Population Dynamics of Underdominance Gene Drive Systems in Continuous Space

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Abstract

Underdominance systems can quickly spread through a population, but only when introduced in considerable numbers. This promises a gene drive mechanism that is less invasive than homing drives, potentially enabling new approaches in the fight against vector-borne diseases. If regional confinement can indeed be achieved, the decision-making process for a release would likely be much simpler compared to other, more invasive types of drives. The capacity of underdominance gene drive systems to spread in a target population without invading other populations is typically assessed via network models of panmictic demes linked by migration. However, it remains less clear how such systems would behave in more realistic population models where organisms move over a continuous landscape. Here, we use individual-based simulations to study the dynamics of several proposed underdominance systems in continuous-space. We find that all these systems can fail to persist in such environments, even after an initially successful establishment in the release area, confirming previous theoretical results from diffusion theory. At the same time, we find that a two-locus two-toxin-antidote system can invade connected demes through a narrow migration corridor. This suggests that the parameter space where underdominance systems can establish and persist in a release area while at the same time remaining confined to that area could be quite limited, depending on how a population is spatially structured. Overall, these results indicate that
realistic spatial context must be considered when assessing strategies for the deployment of underdominance drives.

**Graphical Abstract**

Gene drives are genetic constructs designed to self-propagate through a population.\(^1\)–\(^3\) Such systems could be used for a variety of potential applications, including the dissemination of transgenes in disease vectors that would render them unable to transmit pathogens such as malaria or dengue.\(^1\)–\(^3\) One class of gene drives are underdominance systems, in which heterozygotes have lower fitness than drive or wild-type homozygotes. In a panmictic population, this results in a frequency-dependent rate of spread of the drive allele and an introduction frequency threshold (which is typically a function of the fitness cost of the drive\(^4\)–\(^8\)). When present below this frequency, the drive allele will tend to decrease in frequency and be lost from the population. When introduced above this frequency, it is expected to increase in frequency and potentially fix in the population. Compared to other forms of gene drives, such as CRISPR homing drives and Medea, underdominance systems typically require larger transgenic insect releases to successfully spread through a population and thus a substantially greater initial effort to establish the drive. However, a purported advantage of underdominance systems is that they can successfully establish after a large-scale release and then remain locally confined to the release region. This property could ease regulatory and public approval requirements compared to other drive systems.

Several different forms of engineered underdominance systems have been demonstrated thus far. The earliest systems involved the formation of reciprocal chromosomal translocations (RCT).\(^9\)–\(^12\) More recently, toxin-antidote systems at a single genomic locus (1L1T) have been developed,\(^13\) as well as two-allele toxin-antidote systems at a single locus (1L2T) or two genetically unlinked loci (2L2T).\(^14\) The expected population dynamics of these systems have been examined in several modeling studies, which typically focused on panmictic population models and extensions of such models to two or more discrete panmictic demes linked by migration. The 1L1T system, for example, was found to stably persist without invading a connected deme under a wide range of parameters and fitness values.\(^4\),\(^15\) It was also found to be stable in connected population networks, unless the migration rate between the demes was very high.\(^16\) Introduction threshold frequencies needed for successful establishment in a panmictic population have been calculated for both the 1L2T and 2L2T systems,\(^5\)–\(^8\) and their capacity to invade connected demes has also been studied, which was shown to be possible only with the 2L2T system for similarly sized populations.\(^6\),\(^7\) The
2L2T system has further been assessed for different release strategies, mechanisms of action, ecological parameters, payload fitness effects, and combinations with other systems. Its ability to establish in a population was found to be fairly robust to variation of these parameters.

While the behavior of underdominance systems is reasonably well understood in models of connected panmictic demes, it is more complicated to predict their dynamics for spatially explicit environments where individuals move over a continuous landscape. In such populations, allele frequencies become local quantities that can vary across space, and the overall allele frequencies in the population will no longer be the decisive factor for whether a given underdominance system is expected to spread or be lost. In fact, the bistable dynamics of underdominance systems should result in a tendency to form local regions comprised primarily either of underdominance or wild-type alleles, with nontrivial interactions at the boundaries between such regions that will determine the overall population dynamics.

A rich body of literature already exists on the general dynamics of bistable genetic systems in such continuous-space populations, based primarily on the analysis of reaction-diffusion models. The results from these studies can in principle be mapped directly onto simple underdominance gene drive systems such as the 1L1T or RCT drives. This has provided crucial insights into the expected dynamics of such systems, demonstrating fundamental differences to the dynamics in panmictic population models. For example, diffusion models suggest that only drives that have an introduction threshold below 50% in a panmictic population should be able to also advance a wave of drive alleles in a continuous-space population model. Furthermore, the release of such drives additionally requires a critical propagule size for the drive to be able to spread due to the effects of boundary curvature on the rate at which individuals encounter one another at the boundary. Thus, even for drives with panmictic introduction thresholds below 50%, the area dominated by drive alleles can contract and the drive can eventually be eliminated if it is released in too small a region. These results hold true even if the total frequency of the drive in the entire population is well above or below the panmictic threshold because the dynamics of the system will be determined by interactions at the drive/wild-type boundary. Generally, the ability of a drive to persist in a continuous-space population in the face of incoming gene flow of wild-type alleles should be higher for drives with lower introduction thresholds, and the same should be true for their ability to invade other regions.

Diffusion theory has also provided analytical expressions for the expected rate of advance at which underdominance systems will spread in one- or two-dimensional space as a function of the fitness parameters of the system. At the boundary where a region comprised primarily by drive alleles encounters a region comprised primarily by wild-type alleles, population density should be reduced due to the lower fitness of heterozygotes. Barriers to diffusion were found to stop propagation of the drive if strong enough, while density gradients should generally assist diffusion of a drive allele from higher to lower density. However, even with a boundary that is expected to be stable in a deterministic model, stochastic effects can shift this boundary. Hybrid zones between species have already provided demonstrations of such situations, which often additionally involve Allee effects.
due to population suppression in such regions.\textsuperscript{33,34} These models have also been successfully applied to \textit{Wolbachia} systems,\textsuperscript{35,36} which (when moderate to high fitness costs are present) are conceptually similar to underdominance systems in many aspects and also show frequency-dependent dynamics.\textsuperscript{35,36,45,46,37–44}

Taken together, the results from the study of bistable genetic systems in diffusion models clearly demonstrate that the dynamics of underdominance gene drive systems should be fundamentally different in spatially continuous populations compared to models of panmictic populations. Nonetheless, current assessments of the expected performance of proposed underdominance drives are still often based on models of panmictic populations or networks of such populations linked by migration.\textsuperscript{1,3,19–22,47,48,4–8,15,16,18} This could be problematic because some conclusions about the expected performance and invasiveness of these systems may not be applicable to real-world scenarios.

In addition, some aspects of more sophisticated underdominance drives may not be accurately captured by the diffusion approximation for a simple bistable genetic system. The 1L2T and 2L2T systems, for example, have distinctly different molecular mechanisms than the 1L1T and RCT systems, involving a much larger fraction of nonviable offspring, for example. This should lower population densities at the boundary between wild-type and underdominance alleles differently between these drives, which could in turn affect their quantitative performance in spatially continuous populations. Previous analytical studies have also considered only a narrow set of ecologically relevant environments, and it remains somewhat unclear how diffusion parameters in the analytical models exactly relate to the dispersal and demographic parameters in an individual-based model for an accurate comparison.

Thus, there still remains a need for more realistic, individual-based simulations to improve our quantitative understanding of the behavior of underdominance systems in continuous-space scenarios, compare different proposed drive mechanisms, and confirm the results of analytical models. Only one recent simulation-based study specifically investigated the performance of a 2L2T underdominance gene drive system in a spatially explicit population model, and this study used a grid approximation for modeling spatial dynamics.\textsuperscript{17} It was found that the release threshold required for successful invasion varied based on the release pattern, and that this threshold was often higher than for panmictic populations.\textsuperscript{17}

Here, we conduct a simulation-based investigation of the population dynamics and general performance of four engineered underdominance system (1L1T, RCT, 1L2T, and 2L2T) in several types of spatially continuous environments that may be representative of possible real-world scenarios. We first compare the intrinsic ability of these drives to advance a wave of drive alleles against wild-type alleles in a spatially continuous population under symmetric starting conditions. We then look at more realistic release scenarios in continuous space, where drive individuals are placed in a central contiguous area within a wild-type population, which can have greater density than the surrounding region. Finally, we study the ability of the different underdominance systems to persist in a release deme and invade another deme in a scenario where the demes are connected by a continuous migration corridor. We find that the spatial structure of a population has a profound impact on the fate...
of an underdominance system, often preventing successful persistence but also allowing the 2L2T system to become invasive. Throughout our study, we seek to interpret the results from our individual-based simulations in light of the previously derived analytical results from diffusion models.

MODEL

Deterministic Model.

We used a deterministic, discrete-generation model to calculate expected introduction thresholds of each drive type in a panmictic population. In this model, drive homozygotes are initially added to a population of wild-type individuals at a specified introduction frequency. The life cycle in each generation is then modeled as follows: Females select a mate randomly, with each male’s chance of being selected being proportional to his fitness value, and then generate a number of potential offspring equal to twice their fitness value. Homozygotes for a drive allele carry a fitness cost $F$, and unless otherwise specified, drive heterozygotes are assumed to have a fitness equal to the square root of the fitness of homozygotes (i.e., we assume multiplicative fitness costs of the drive allele). Certain offspring genotypes are nonviable and removed, depending on the particular drive strategy (as specified in further detail below for each specific drive type). Calculated genotype frequencies are finally normalized to obtain the true population genotype frequencies, and the process is evaluated iteratively for each generation. Note that we only model genotype frequencies, effectively assuming an infinite population. To calculate the introduction thresholds, we systematically varied introduction frequencies to detect the lowest frequency at which the drive was able to invade.

Underdominance Systems.

We studied four different types of underdominance systems that span a variety of molecular mechanisms and introduction threshold frequencies, as well as a “normal” nondriving allele for comparison:

1. **One-locus one-toxin-antidote (1L1T) system.** This system consists of a single drive allele, inserted into a single genomic locus (Figure 1A). The drive allele encodes an RNAi targeting a haploinsufficient gene (the “target”), located at the same or a different locus as the drive allele. In addition, the drive allele contains a functioning copy of the gene (the “rescue gene”), sufficiently recoded such that it is not itself prone to being targeted by the drive’s RNAi. In a homozygote for the drive allele, the target gene will be silenced, but since two copies of the rescue gene are present, the function of the haploinsufficient target will be completely restored. In heterozygotes, however, only one copy of the rescue gene is present, resulting in a lower fitness compared to either homozygote. The dynamics of this system will be determined by the relative fitness values of the heterozygote and drive homozygote in relation to the wild-type homozygote. In our model, we assume that the drive allele contains a payload that reduces fitness by a factor $F \leq 1$ in drive homozygotes relative to wild-type homozygotes. The silencing of the haploinsufficient gene in heterozygotes additionally reduces
fitness by a factor of 0.26, a value that is inspired by a previous experimental demonstration of such a system,$^{13}$ where homozygotes for the drive had a fitness of $F = 0.71$ and heterozygotes had a fitness of 0.22. Assuming that the fitness factors are multiplicative, heterozygotes then have a relative fitness of $0.26 \sqrt{F}$ in our model.

2. **Reciprocal chromosomal translocation (RCT) system.** This system consists of two drive alleles, generated by reciprocal translocation between two different chromosomes (Figure 1B). In such a system, the only three viable genotypes are homozygotes for the translocated alleles at both chromosomes, heterozygotes for the translocated alleles at both chromosomes, and homozygotes for the wild-type alleles at both chromosomes. The viable heterozygotes will then have at most 50% viable offspring, while mating pairs of homozygotes of either type will have normal numbers of offspring. We will assume more generally that one of the translocated chromosomes also carries a payload gene, and that homozygotes for both translocations have a relative fitness $F$ compared to homozygotes for the wild-type alleles at both chromosomes. The viable heterozygotes have a relative fitness of $\sqrt{F}$. When reporting drive allele frequencies, we report the frequency of the element with the payload, though both frequencies will be equal to each other.

3. **One-locus two-toxin-antidote (1L2T) system.** This system requires two different drive alleles at a single genomic locus, each encoding a different toxin, while at the same time carrying an RNAi (the “antidote”) that silences the toxin of the other drive allele (Figure 1C). In this case, the only viable genotypes are heterozygotes for the two drive alleles and homozygotes for the wild-type allele. To model possible additional fitness costs, including those of a payload gene (which could be located inside one or both drive alleles), we assume that these heterozygotes have a relative fitness $F$ compared to wild-type homozygotes. When reporting drive allele frequencies, we report the frequency of both alleles together (with each representing exactly half the total).

4. **Two-locus two-toxin-antidote (2L2T) system.** This system is a variation of the 1L2T system in which the two drive alleles are inserted into two genetically unlinked genomic loci (Figure 1D). We further assume that the antidote from one copy of a drive allele can completely silence two toxin copies from the other drive allele. In that case, the only nonviable offspring would be those individuals that inherited either one or two copies of either drive allele while not inheriting at least one copy of the other allele. We assume that one of the drive alleles could also contain a payload gene with a relative fitness $F$ in homozygotes and $\sqrt{F}$ in heterozygotes compared with wild-type individuals, while the drive allele at the other locus carries no payload or additional fitness cost. When reporting drive allele frequencies, we report the frequency of the element with the payload, though both elements should have similar frequencies.

5. **“Normal” nondriving allele.** We also considered a nondriving allele with standard Mendelian inheritance patterns. Like the drives, the allele has a
codominant fitness cost, with a relative fitness $F$ in homozygotes and $\sqrt{F}$ in heterozygotes compared to wild-type homozygotes.

We note that the experimental demonstrations of both the 1L2T and 2L2T systems are based on maternally active Medea elements, yet this system has proven difficult to transfer from Drosophila to other relevant target organisms. Thus, for our study we chose to model conceptually similar but more general underdominance systems in which the toxin and antidote effects are based on the genotype of any individual, regardless of parent.

**Basic Panmictic Population Model.**

We implemented each of the four underdominance systems in an individual-based, forward-in-time population genetic simulation framework, using the SLiM software version 3.1. Here we will first outline the general life cycle of these simulations for the basic panmictic population model. The extension to continuous space will be discussed below.

Our basic panmictic model simulates a population of sexually reproducing diploid hermaphrodites. The life cycle is based broadly on a Wright–Fisher-type model, where individuals evolve over discrete generations during which they reproduce and then die. To obtain the individuals of the next generation, we first calculate how many such individuals will be generated. In our model, this is determined by the number of individuals in the previous generation and the carrying capacity of the population. Specifically, if $N$ individuals were present in generation $t$, we will generate $10N/(1 + 9N/K)$ offspring in generation $t + 1$, where $K$ is the carrying capacity. This model produces logistic dynamics and was selected to smoothly but quickly restore the population to carrying capacity after perturbation (e.g., after the initial release of drive-carrying individuals into a wild-type population). The population size would be expected to approach $K$ under this model if all offspring were viable. However, some of our underdominance systems can have nonviable offspring, so the actual population size is often below carrying capacity.

The next step is to generate these individuals. For each one, we first draw a random individual from generation $t$ as its first parent. The probability to be drawn is proportional to each individual’s fitness. A second parent is drawn accordingly. The offspring’s genotype is then determined by Mendelian inheritance. After all offspring have been generated this way, we remove the nonviable offspring to finalize the population in generation $t + 1$.

We also study an extension of the panmictic scenario where two panmictic demes are linked by migration at rate $M$, specifying the probability that an offspring created in one deme has its parents drawn from the other deme. This represents parents mating in one population and then the female migrating to another population before laying eggs. The specific setup of this scenario and the parameters used will be detailed in the Analysis section. In one test case scenario involving drive release into one panmictic population that is connected to another by migration (a standard scenario for assessing such constructs), our results were a match to previous studies (Figures S1–S2).
Extension to Continuous Space.

In our two-dimensional continuous space model, four fundamental aspects are modified from the panmictic model. First, each individual now has properties representing their x and y coordinates in space. These coordinates are set when a new offspring is generated, by displacing its position from that of its first parent into a random direction and by a distance drawn from an exponential distribution with mean $D$, which we simply term the “dispersal rate” ($D$) of the spatial model. If a new offspring is assigned coordinates that would place it outside of the boundaries, its position is redrawn until it falls inside the arena (except for the circular release scenarios, where we used periodic toroidal boundaries).

Next, we define how spatiality impacts the mating behavior of individuals. In the panmictic model, mates could be picked among all existing individuals in the population. In the spatial model, we assume that only mates within a certain radius of the first parent can be chosen. For simplicity, we further assume that this mating radius is equal to the average dispersal distance $D$. The probability of potential mates to be picked is again proportional to their fitness. If no possible mate is present within the specified area, the first parent is redrawn until an offspring has been successfully generated. This model could be considered somewhat representative of mosquitoes where a female mates with a male that has potentially migrated to her eclosion area (after eclosing within distance $D$). Then, the female moves over an area with radius $D$ while generating her offspring.

Third, we adopt a mechanism of local density regulation. This represents local competition and prevents unrealistic agglomeration of individuals in small areas, which should be impossible in a real population due to limited local supply of resources. We implement local density regulation by defining a carrying density $ρ_K = K/A$, where $K$ is the global carrying capacity and $A$ is the total area in which the population lives. For every individual in the population, we calculate the local density $ρ_i$ of individuals present within a circle of radius $r$ centered around its location. The fitness of the individual is then rescaled using the same logistic form we used for the global carrying capacity in the panmictic scenario but using densities instead: $ω'_i = ω_i \times 10/(1 + 9ρ_i/ρ_K)$. Individuals located in more dense areas will thereby tend to have lower fitness, and thus fewer offspring, which will attenuate regional density fluctuations. For all spatial scenarios, we only studied dispersal rates of $D \geq 0.02$ (the density interaction radius $r$). This is because for $D < r$, the population becomes unrealistically fragile since many individuals can no longer find mates or disperse away from areas of high density, leading to strong clustering.

Finally, we need to specify how many offspring will actually be generated in the next generation. In the panmictic model, this was simply determined by the global carrying capacity. If we were to adopt the same approach in the spatial model, however, this would often result in biologically unrealistic behavior due to artifacts resulting from Wright–Fisher assumptions. For example, if most individuals reside in a very small area at high density, or if the overall population size was initially very low, the Wright–Fisher model would tend to generate far more offspring in the next generation than might be biologically possible due to resource competition or maximum reproductive capacity. To address this, we set the overall number of individuals present in the next generation to be the sum of the net fitness of
individuals in the previous generation. For the RCT, 1L2T, and 2L2T systems, where a fraction of offspring is expected to be nonviable, we further assume that some individuals only contributed a fraction of their net fitness to the count of offspring in the next generation (details are described in the SLiM configuration files for these models).

These complexities illustrate how the Wright–Fisher model approaches its limits for modeling spatial populations. More realistic models would likely depart from this framework and instead model mating events and litter sizes explicitly, such that the population size in the next generation would emerge naturally from these events. While this is possible in the latest versions of SLiM, we used a Wright–Fisher framework for our spatial models to ensure comparability with the panmictic scenario.

In our analyses of the behavior of the different underdominance systems in the spatial population models, we will study four specific scenarios defined by the geometry of the spatial area and the initial distribution of drive individuals. These scenarios will be described in detail in the Analysis section.

**Data Generation.**

Simulations were run on the high-performance computing cluster of the Department of Computational Biology at Cornell University with ten replicates per data point (averages are reported). All SLiM configuration files for the different underdominance strategies and study scenarios and all simulation data are available on Git Hub (https://github.com/MesserLab/UnderdominanceGeneDriveSystems). Movie examples of several simulations are available on YouTube (https://www.youtube.com/playlist?list=PLXBGSqKW8wIbbSPgHXkkeP1TDd36ZaiHv6).

**ANALYSIS**

**Introduction Thresholds in a Panmictic Population.**

To recapitulate previous findings on the ability of the four drive systems to spread in a panmictic population, we first calculated their introduction threshold frequencies as a function of the drive fitness parameter \( F \) (Figure 2). These threshold frequencies represent unstable equilibria below which the drive is expected to decrease in frequency in a panmictic population (until eventual loss) and above which it is expected to increase in frequency (either to fixation or to a high equilibrium frequency for the 2L2T drive). When wild-type and drive homozygotes have equal fitness, both the 1L1T and RCT systems have a threshold frequency of exactly 50%. The 1L2T system has a higher introduction threshold of 67%, while the 2L2T system has a lower threshold of 27%, consistent with previous results.\(^4,5,20,24,6–8,15–19\) For all four drives, these thresholds increase with increasing drive fitness cost.

**Ability of the Drives to Persist and Spread in a Symmetric Scenario.**

For organisms that live in continuous space, the global drive allele frequency in the population may not be sufficient to determine whether the drive will spread or decline. In this case, local allele frequencies could vary across space, and the spatial distribution of
alleles could become important. Underdominance systems in spatially continuous populations should in fact exhibit a tendency to separate the space into areas where drive alleles dominate and where wild-type alleles dominate. The outcome will then depend on how the boundaries between drive-dominated and wild-type-dominated areas tend to shift over time, which could be affected not only by the type of drive but also by the initial distribution in space and the geometry of the landscape.

Analytical results based on a one-dimensional reaction-diffusion model predict that a wave of drive alleles is expected to advance for drives with an introduction threshold below 50% in the panmictic model and to retreat for drives with an introduction threshold above 50%. Drives with a threshold of exactly 50% should be able to retain a stable boundary (with some diffusion and stochastic movement). For our drive systems, this would imply that only the 2L2T system should be able to actively spread in a continuous space model as long as its fitness costs are not too high (with the threshold being at roughly $F > 0.7$, according to Figure 2). The 1L2T and RCT systems should be able to retain a stable boundary only in the absence of drive fitness costs. In all other scenarios, the drive is expected to retreat.

To test whether these predictions are accurate for our 2D continuous space simulation model, we studied a symmetric scenario of a square arena where drive homozygotes (heterozygotes for both drive alleles for the 1L2T system) initially occupied the left half of the arena while wild-type homozygotes occupied the right half (Figure 3A). We assumed an edge length of 1 for the arena (and thus a total area of $A = 1$) and a carrying density of $\rho_K = K/A = 10,000$. Local population densities were estimated over a circle of radius equal to 2% of the edge-length of the arena (i.e., $r = 0.02$). The scenario was initialized by randomly placing 10,000 individuals and then converting all individuals in the left half to drive homozygotes and all individuals in the right half to wild-type. After 60 generations (at which point the behavior of the drive was clearly demonstrated), we recorded the drive allele frequencies in the left half of the arena to assess the ability of the drive to persist in the area where it was initially present and in the right half of the arena to assess its ability to spread.

We first checked that when a nondriving allele was introduced instead of an underdominance system, it indeed diffused quickly throughout the population (Figure S3). By contrast, all underdominance systems were able to maintain a distinct boundary between the region with drive individuals and the region with wild-type individuals, with the sharpness of the boundary depending on the dispersal rate and type of drive based on its ability to suppress heterozygotes (1L2T, 1L1T, RCT, and 2L2T in declining order of sharpness). Consistent with the analytical predictions of a 1D model, the 1L1T and RCT systems were able to maintain the boundary at nearly the same location over the whole 60 generations for $F = 1$, but with increasing fitness costs, the boundary started receding into the left half of the arena (Figure 3B,C). The 1L2T system was rapidly eliminated from the entire arena, even with no fitness costs and low dispersal (Figure 3D). The 2L2T system could persist in its initial region even with moderate fitness costs (Figure 3E). For low fitness costs, it could also successfully spread into the right half by pushing the boundary (Figure 3F). Higher dispersal generally accelerated the observed behavior in all these cases. Note, however, that for $F = 0.7$ (which should have resulted in an introduction threshold of approximately 50% in the panmictic model according to Figure 2, and thus a stable boundary according to analytical
predictions) the 2L2T system was still not able to always persist. This was presumably because the fitness cost of the drive led to somewhat lower overall population density in the drive-dominated area in our simulation model, which may have affected drive propagation dynamics compared to an analytical model that assumes constant population density or symmetric suppression.

**Ability of the Drives to Persist and Spread from a Central Release.**

The symmetric scenario can illustrate the general ability of the different drive systems to prevail against wild-type under symmetric starting conditions in a spatially continuous population, but it is not very representative of actual release scenarios. In practice, a drive might often be released into a smaller area of the population, for example. In that case, the boundary between drive and wild-type regions will no longer be symmetric, thereby potentially affecting its spatiotemporal dynamics in complex ways. Analytical studies specifically predict that underdominance systems should never be able to form the critical propagule required for spread in a 2D spatial model unless they have an introduction threshold below 50% in a panmictic population, with the minimum propagule size dependent on the threshold.

To study how a circular boundary impacts the ability of the four drive systems to persist and spread in our spatial model, we considered a scenario where drive individuals were released into a circle located in the center of a square arena with periodic (toroidal) boundaries (Figure 4A). The population was first allowed to equilibrate for 10 generations, and drive individuals were then released into a central circle of radius 0.25 so that they comprised 80% of the individuals in that region. For all four underdominance systems, this release size assured initial establishment in the release circle under most of the parameters studied, and higher release sizes would therefore presumably not have changed the outcome substantially. After 30 generations, at which point the wild-type allele had typically fixed over most of the parameter space, we recorded drive allele frequencies inside the initial release circle to assess persistence, and outside of the initial release circle to assess spread.

All four underdominance systems were less effective at persisting in this circle release scenario than in the symmetric scenario. Indeed, we observed that even in the absence of fitness costs, the 1L1T and RCT systems both receded in this scenario across the entire parameter range and were usually completely eliminated within 30 generations (Figure 4B,C), which is consistent with analytical results. Higher fitness costs and dispersal rate further accelerated this process. The 1L2T system was generally the fastest to recede among all systems (Figure 4D), consistent with its high introduction threshold. The 2L2T system was able to persist for low fitness costs and low dispersal (Figure 4E) and could even spread into the surrounding area at somewhat higher dispersal (Figure 4F). Yet, the parameter range under which this was observed was much more limited than in the symmetric scenario.

A drive release may be most effective if the release is sufficient to locally overwhelm wild-type individuals, but otherwise spread out as large an area as possible. A drive with a threshold of below 50% will even be able to expand with a sufficiently high release radius. To investigate this, we kept the overall number of released individuals constant (representing 80% of the population in the release area only for a release radius of 0.25), but
allowed the release radius to vary (Figure 5A). We found that the 1L1T and RCT drives would persist the longest at a high release radius, as long as the radius was small enough to allow for initially successful drive establishment (Figure 5B,C). Higher levels of dispersal tended to increase the optimal release radius and reduce drive persistence. However, nowhere over the parameter range tested was the 1L2T able to persist (Figure 5D). The 2L2T drive was able to persist when the release radius allowed it to establish a critical propagule\textsuperscript{23,24} (Figure 5E). If the radius was even slightly higher, the 2L2T drive became invasive and was able to spread throughout the arena.

These results suggest that for some populations, an optimal underdominance release strategy may be to evenly inundate the region with a sufficient number of individuals to exceed the drive’s panmictic release threshold. To test this, we performed an even release of individuals with underdominance drives carrying no fitness costs and compared the final drive frequency after 20 generations to results from identical releases in panmictic populations (Figure S6). For the 1L1T and RCT systems, there was little difference between the spatial and panmictic results. However, when dispersal was low, the drive took longer to go to fixation or be eliminated from the population. This could be because a random release always results in some clustering where some areas have higher frequencies of drive or wild-type alleles than the population average, and these clusters could be more difficult to eliminate.

If such clusters do form, we might except that they have a larger effect if the drive’s panmictic introduction threshold frequency is well above or below 50%. This is because a critical drive propagule (with a threshold under 50%) may form due to local fluctuations in frequency and then expand, even if the average frequency in a panmictic population would not be sufficient for the drive to avoid elimination. Conversely, for a drive with a threshold over 50%, a wild-type critical propagule may form under similar conditions and eventually eliminate the drive. This is consistent with our results for the 1L2T drive, which required higher release sizes to ensure drive success than in panmictic populations, particularly when dispersal was low (Figure S6). The 2L2T system similarly could invade successfully even when released slightly below its panmictic introduction threshold, though the difference from the panmictic scenario was substantially smaller than for the 1L2T drive.

**Ability of the Drives to Persist and Spread from a Central Release into a High-Density Region.**

Certain applications of underdominance systems may involve the release into an area where population density is higher than in the surrounding regions. For example, a mosquito-targeting drive could be released into a city or a wetland region, where mosquito densities can be higher than in surrounding rural areas. One dimensional analytical studies of the dynamics on underdominance systems in scenarios with density gradients predict that the spread of an allele is facilitated if it is moving from an area of high to low density.\textsuperscript{23,24} For steep enough gradients, an underdominance system with a lower than 50% threshold would be unable to advance, and conversely, a wild-type allele may be unable to advance across a gradient even if the drive introduction threshold was over 50%.

To model a scenario involving regions of different densities, we modified the circle release scenario described above so that the carrying density inside the central release circle could
be varied by a factor $x$, while keeping the carrying density outside of the circle the same as before (Figure 6A). For a given value of $x$, the release number was then adjusted accordingly such that drive individuals still initially constituted 80% of individuals inside the release circle. Persistence and spreading ability were again measured after 30 generations, at which point allele frequencies had usually reached an equilibrium over most of the parameter space.

When we doubled the carrying density of the release circle compared to that of the surrounding region ($x = 2$), both the 1L1T and RCT systems were now able to persist in the release area for low fitness costs and dispersal (Figure 6B,C). At equilibrium, the boundary typically extended somewhat beyond the initial release circle. As carrying density in the center was further increased, the 1L1T and RCT systems, for low fitness costs and high dispersal, were even able to spread into the area surrounding the circle (Figure S9B). However, in a larger arena, this would presumably take the form of an equilibrium with surrounding wild-type individuals, and the drive would still remain confined to the area immediately surrounding the region of higher density. Thus, for the 1L1T and RCT drives, a successful but confined release could potentially take place in a region of higher density if the release encompasses nearly the entire region. The 1L2T drive was unable to persist over most of the examined parameter space, except for very high carrying densities in the release circle and low fitness costs (Figure 6D). With 2-fold higher central population density, the 2L2T drive could persist over a wide range of parameters (Figure 6E) and quickly began to spread into the surrounding areas unless it had a high fitness cost (Figure 6F). Overall, the presence of a target area with higher carrying capacity seems quite effective at enabling persistence of even weaker drive systems compared to a scenario with uniform carrying capacity. However, spread by the 2L2T system was also facilitated in this case.

**Ability of the Drives to Invade a Connected Population via Migration.**

A key concern regarding any gene drive system is whether it can invade other populations that are connected to the release population by some level of migration. Due to their frequency-dependent introduction thresholds, underdominance systems are generally considered to be less invasive in this regard than other types of drives such as homing drives. This notion derives from the analyses of models where distinct demes are linked by migration (assuming panmixia within each deme). In such models, all four underdominance systems we included in this study can be prevented from spreading from one deme into another if the migration rate between them is kept sufficiently low.4,5,20,6–8,15–19

It is not immediately clear how such a scenario is naturally extended to spatially continuous populations since there are different ways in which migration between demes can be implemented. One possibility is to assume that migrants are placed randomly within the arrival deme, depicting travel by mosquitoes via high altitude winds, for example. In this case, the invasion ability of a drive should be similar to a model of two linked panmictic demes (though it may be somewhat different if the dispersal distance of individuals is low, see Figure S6). However, an alternative possibility would be that migrants tend to arrive together at certain geographic locations inside the arrival deme. This too could be a realistic assumption for many real-world populations, such as when migration occurs by human-
facilitated travel on ships moving between harbors. In this case, allele frequencies could locally be much higher in the arrival regions compared to the overall frequency in the whole deme, potentially affecting the ability of a drive to persist in the release deme and its ability to invade the wild-type deme.

To explore this possibility, we studied an idealized instantiation of such a model where two spatially continuous demes are connected by a migration corridor (Figure 7A). Such a scenario could represent a mosquito population in a marshy area connected by a stream, for example, or two cities linked by a road containing dwellings along its length. In particular, we considered two circular regions, each with radius 0.4, and connected by a migration corridor of length 0.4 and variable width w. The total area of the arena is therefore \( \approx 2\pi \times 0.4^2 + 0.4w \). Assuming a uniform carrying density of \( \rho_k = 10,000 \), this yields an expected population size of \( \approx 10,000 + 4000w \) individuals. We initialized the model with a randomly distributed population of this size. All individuals in the left circle and left half of the migration corridor were assigned to be drive individuals, while all individuals in the right half were wild-type. After 100 generations—a period long enough to ensure that alleles had time to move through the corridor and potentially invade the other deme—we recorded drive allele frequencies in the left deme to assess persistence and in the right deme to assess invasion.

For a corridor width of \( w = 0.1 \), both the 1L1T and RCT systems were able to persist in the left deme with even moderate fitness costs (Figure 7B,C), receding only inside the corridor region. The 1L2T system could persist successfully only in the absence of fitness costs and when the corridor width was small (Figure 7D). Otherwise it quickly receded. Interestingly, a high rather than a moderate level of dispersal was actually beneficial toward the persistence of these drives, presumably due to the specific geometry at the interface between the circle and the corridor where wild-type individuals trying to invade the left deme would have a hard time reaching a high enough local frequency in the presence of strong diffusion. The drive could only persist if the ratio between dispersal and corridor width was below a critical level (approximately two). The 2L2T system, on the other hand, was able to persist in the release deme even with high fitness costs (Figure 7E). It was also the only system that could successfully invade the right deme, as long as corridor width and dispersal was high and fitness costs were small (Figure 7F). For intermediate corridor width, a more moderate level of dispersal was in fact optimal for invasion, analogous to moderate dispersal levels facilitating invasion of wild-type alleles in the left deme. This again suggests that the ratio between dispersal and corridor width is an important factor affecting the outcome of a specific scenario.

Thus, under certain conditions, underdominance systems can persist in one deme of a spatially continuous population while failing to invade another deme that is connected to the former by a migration corridor. Drives that could not persist in the symmetric scenario (see Figure 3) partially regained their ability to persist in the corridor scenario, while the 2L2T system correspondingly lost some, though not all, of its ability to spread into areas where it was not initially present. Qualitatively, these results are consistent with the behavior observed in previous studies of two connected panmictic demes.⁴,⁵,²⁰,⁶–⁸,¹⁵–¹⁹ These results can also be interpreted in the light of previous analytical results derived for a one-

ACS Synth Biol. Author manuscript; available in PMC 2021 July 16.
dimensional model that included a "barrier" to migration,24,29,30 which would be seen as conceptually similar to the effects of the corridor in our model. In the diffusion model, such a barrier was found to generally reduce the capacity of an underdominance allele to spread across the barrier. While the nature of these barriers was quite different than our corridor scenario, they had the same result of reducing the capacity for successful invasion.

We next set out to compare the invasiveness of the 2L2T system between our corridor model and a model of two panmictic demes connected by migration. In particular, we modeled two demes (with panmixia within each deme) with equal carrying capacity $K = 5000$, linked by symmetric migration at rate $M$, which in this case represents the fraction of individuals being exchanged between the demes per generation. The scenario was initialized by first introducing 5000 drive homozygotes (or heterozygotes for the two different drive alleles in the 1L2T system) into the first deme and 5000 wild-type individuals into the second deme (Figures S13–S14).

For a quantitative comparison between the two-panmictic-demes model and our spatially continuous corridor model, we need a way to relate their migration parameters. This is complicated by the fact that the effective level of migration in the corridor model depends on various factors, including the geometry of the corridor and the dispersal rate $D$ (the dispersal distance of individuals, different than the migration rate $M$ in the two-panmictic-demes model, which directly specifies the exchange rate between the demes). We used the observed diffusion rate of a nondriving “normal” allele with no fitness costs as a proxy for the effective cumulative migration level between the two demes over the course of the scenario. Specifically, we considered a two-panmictic-demes scenario and a migration-corridor scenario to have comparable effective migration levels when a normal allele that was initially fixed in the first deme (and absent in the second) was able to diffuse to the same overall frequency in the second deme after a fixed number of generations.

Figure 8 shows that for comparable migration levels according to this definition, the 2L2T system is substantially more invasive in the migration-corridor model compared to the two-panmictic-demes model. In fact, after 200 generations, the drive allele in the corridor scenario typically reaches a much higher frequency in the right deme than a nondriving allele for the parameters tested, suggesting that the drive was not just diffusing into this deme, but actively spreading. Note, though, that for smaller corridor widths, there is an optimal dispersal/migration level for 2L2T invasiveness (Figure S15). In contrast, the 2L2T invasion frequency in the two-panmictic-demes model stayed well below that of the nondriving allele over the entire parameter space, suggesting that drive spread was actively hindered by its underdominance mechanism. While these differences may seem striking, they simply reflect the ability of the 2L2T system to advance a wave of drive alleles in continuous space into wild-type areas due to its low introduction threshold (as we have seen in our symmetric model in Figure 3). In this case, the wave first advances through the corridor and then across the right deme (except for small corridor sizes, where drive invasion can potentially be prevented at some rates of dispersal, see Figure S13). In the two-panmictic-demes model, on the other hand, most drive-carrying individuals that migrate to the second deme will mate with wild-type individuals, so their offspring will be heterozygous and thus less fit. This results in continuous removal of the drive from the
second population and a drive equilibrium frequency that is still well below its panmictic introduction threshold unless migration is very high.

**DISCUSSION**

The primary appeal of underdominance systems lies in the promise of a gene drive mechanism that could remain locally confined due to threshold-dependent invasion dynamics. In a panmictic population, it is relatively straightforward to predict if a given underdominance system should be able to spread since this will depend primarily on whether the overall frequency of the drive in the population is above or below its intrinsic introduction threshold.\(^4,5,20,6–8,15–19\)

This notion can be directly extended to scenarios where two panmictic demes are linked by migration. Here, whether a drive can spread between demes depends on whether the migration rate can eventually push the frequency of the drive allele above its introduction threshold in the second deme. Previous modeling studies have provided us with a relatively good understanding of the behavior of different underdominance systems in such scenarios. These studies have shown, for example, that there is typically a “safe” parameter range under which a drive can successfully spread and persist in a target deme, while still remaining unable to invade other connected demes. Drives with lower introduction thresholds tend to be more persistent than those with higher thresholds, but they also require lower migration rates to prevent invasion.\(^4,5,20,6–8,15–19\)

One important question regarding these models is how well their results translate to real-world populations that are often not panmictic, for instance when organisms occupy a large, continuous landscape. Theoretical studies suggest that the dynamics of underdominance systems should be fundamentally different in such spatially continuous populations compared to panmictic ones.\(^23–30\) For example, whether a given underdominance system can spread across such a landscape will depend not on the overall frequency of drive alleles in the population, but mainly on the intrinsic threshold-frequency of the system and whether it is initially present in a sufficiently large propagule.\(^23,24\)

In this study, we used individual-based simulations to systematically assess underdominance systems in a variety of continuous space scenarios, focusing specifically on four proposed systems (RCT, 1L1T, 1L2T, and 2L2T) that appear to be feasible with current technology. We found that their dynamics in spatially continuous populations are indeed very different from those in panmictic population models, confirming the general predictions of previous analytical studies. For example, while all four underdominance systems we studied are able to spread and persist in a panmictic population when released at sufficient frequency, in continuous space models only the low-threshold 2L2T drive was able to advance a wave of drive alleles against wild-type alleles, or spread into surrounding areas after a central release. This is consistent with analytical results predicting that only drives with introduction thresholds below 50% in panmictic models should be able to spread effectively in such spatial scenarios.
Our results also suggest that even those underdominance systems with a threshold of approximately 50% in a panmictic model may have only limited ability to persist in a spatially continuous population after a release. Indeed, neither the RCT nor the 1L1T drives were able to persist in our circular release scenario, unless the release area also had a higher carrying density than the surrounding area. This is likely a general consequence of the geometrical disadvantage drive alleles experience compared to wild-type alleles in such a release scenario, since they encounter wild-type individuals at a concave boundary. An individual located at the boundary will thus observe a local drive allele frequency of <50% in its immediate vicinity, which is below the threshold frequency of the 1L1T and RCT systems. Only the 2L2T system could potentially persist in such a scenario, with the outcome (including its ability to spread) determined by the radius of the initial release, the drive fitness, and the dispersal rate.

One of the most striking differences we found between the panmictic and spatially continuous models was the much higher invasiveness of the 2L2T system when migration was able to proceed through a corridor in the spatial model, as compared to a model of two linked panmictic demes with similar overall levels of migration. Thus, we argue that the 2L2T system must be considered invasive in the absence of moderate to high fitness costs for a wide range of possible scenarios. This is in stark contrast to population models of two panmictic demes linked by migration, where this system was not found to be invasive for low migration rates.

The high invasiveness of the 2L2T system in the corridor scenario can be explained by the ability of this system to advance a wave of drive alleles in continuous space, but the magnitude of the effect was still remarkable. Furthermore, while migration through a corridor could be quite common in real-world population, this phenomenon may not actually rely on the existence of a continuous corridor in space. It could be generally applicable to any scenario where migrants tend to cluster in specific geographic locations of the arrival population, such as harbors. In this case, there could be areas with sufficiently high drive allele frequencies in the arrival population that could serve as “seeds” for invasion, even if migration is comparatively low on the scale of the population as a whole. In practice, it would be quite difficult to rule out such a scenario for any given population. Approaches that aim to infer effective migration rates between distant regions based on neutral genetic differentiation, for example, would presumably have difficulty in reliably distinguishing such a scenario from one where migrants are distributed uniformly. Thus, caution should be used when relying on the predictions of panmictic deme models for assessing the invasiveness of an underdominance system in a real-world application, since this may substantially underestimate drive invasiveness. Similar considerations apply to assessments of a high-threshold drive’s ability to persist in the face of wild-type reinvasion.

To accurately predict the dynamics of underdominance systems in real-world populations, model realism may still need to go well beyond the basic level we considered here and include factors such as overlapping generations and various other details of the lifecycle that could affect drive dynamics. For example, habitats of Anopheles mosquitoes are often highly seasonal, with both persistence in the dry season and long-distance migration potentially playing an important role in reestablishing a population at the beginning of a season.
Underdominance systems may have markedly different behavior in models of such environments compared to both panmictic and basic continuous-space models. Furthermore, the migration corridor scenario we used to illustrate the invasiveness of the 2L2T system in continuous-space populations was necessarily highly idealized. Real corridors may have different ecological characteristics than the primary demes, such as different dispersal levels and carrying capacities, changing the effective critical ratio between dispersal and corridor width. If the “corridor” represents shipping routes, for instance, populations could potentially even evolve on the ships during transit, or perhaps arrive in larger batches with multiple generations in between arrival batches. All these system-specific factors could potentially alter the actual invasiveness of a drive.

In comparing the relative merits of the four different underdominance systems in spatial scenarios, we observed several general patterns. While we found that the 1L2T system can establish in a local region the most quickly, it is also highly vulnerable to reinvasion by wild-type individuals. Thus, this system would likely be of use only on small islands or in otherwise highly isolated regions with low levels of migration. The 2L2T system establishes the most slowly but can persist more stably due to its low threshold. However, this also makes it the most invasive. The intermediate threshold 1L1T and RCT systems can establish quickly, but often have trouble persisting. Comparing the two systems, RCT has lower ability to suppress wild-type alleles, making it more vulnerable to migration than 1L1T. On the other hand, RCT alleles may be less vulnerable to genomic instability causing the separation of toxin and antidote components. This advantage may be of low importance compared to other underdominance systems, particularly the 1L1T RPM-Drive system, which was recently shown to be highly stable for an extended period of time. RCT systems would also presumably suffer from reduced levels of crossovers. This could prevent the introgression of higher fitness wild-type chromosomes and thereby effectively add a fitness cost. For other systems, this reduction in fitness from laboratory genetic backgrounds compared to wild-type individuals could possibly be overcome by crossing of wild-type individuals to drive individuals prior to generating homozygous stocks for release. Without such a method, all underdominance systems would likely suffer additional fitness costs compared to wild-type individuals, resulting in higher introduction thresholds. It should be noted that population suppression is a potentially useful application of gene drive, but all the engineered systems considered here lack the power to induce substantial population suppression. However, several new CRISPR-based toxin-antidote designs have recently been proposed that would support population suppression. “Tethered” suppression drives could also be linked and confined with an underdominance system. Modeling of such systems in spatially continuous environments may be particular interesting due to the often chaotic dynamics of suppression type gene drives in structured populations.

Our results suggest two possible strategies for increasing the chance that an underdominance drive can successfully establish and persist in a spatial population. The first strategy is to ensure that the release covers the entire area of the target population at a level well above the threshold for a high-threshold drive. For a medium-threshold drive, coverage over most of the area is necessary, so that remaining pockets of wild-type individuals will experience a geometrical disadvantage after initial establishment of the drive. Importantly, this also needs to include any areas connected to the target area by moderate migration. The second strategy
is to release the drives into an area with a higher carrying capacity than the surrounding area. This could allow a medium-threshold system to persist, and potentially even a high-threshold system if the difference in carrying capacity from the surrounding area is sufficiently large with a sharp boundary. However, even a narrow migration corridor of similar density would likely result in the replacement of any high-threshold system. A 2L2T system could support a wider range of release strategies but is also much more invasive.

Our study represents one step toward improving our understanding of the behavior of underdominance systems in realistic spatial populations, but more work remains to be done. While we restricted our analysis to only those underdominance systems that have been experimentally demonstrated, other designs have also been proposed\(^7\),\(^{21,55,56,60-65}\) that could exhibit interesting dynamics in spatially continuous populations. The results we presented were all based on simulations, yet a better analytical understanding of the processes and parameters involved would certainly be helpful. Indeed, such analytical studies have already considered the effects of reduced dispersal on the containment of an underdominance system.\(^{24}\) Future studies could explore other ecological parameters and migration patterns and investigate how specific underdominance systems differ from the idealized one-locus\(^{23,36}\) and RCT\(^{25-27}\) systems on which most analytical studies have focused thus far. Overall, our results suggest that realistic spatial modeling remains critical for assessing the chances of success for any underdominance application prior to its release.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

We thank Benjamin Haller for helpful discussions and assistance with the implementation of models in SLiM. We further thank five anonymous reviewers, as well as Nicolas Bierne and Matt Edgington for valuable comments on this manuscript. This study was supported by funding from New Zealand’s Predator Free 2050 program under award SS/05/01 to P.W.M. and grants from the National Institutes of Health under awards R01GM127418 to P.W.M. and F32AI138476 to J.C.

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Figure 1.
Underdominance systems. The figure illustrates the mechanisms of action and viable genotypes for each of the four drives (blue, viable; red, not viable). (A) The 1L1T system works by targeting a haploinsufficient gene with RNAi. (B) The RCT system involves translocations of two different chromosomes. (C) The 1L2T system has two drive alleles, each containing a toxin that is compensated by a rescue gene in the other allele. Both alleles are located at the same locus. (D) The 2L2T system is a variation of the 1L1T system where the two drive alleles are located at different loci and a single copy of a rescue gene can fully compensate two copies of the toxin.
Figure 2.
Introduction threshold frequencies of underdominance systems. In a deterministic model of a panmictic population of infinite size, the introduction threshold frequencies of the four drive systems vary as a function of the fitness parameter $F$. These threshold frequencies represent unstable equilibria below which the drive is removed and above which the drive increases in frequency (either to fixation or to a high equilibrium frequency for the 2L2T drive, shown by the dashed line).
Figure 3.
Symmetric scenario. (A) The square arena is initialized with drive individuals in the left half and wild-type individuals in the right half. (B–E) Ability of the four underdominance systems to persist in the left half after 60 generations. (F) Ability of the 2L2T system to spread to the right half after 60 generations. Color gradients show final drive frequencies in the left (blue) and right (red) half of the arena. Persistence and spread heatmaps for all four systems and comparison to a nondriving allele are shown in Figure S3.
Figure 4.
Circle release scenario. (A) Square arena with drive individuals released in a central circle. (B–E) Ability of the four underdominance systems to persist after 30 generations inside the circular area of the initial drive release. (F) Ability of the 2L2T system to spread to the area outside of the initial release circle after 30 generations. Color gradients show final drive frequencies in the initial release (blue) and outer (red) areas of the arena. Persistence and spread heatmaps for all four systems and comparison to a nondriving allele are shown in Figure S4.
Figure 5.
Circle release scenario with variable introduction radius. (A) A 1 × 1 square arena with a constant number of drive individuals (the same number released in the Figure 4 scenario) with $F = 1$ released in a central circle of variable radius. (B–E) Ability of the four underdominance systems to persist inside the circular area of the initial drive release after 30 generations (note that the size of the release area varies in this scenario). (F) Ability of the 2L2T system to spread to the area outside of the initial release circle after 30 generations. Color gradients show final drive frequencies in the initial release (blue) and outer (red) areas of the arena. Persistence and spread heatmaps for all four systems and comparison to a nondriving allele are shown in Figure S5.
Figure 6.
High-density circle release scenario. (A) Rectangular arena with drive individuals released in a central circle of x-fold higher carrying density compared to the surrounding area. (B) Persistence of the 1L1T system for x = 2 in the circular area of higher density where the drive is initially released. (C) Persistence of the RCT system for x = 2. (D) Persistence of the 1L2T system as a function of x and dispersal for F = 1. (E) Persistence of the 1L2T system for x = 2. (F) Spread of the 2L2T drive for x = 2 outside the high-density area of initial drive release. Color gradients show final drive frequencies in the initial release (blue) and outer (red) areas of the arena. Figures S7–S9 show additional persistence and spread heatmaps for all four systems and additional parameter variations.
Figure 7.
Migration-corridor scenario. (A) Two circular demes are connected by a migration corridor, with drive individuals initially present in the left half of the arena and wild-type individuals in the right half. (B) Persistence of the 1L1T system for \( w = 0.1 \). (C) Persistence of the RCT system for \( w = 0.1 \). (D) Persistence of the 1L2T system as a function of \( w \) and dispersal for \( F = 1 \). (E) Persistence of the 2L2T system for \( w = 0.1 \). (F) Spread of the 2L2T system as a function of \( w \) and dispersal for \( F = 1 \). Color gradients show final drive frequencies in the left (blue) and right (red) half of the arena. Figures S10–S12 show additional persistence and invasion heatmaps for all four systems and additional parameter variations.
Figure 8.
Comparison of invasiveness of the 2L2T system between the two-panmictic-demes scenario and the migration-corridor scenario. The corridor scenario uses a corridor width of \( w = 0.1 \). The horizontal axis shows the average frequency a nondriving "normal" allele reaches in the right deme after 200 generations under the given scenario, assuming the allele was initially fixed in the left deme and absent in the right deme at the onset. To obtain the different data points shown for a given model, we varied the migration parameter over a range of values (\( M \) for the two-panmictic-demes model and \( D \) for the corridor model). For each data point, the vertical axis then shows the corresponding final frequency a 2L2T allele reaches in the same scenario, when initially present in the left deme instead of the normal allele. Points
above the dashed line ($y = x$) specify scenarios where the 2L2T allele is able to invade more effectively than the normal allele, while points below the dashed line mean that invasion of the 2L2T allele is suppressed. In the two-panmictic-demes model, the 2L2T allele remains confined to the left deme for all migration parameters tested. By contrast, in the migration-corridor model, the 2L2T allele typically invades the right deme and does so much faster than a normal allele. Figure S15 shows results for additional corridor widths and a wider range of normal allele invasion frequencies.