewness and kurtosis of the fitness distributions are non-zero, indicating non-Gaussianity, and they approach the known values of the GOE TW distribution.

It is also possible to compare the fitness distribution directly to the TW distribution. The parameters \( V \) and \( \Gamma \) can be found from the simulation data by applying linear regression to the means of equations (1) and (2). The fitnesses from the simulation are then rescaled as

\[
\chi_{\text{sim}} = \frac{\log f - \langle f \rangle}{\langle f \rangle^{1/3}}.
\]

Figure 3 shows that in the non-stationary regime, the fitnesses
fall onto the universal GOE TW distribution, which is skewed towards higher fitnesses, with tail behaviors \(-\ln P(x) \sim x^{3/2}\) and \(-\ln P(x) \sim x^3\). To demonstrate the robustness of this result, we simulated a variant of the model where the selective advantage of beneficial mutations, \(s\), is a random variable generated from an exponential distribution, a common choice in this field [12, 14]. The two data sets can be seen to be indistinguishable.

In addition, two other initial conditions were simulated. The droplet geometry in the PNG model is when the initial condition is a single nucleation site, with no additional nucleations (or mutations) allowed outside. The boundary of the initial seed grows over time, making the fitness profile curved. The deviations from this curved profile converge to the TW distribution of the Gaussian unitary ensemble [46, 47, 56]. The droplet geometry has an interesting evolutionary analogy: it corresponds to a mutation that raises the mutation rate significantly (a mutator strain), and competes with a population that has essentially no mutations. The third initial condition corresponds to a system with fully developed, stationary diversity (surface roughness). In this case the distribution of the deviations from the initial fitness profile is predicted to converge to a universal distribution \(F_0\), which does not appear directly in random matrix theory but is closely related to the TW distributions [56]. Again, the data fall nicely onto the predicted distribution. The three universal distributions shown in figure 3 have similar overall shapes and share the same tail behavior mentioned above for the GOE TW distribution, but the distribution \(F_0\) is distinguished from the others by having zero mean [56].

4. Deleterious mutations

Our model may be modified to include only deleterious mutations by having a single negative selection coefficient \(s < 0\). Once a mutation appears, its expansion is unfavorable, and happens only due to genetic drift. For a single mutation, the probability of fixation vanishes exponentially in \(N\) as \(\pi \sim e^{Ns}\) for large negative \(Ns\) [35, 36]. When many deleterious mutations are present simultaneously in the population, the rate of fitness decline is governed by the time scale on which the subpopulation of individuals with the smallest number of mutations (the ‘least loaded class’) goes extinct by genetic drift. In the well-mixed case the number of individuals in the least loaded class is on the order of \(n_0 \sim N e^{-U_d/s}\), where \(U_d\) is the deleterious mutation rate [17]. Correspondingly for

\[ n_0 \sim N \sim e^{-U_d/s} \gg 1, \]

the probability of fixation of an additional deleterious mutation in this class is exponentially small. Detailed analysis shows that under condition (4) the rate of Muller’s ratchet is also exponentially small in \(N\) [21, 23, 25], whereas for \(n_0 |s| < 1\) the fitness of the population declines continuously, and a description in terms of a traveling wave in fitness space, similar to that used in the context of adaptation (\(s > 0\)), is applicable [11]. Importantly, for a given set of mutation parameters \((U_d, s)\) the slow ratchet condition (4) is always attained for large populations, which implies that the fitness decline effectively ceases for \(N \to \infty\).

4.1. Muller’s ratchet in spatial populations

Simulations of the one-dimensional spatial model show a fundamentally different behavior in the rate of fitness decline, which we measure with \(F = \langle \log f \rangle\), so that \(V\) is approximately \(F/t\) after some long time. Figure 4 shows that for sufficiently large \(U_d\) deleterious mutations accumulate at a constant rate, which becomes independent of the habitat size, \(L\), for large \(L\). Exploration of the parameter space reveals that this transition in the fitness decline is sharp for certain values of \(U_d\) and \(s\) (figure 5). The rate of fitness decline is non-monotonic in \(s\). Initially the larger mutation effects lead to a higher rate of fitness decline with increasing \(s\), but at the same time selection becomes more effective in eliminating the deleterious mutations, which eventually halts the fitness decline. Rescaling the fitness by \(U_d\) collapses the curves in the region of large \(s\), where \(F \sim U_d/s\), while for very small \(s\), mutations accumulate at close to the maximal possible rate, \(F \approx U_d s\).

To further elucidate the nature of the transition we examine the density of sites with no mutations, \(n_0\). Figure 5(c) shows a sharp transition in \(n_0\) between regimes where the fitness is steadily declining (the moving ratchet) and where the fitness is not declining (the stationary ratchet). The collapse of curves in figure 5(d) indicates that the transition occurs when

\[ \frac{U_d}{s^2} \approx 1. \]

To explain this relation, consider a patch of deleterious mutants created in a single mutational event. Because \(|s| \ll 1\),
the boundaries of the patch perform almost symmetric random walks that are weakly biased inwards by selection. The patch disappears when the two boundaries meet. The life time $\tau$ of such an isolated patch is therefore equal to the first passage time of a random walk on the half-line with a bias $\sim |s|$ towards the origin, which has a distribution of the form [62].

$$P(\tau) \sim \tau^{-3/2} e^{-s^2 \tau}. \quad (6)$$

When $U_d$ is small, deleterious patches are created and disappear independently of each other (figure 6).

To estimate the density $\rho_0$ of sites without deleterious mutations, we note that $1 - \rho_0$ is the probability that a deleterious mutation is found at a randomly chosen point in space, $x$, at a random time $t$. In other words, $1 - \rho_0$ is the fraction of the space-time area in figure 6 that is covered by deleterious patches. A patch with life time $\tau$ reaches a spatial extension of order $\tau^{1/2}$, and hence its area is $a \sim \tau^{3/2}$. Using (6) the distribution of $a$ is found to be $P(a) \sim a^{-4/3} e^{-s^2 a^{3/2}}$.

Figure 5. (a) The rate of fitness decline, as indicated by the mean log fitness $F$, changes sharply for certain parameters $U_d$ and $s$. (b) Rescaling by $U_d s$ collapses parts of the curves. Dashed line indicates $r^{-2}$. $F$ was measured after $10^7$ generations with $L = 2^8$, and mutation rates were $U_d = 10^{-6}$ (blue diamonds), $10^{-5}$ (green plusses), $10^{-4}$ (red crosses), $10^{-3}$ (cyan squares), and $10^{-2}$ (magenta circles). (c) A sharp transition in the density of sites with no mutations, $\rho_0$, as a function of mutation effect size. When $\rho_0$ is large the fitness does not decline, while when $\rho_0 = 0$ the fitness declines indefinitely. (d) Scaling the $s$-axis by $U_d^{3/2}$ reveals that the critical parameters are $U_d/s^2 \approx 1$. Results were averaged over 30 simulations, except for $U_d = 10^{-4}$ and $U_d = 10^{-3}$, which were only run once.

Figure 6. Schematic space-time view of the creation and extinction of patches of deleterious mutations in the spatial Muller’s ratchet problem. The boundaries of a patch are weakly biased random walks and the patch disappears when the two walks meet. A patch of life time $\tau$ reaches a maximal width $\sim \tau^{1/2}$. The distribution of life times is heavy-tailed for small $|s|$ (see equation 6).
from which the average area of a patch is deduced as $\langle a \rangle \sim s^{-2}$. Since patches are created with probability $U_d$ per unit time and space, it follows finally that

$$1 - \rho_0 \sim \frac{U_d}{s^2}$$  \hspace{1cm} (7)

at least when $U_d/s^2 \ll 1$ so that the patches remain isolated. Assuming that the dependence of $\rho_0$ on the parameter combination $U_d/s^2$ continues to hold up to the point where the merging of patches leads to the global extinction of the least loaded class ($\rho_0 = 0$), we conclude that the transition from the stationary to the moving ratchet is indeed determined by a condition of the form (5). Support for this assumption is provided in figure 7(a), which shows that simulation results for $\rho_0$ obtained for different values of $s$ and $U_d$ collapse onto a single curve when plotted against $U_d/s^2$.

The relation (7) also explains the behavior of the fitness in the regime of large $|s|$ in figure 5. In the stationary phase of the ratchet the fitness is independent of time and given by $F = s(1 - \rho_0) \sim U_d/s$, hence $F/U_d s \sim 1/s^2$ independent of $U_d$. Note that the behavior of $\rho_0$ in (7) is different from the well-mixed case, where $\rho_0 = e^{U_d/s} \approx 1 - \frac{U_d}{s^2}$. For a given selection strength $|s|$, the deleterious mutation rate required to set the ratchet into motion is $U_d \sim s^2$ in the spatial case, much smaller than the corresponding value $U_d \sim |s| \ln(N|s|)$ obtained from (4) in the well-mixed setting.

4.2. Non-equilibrium wetting and critical exponents

For a detailed characterization of the transition between the stationary and the moving spatial ratchet we exploit the similarity of our model to a class of surface growth models that are referred to as non-equilibrium wetting models [63–66]. In a wetting transition a macroscopic layer of one phase (typically a liquid) forms on top of another phase (typically a solid substrate). Non-equilibrium wetting describes the transition between a layer that is bound to the substrate (the stationary ratchet), and one that grows indefinitely (the moving ratchet). Specifically, in the limit $|s| \to \infty$ our model becomes equivalent to an unrestricted solid-on-solid model with no evaporation inside plateaux [64]. The solid-on-solid constraint implies that the surface has no overhangs, that is, each particle is supported by another solid particle below it. The absence of evaporation from plateaux corresponds to the fact that fitness can increase only by selection, and there is no restriction on the fitness/height differences between adjacent sites. For this model the wetting transition has been shown to be governed by directed percolation (DP) [67]. DP is a broad universality class of non-equilibrium phase transitions that occur between an ‘active’ and an ‘extinct’ state, for example, an infectious disease spreading in a population. In the present context the active phase is the population in the least loaded class that persists indefinitely in the stationary ratchet state and goes extinct at the transition.

The association with DP predicts power law behaviors of various quantities near the transition. In particular, at the transition, $\rho_0(t) \sim t^{-\theta}$, where $\theta = 0.159 464 ...$ [67]. Figure 8 shows that $\rho_0$ decays slowly for parameters close to $U_d/s^2 = 1$, consistent with the power law predicted by DP. Moreover, the stationary density of sites with no mutations and the rate of fitness decline are predicted to behave as

$$\rho_0 \sim (u_c - u)^{\beta_D}$$ for $u < u_c$ and

$$|V| \sim (u - u_c)^{\nu_D}$$ for $u > u_c$,  \hspace{1cm} (8)

at the transition, where $u = U_d/s^2$ is the scaled mutation rate with critical value $u_c \approx 1$, and $\beta_D = 0.276 486 ...$ and $\nu_D = 1.733 847 ...$ are the order parameter exponent and the temporal correlation length exponent of DP, respectively [67].
While the additional stochasticity associated with the smallness of the selection coefficient in our model makes it difficult to find these exponents numerically with any accuracy, the data shown in figure 7 are clearly consistent with the power laws (8). At the transition the (negative) mean fitness and the variance of the fitness are predicted to grow logarithmically with time [63, 65], which is also borne out by the simulations (figures 8(b) and (c)).

5. Discussion

In this paper we have explored the effects of spatial structure on two common evolutionary scenarios characterized by a large and constant supply of beneficial or deleterious mutations. In both cases the fact that selection acts through local, rather than global competition leads to profound modifications of the familiar well-mixed dynamics. For the case of adaptation the most conspicuous effect is the existence of a limiting rate of adaptation that becomes independent of the population size for large populations. At the same time the lack of communication between different parts of the habitat implies that the fitness variance grows without bound, invalidating the proportionality between these two quantities expected from Fisher’s fundamental theorem [39, 40]. Similarly, our results for Muller’s ratchet show that selection in spatial habitats is weakened to the extent that the fitness declines at a finite rate even for infinitely large populations, provided the condition $U_d/s^2 > 1$ is satisfied. Figure 9 summarizes the behavior of the rate of fitness change in the different regimes considered in this paper.

By exploiting analogies with models of surface growth, we have arrived at a detailed statistical characterization of the fitness evolution in one-dimensional spatial habitats. The model with beneficial mutations has the scaling exponents and universal distributions that belong to the KPZ universality class, and we provide evidence that the model with only deleterious mutations is in the DP class. While our model becomes similar to the PNG and non-equilibrium wetting models in the limit of strong selection, it was not...
a priori evident that the additional stochasticity associated with genetic drift would leave the asymptotic behavior unchanged.

Knowing the universality class has implications for generalizations of the model. For example, based on our understanding of KPZ-type surface growth processes, we may conclude that the saturation of the speed of adaptation holds in any habitat dimension and for a broad class of distributions of selection coefficients, including those that are fatter than exponential. Also the association between the spatial Muller’s ratchet and DP is expected to extend to two-dimensional (planar) habitats, including the dependence of the transition on the parameter combination $U_d/s^2$. The scaling exponents $\beta$ and $\alpha$ governing the transient growth of the fitness variance and its dependence on habitat size in steady state are not known exactly for dimensions larger than one [43, 44]. However, a recent simulation study of various two-dimensional KPZ-models has identified a set of geometry-dependent universal distributions that are qualitatively similar to those found in the one-dimensional case [68]. Spatial evolution models in planar habitats have been considered in the context of cancer progression, where the distribution of waiting times $t_k$ until the occurrence of a given number $k$ of mutations is of central interest [69]. In the surface growth analogy, this corresponds to the time when the surface reaches a given height. Using the probabilistic concept of first passage percolation, it can be shown that such waiting times in KPZ-type growth processes again follow KPZ statistics [46]. This implies that the distribution of ‘waiting times to cancer’, which was argued in [69] to be Gaussian for small $k$, should asymptotically approach the two-dimensional analogue of the TW distribution found in [68].

A natural open question concerns the behavior of spatial populations that can acquire both deleterious and beneficial mutations. In the well-mixed case it is known that beneficial mutations dominate the behavior of large populations, in the sense that the fitness increases at a positive rate provided that a finite fraction of mutations are beneficial [13, 15]. In preliminary simulations we have explored a one-dimensional model where both types of mutations occur at rates $U_b$ and $U_d$, respectively, with a single selection magnitude $|s| = 0.01$. When $U_d$ is small the deleterious mutations do not accumulate, but do provide a genetic load. The genetic load does not affect the adaptation of beneficial mutations, and the associated growth exponents and fitness distribution are the same as for the model without any deleterious mutations. When $U_d$ is larger, there is a competition between the accumulation of deleterious and beneficial mutations, and the fitness may go either up or down. Nevertheless, also in this situation the growth exponents are close to their KPZ values, even if the fitness is declining. A detailed investigation of this model in the light of the analogy to non-equilibrium wetting processes appears to be an interesting problem for further research.

Our one dimensional model is similar to the one dimensional frontier of an expanding planar population. Theoretical and experimental studies have found enhanced genetic drift in such populations due to smaller population densities at the front. This was called gene or allele surfing [70–72], and the literature is mostly concerned with the decreased genetic variation as a signature of recent expansions. Hallatschek and Nelson [52] studied the accumulation of deleterious mutations on an expanding front and found a genetic load analogous to equation (7) and a sharp transition where the deleterious mutants take over (see [73] for another study of ‘expansion load’). If separate mutations of the same phenotypic (or fitness) effect are distinguishable genetically, known as parallel adaptation, then they may also form patterns of interfering spatial waves [74].

An experimental test of our results would be difficult in a model system such as expanding Escherichia coli colonies, because the physical growth of the colony may induce additional effects, such as super-diffusive motion of the boundaries between genetic clones [72]. Also, the success of a beneficial mutation may depend on the inflation of the edge of the colony [75], or where the mutation occurs relative to the edge [76]. Kuhr et al [77] modeled an expanding population with two types of cells and unidirectional mutations. They found that the spatial roughening of the colony boundary changes the critical behavior of the transition to where deleterious mutants invade the front, compared to the DP behavior described above for the spatial Muller’s ratchet. Similarly, Lavrentovich et al [75] found that in a radially expanding population with deleterious mutations, there was a DP-like transition whose properties are modified by the radial expansion. Our model provides a theoretical understanding of the dynamics of beneficial and deleterious mutations in one-dimensional habitats that is separate from these additional complications.

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