1 Invasive Allele Spread under Preemptive Competition

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Summary. We study a discrete spatial model for invasive allele spread in which two alleles compete preemptively, initially only the “residents” (weaker competitors) being present. We find that the spread of the advantageous mutation is well described by homogeneous nucleation; in particular, in large systems the time-dependent global density of the resident allele is well approximated by Avrami’s law.

1.1 Introduction and Model

The spatial and temporal characteristics of the spread of an advantageous mutation are fundamental questions in population dynamics. Fisher [1] and Kolmogorov et al. [2] first addressed these questions using the framework of a simple reaction-diffusion equation [3]. That work and many others focused on the velocity of the propagating front, which exists initially and separates the two spatial regions occupied separately by the two alleles. Both continuum and discrete spatial models have successfully tackled various aspects of these problems [3, 4]. In this work we investigate how the advantageous allele emerges from “scratch”; i.e., initially the region is fully dominated by the resident allele and the advantageous allele is introduced by rare mutations. While the mutant allele has an individual-level advantage over the original one, the low probability of mutations, combined with a discrete spatial dynamics, can prevent the spread of the mutant for long times. Here we consider a model where the original “resident” and the competitively superior “invasive” allele compete for a common limiting resource preemptively [5–8].

The details of our model are as follows. We consider an $L \times L$ lattice with periodic boundary conditions. Each site can be empty or occupied by a single allele (either a resident or an invader). A lattice site represents the minimal level of locally available resource required to sustain an individual organism, hence the “excluded volume” constraint. We introduce the local occupation numbers at site $x$, $n_i(x) = 0, 1$, $i = 1, 2$, representing the number of resident and invader alleles, respectively. By virtue of the excluded volume constraint, $n_1(x)n_2(x) = 0$. New individuals arise through local clonal propagation only.
That is, an individual occupying site $x$ may reproduce if one or more neighboring sites are empty (here we consider nearest neighbor colonization only). Competition for resources, hence space, is preemptive, therefore, an occupied site cannot be colonized by either allele until the current occupant’s mortality leaves that site empty. Each individual may mutate and so carry the alternate allele; mutation is a two-way, recurrent process.

We performed dynamic Monte Carlo simulations to study the above model. Our time unit is one Monte Carlo step per site (MCSS) during which $L^2$ sites are chosen randomly. If a site is empty, it may be colonized by individuals of allele $i$ occupying neighboring sites, at the rate $\alpha_i \eta_i(x)$; $\alpha_i$ is the individual-level colonization rate and $\eta_i(x) = (1/4) \sum_{x' \in n(x)} n_i(x')$ is the density of allele $i$ around site $x$ [nn($x$) is the set of nearest neighbors of site $x$]. If a site is occupied by an individual, it can die at rate $\mu$ (regardless of the allele) or mutate to the other allele at rate $\phi$. We can summarize the local transition rules for an arbitrary site $x$ as

$$0 \xrightarrow{\alpha_1 \eta_1(x)} 1, \quad 0 \xrightarrow{\alpha_2 \eta_2(x)} 2, \quad 1 \xrightarrow{\mu} 0, \quad 2 \xrightarrow{\mu} 0, \quad 1 \xrightarrow{\phi} 2,$$

where $0, 1, 2$ indicates whether the site is empty, occupied by an individual with the resident, or an individual with the invader allele, respectively.

In the simulations, we initialized the system fully occupied by the resident allele ($n_1(x)$=1 for all $x$). We are interested in the parameter region where $\phi \ll \mu < \alpha_1 < \alpha_2$, so that mutation is a rare process, but the invader allele has a reproductive-effort advantage. Then, due to mortality, the system quickly relaxes (much too fast for mutation to play a role) to the “quasi-equilibrium” state where the resident’s population is balanced by its own clonal propagation and mortality rates (in the near absence of invaders). Throughout the simulations, we track the time-dependent global densities of the two alleles, $\rho_i(t) = (1/L^2) \sum_x n_i(x, t)$. We define the lifetime $\tau$ of the resident allele as the first passage time of $\rho_1(t)$ to one-half of its quasi-equilibrium value $\rho_1^*$.  

### 1.2 Single-Cluster and Multi-Cluster Spread

As a result of the rare mutations, individuals with the invasive allele occasionally appear in the population. An invader lacking access to nearby resources may die without propagating. If a site opens in the local neighborhood (resource becomes available), the invader may colonize it. However, the empty site is likely surrounded by more than one resident. The resident’s greater local density can compensate for its lower individual-level colonization rate, so the resident has the better chance of colonizing an empty site. Consequently, one expects small clusters of the invading allele to shrink and disappear. Residents, although weaker competitors, can prevail for some time, since preemptive competition imposes a strong constraint on the growth of the invaders.
Individuals with the advantageous allele can succeed only if they generate a cluster large enough that it statistically tends to grow at its periphery.

Snapshots of configurations and preliminary studies [9] confirm the existence of a critical cluster size, beyond which the spread of the invading allele becomes statistically favorable. Further, they also show strongly clustered growth of the invading allele. For a given set of parameters, there exists a length scale $R_o$, the typical spatial separation of invading clusters; for $L \ll R_o$, the invasion almost always occurs through the spread of a single invading cluster [single-cluster (SC) invasion], while for $L \gg R_o$ the invasion is the result of many invading clusters [multi-cluster (MC) invasion]. Conversely, fixing the linear system size $L$ and other parameters (except the mutation rate) there is a characteristic value of $\phi$ (now controlling $R_o$), such that for sufficiently low values of $\phi$, MC invasion by the advantageous allele crosses over to the SC pattern.

The above picture suggests that we can apply the framework of homogeneous nucleation and growth [10–12] to describe the spatial and temporal characteristics of the spread of the invasive allele. This framework has successfully described analogous dynamic phenomena in ferromagnetic [13–15] and ferroelectric materials [16,17], flame propagation in slow combustion [18], chemical reactions [19], and other ecological systems [9,20,21]. While local mutation is a Poisson process, lacking a Hamiltonian or an effective free energy for the model, it is not known a priori whether the nucleation of a “supercritical” cluster will also be Poisson. To this end, in the SC regime, we constructed cumulative probability distributions for the lifetime of the resident allele $P_{\text{not}}(t)$, i.e., the probability that the global density of the resident has not crossed below $\rho^*_1/2$ by time $t$. We found that these distributions are indeed
exponentials (indicating that the nucleation of a successful invading cluster is a Poisson process): $P_{\text{not}}(t) = 1$ for $t \leq t_g$ and $P_{\text{not}}(t) = \exp\left[-\left(t - t_g\right)/\langle t_n \rangle\right]$ for $t > t_g$. Here $\langle t_n \rangle$ is the average nucleation time and $t_g$ is the close-to-deterministic growth time until the advantageous mutation dominates half the system. We show results for a fixed (sufficiently small) system size for three mutation rates in Fig. 1.1(a). From the slopes of the exponentials we obtained the average nucleation times [Fig. 1.1(b)], hence the $\phi$-dependence of the nucleation rate per unit volume $I(\phi)$. Since $\langle t_n \rangle = [L^2 I(\phi)]^{-1}$, we have $I(\phi) \sim \langle t_n \rangle^{-1} \sim \phi$. In the SC regime, the invasive spread is inherently stochastic; it is initiated and completed by the first randomly nucleated successful cluster of the advantageous allele. For very low values of $\phi$, the lifetime is dominated by the very large average nucleation times, hence $\langle \tau \rangle = \langle t_n \rangle + t_g \approx \langle t_n \rangle \sim \phi^{-1}$.

In the MC regime the invasion processes becomes self-averaging and the global densities approach deterministic functions in the limit of $L \to \infty$. At the same time, $\langle \tau \rangle$ approaches a system-size independent limit. For large systems we applied the KJMA theory [10–12] (or Avrami’s law) to predict the density of the resident allele,

$$\rho_1(t) \simeq \rho_1^* e^{-\ln(2)(t/\langle \tau \rangle)^3}. \quad (1.2)$$

Our results in Fig 1.2(a) show that it is, indeed, a very good approximation. Assuming that the spreading velocity of the invading clusters is constant, KJMA theory predicts that $\langle \tau \rangle \sim [I(\phi)]^{-1/3} \sim \phi^{-1/3}$ in the MC regime. The measured exponent, $-0.304$, is not too far off [Fig. 1.2(b)], but it indicates that the assumption of a constant spreading velocity (possibly as a result of the nontrivial surface properties of the clusters) may break down.
1.3 Summary and Outlook

We studied the spread of an advantageous mutant in a two-allele population where rare mutations introduce the favored allele. We found that nucleation theory, in particular Avrami’s law, describes this phenomenon very well. Systematic studies of the critical cluster size and the cluster-size dependence of the spreading velocity are under way. The structure of the spreading clusters, in particular, the roughness of their surface, is expected to play an important role in the latter.

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22. This research is supported in part by the US NSF through Grant Nos. DMR-0113049, DMR-0426488, DEB-0342689 and by the Research Corporation through Grant No. RI0761.