Conflict is everywhere. It not only takes place between species or between individuals, but also within individuals (Burt & Trivers, 2006; Queller & Strassmann, 2018). In general, all genetic elements are selected to increase the frequency at which they are copied to future generations. Most elements achieve this by increasing the fitness of the organism that carries them, which aligns the interests of the organism and its genome. However, there are also elements that increase their own representation in the future generations at the expense of the rest of the genome, without a positive fitness effect on the organism. Since some even cause harm to the organism’s fitness, these elements are known as selfish genetic elements (Burt & Trivers, 2006). Selfish genetic elements come in a variety of forms. For example, killer meiotic drivers increase their frequency in the functioning gametes of an organism by inhibiting or destroying gametes that do not carry the driver (Núñez et al., 2018).

Killer meiotic drivers work in one of two ways (Núñez et al., 2018): Either they release a killer element that attacks a target locus on the homologous chromosome, or they create a poison that attacks all meiotic products (indiscriminate of whether they carry the driver), together with an antidote that acts in cis and thus rescues only driver-carrying meiotic products. These poison-antidote drivers commonly work only in males and could cause reduced sperm.
competitiveness for reasons such as imperfect rescue and reduced gamete counts (Price & Wedell, 2008). In such a scenario, the fitness outcomes for the driver differ dramatically between monandrous and polyandrous matings. In the latter case, where sperm from multiple males compete over fertilization, the driver-carrying poor sperm competitors are at a significant disadvantage.

Females commonly mate with multiple males in wild populations (Taylor et al., 2014). The frequency of polyandry has been linked to genetic and environmental factors, for example male fertility (Sutter et al., 2019), local density (Dean et al., 2006; Firman & Simmons, 2008; Manser et al., 2020) and presence of meiotic drivers (Price et al., 2008). Less is known about meiotic drivers themselves adapting to local variation in polyandry: if drivers do better in single matings, can they somehow avoid ending up in polyandrous situations? One possibility is that drivers could increase the dispersal propensity of their carriers. This hypothesis is based on the argument that dispersal via movement to less dense populations on average may bring driver-carriers to areas with less polyandry. Dispersal could also help avoid matings with another driver-carrier; such matings cause some offspring to be homozygous for the driver, which is detrimental in several drive systems (Fishman & Kelly, 2015; Larracuente & Presgraves, 2012; Lewontin & Dunn, 1960).

We investigate these possibilities for a naturally occurring poison-antidote male meiotic driver in house mice (Mus musculus), the t haplotype, for which there is a wealth of knowledge of its traits, but we also extend our work to varying key traits in order to generalize the conclusions. The t haplotype comprises a 35 Mb linked region on an autosome, estimated to be two million years old (Kelemen & Vicoso, 2018; Silver, 1993). It manipulates spermatogenesis to increase its own chances of transmission (Amaral & Herrmann, 2021; Charron et al., 2019; Lindholm et al., 2019). Heterozygous (notation: +/-) males transmit the t haplotype with 90% probability, leaving only 10% for the homologous wildtype chromosome (denoted +). This marked contrast with the ‘fair’ Mendelian rate of transmission of 50% makes the t ‘selfish’.

Despite enjoying a transmission advantage, t does not fix or persist at high frequencies in natural populations (Ardlie & Silver, 1998). One reason is that homozygous (t/t) carriers of the t haplotype are either inviable (Klein et al., 1984) or sterile as males (Lyon, 1986), which is a large cost to the t’s fitness (Dunn & Levene, 1961; Lindholm et al., 2013; Safronova, 2009; Sutter & Lindholm, 2015). The t is, however, even less frequent in natural populations than would be predicted based on its homozygous disadvantages (Ardlie & Silver, 1998; Bruck, 1957), a pattern known as the ‘t paradox’ (Manser et al., 2011). This paradox was explained by another deleterious trait of the t: the sperm of t-carrying males (+/t), while almost exclusively transmitting the t, are less competitive than sperm of wildtype (+/+)

An increased dispersal propensity conceivably improves the t’s chances of being present in multiple populations, new populations and populations in which it is (temporarily) fitter than the wildtype (Comins et al., 1980; Hamilton & May, 1977; Levin et al., 1969). In general, dispersal leaves more resources for related kin (Hamilton & May, 1977) (in this case, other t alleles). This might not promote dispersal of t above that of the wildtype per se, since +/+ enjoy equivalent benefits as well (likewise, arguments such as ‘being present in multiple populations is beneficial’ apply to +/+ too), but for t there is a unique benefit of leaving a t-rich habitat patch. Their departure counteracts the possibility of two philopatric +/t individuals mating with each other and producing infertile or sterile t/t offspring. If dispersal of t brings its carrier to a population with a lower t frequency, the benefit occurs both at the new as well as the natal site.

As a flipside, however, entering dense, +/+ rich habitat patches induces a larger risk of losing out in sperm competition, because the frequency of polyandrous matings increases with population density in house mice (Dean et al., 2006; Firman & Simmons, 2008; Manser et al., 2020). This is the first reason why it is not straightforward to predict whether t should lead to higher dispersal. The second reason is that the spatial clustering, which is responsible for making matings risky (t individuals might often mate with other t-carriers) itself tends to dissolve as dispersal rates of t increase. To see if the emergent population structure can make higher t dispersal a stable outcome, we simulate the coevolution of t frequencies with t-induced higher dispersal, which also can be density-dependent.

The fact that the success of t is weaker in situations involving sperm competition also makes us hypothesize that net selection on t-associated density-dependent dispersal will be sensitive to assumptions regarding polyandry. If females mate with fewer males at low density, t should encourage dispersal specifically from high-density situations. On the other hand, if the homozygous costs are larger than the polyandrous disadvantage, then we would expect +/+ to disperse preferentially out of low density sites (where t frequency is expected to be high due to the effectiveness of the meiotic drive). We therefore also vary our assumptions regarding polyandry.

In this framework, t behaves somewhat like an infection (Lion et al., 2006), though for unique reasons (homozygote inviability). If t increases in frequency as a result of successfully entering new local populations, the relative fitness of t will decrease over time. Whether this selects for dispersal even out of low density habitats (with low multiple mating frequencies), depends on the balance of all the costs and benefits of dispersal. As a whole, we expect the costs and benefits of dispersal to differ between the wildtype and the t haplotype. Indeed, our previous empirical work on free-living wild house mice found that t-carrying juveniles were more likely to emigrate, and were over-represented in migration events (Runge & Lindholm, 2018, see Figure 1) as well as among dispersers in experimental setups (Runge & Lindholm, 2021).

In this study we present results from individual-based models that simulate the evolution of the t haplotype’s influence on its carrier’s dispersal propensity. We chose to analyse this question with this modelling strategy rather than an analytical one, which may provide more easily interpretable results, to incorporate ecological complexities and feedback between + and t dispersal propensities, which would have otherwise been left out.
Dispersal is the act of changing the patch and there is no other way to move between the patches, effectively making them islands. Mice that share a patch have indistinguishable physical locations.

2.2 | The population

The model tracks the haplotypes of diploid individuals of differing sex and age (overview: Table 1). An individual carries two homologous chromosomes. Each chromosome is a haplotype that comprises two or three linked loci, which differs based on whether we simulated density-dependent or density-independent dispersal propensities. One locus determines whether the haplotype is + or t. Thus, an individual can be +/- or +/-, with t/t not fully viable or fertile in some simulation conditions. The other loci determine the dispersal phenotype as described in Dispersal below. An individual’s age is the number of turns (see below) since birth.

2.3 | Initialization

At the beginning of each simulation, 5,000 mice of age 1 are placed randomly onto patches. Initially, all mice are +/- and 50% are female. All mice that are placed onto patches start with a propensity to disperse between 0 and 1 (uniformly drawn), independent of density (i.e. 0 ≤ D0 ≤ 1; D1 = 0, see below). After 10% of the simulation’s turns, 50% of all mice in the simulation, chosen randomly, are converted from +/- to +/- by converting one chromosome from + to t while keeping all dispersal loci values of that chromosome unchanged. The temporal delay in placing the t haplotype into the world is to ensure that the population has time to equilibrate to carrying capacity across the landscape before the competition between the + and the t allele begins, and to have proceeded past transient effects that are due to initializing the population with a wide range of dispersal propensities.

2.4 | Turns

Within each turn, the following procedures are run for all individuals sequentially (i.e. every procedure is done for all individuals before the next procedure begins): dispersal, mating, birth and death together with aging of the survivors. Within each behaviour, the order of individuals performing it is randomized.

2.5 | Behaviours

2.5.1 | Dispersal

One or two loci, depending on the simulated scenario, determine the dispersal phenotype. In the one-locus models, only a density-independent propensity to disperse (D0) can evolve. In the two-locus models, D0 is the intercept and D1 is the slope of dispersal propensity in relation to the number of mice on a patch (density).
The intercept $D_0$ can take values between 0 and 1 (0 and 100 per cent or percentage points) dispersal propensity, while the slope $D_1$ can go from $-1$ to 1. Individuals evaluate the density of their patch at the beginning of a turn and do not update it as some individuals begin to disperse; this ensures all individuals have the same information on the patch’s density.

One of the two haplotypes carried by each individual acts as dominant and only the values of the dominant alleles are used to determine the dispersal phenotype. In $+/t$, $t$ is always dominant, while in $+/+$ and $t/t$ one haplotype is chosen at random to be dominant. The reasons for this decision were 1) that it allows us to analyse the optimal phenotypes of the two genotypes unconstrained by the direct influence of the other genotype on an individual’s phenotype (i.e. by averaging genotype effects), 2) that additive effects led to many failed ($t$ extinction) simulations due to the increased dimensionality of selection (i.e. selection could not work on the optimal phenotype directly, but had to optimize for counteracting e.g. the effects of potential $+/+$ and $+/t$ genotypes in an individual, 3) that it should work as similar as possible for both genotypes as for example a dominant $t$, but an additive + restricted + evolution for the aforementioned reason more than $t$ evolution.

A mouse’s dispersal propensity (at the patch’s current density) is evaluated against a uniformly drawn real number between 0 and 1 to determine whether the individual disperses. A dispersing focal mouse will move to a randomly chosen new patch (dispersal is global). Dispersal is also costly, leading to death with probability $M_{disp}$.

### 2.5.2 Mating

In the mating procedure, focal females with age $\geq 1$ are approached sequentially by all males of age $\geq 1$ on the same patch, with the list of...
females ordered randomly every turn and the list of males ordered randomly for every female. The female will always mate with the first approaching male and mate with each of the subsequent approachers with a probability of \( a \), that is with on average \( 1 + a (n - 1) \) males if the local patch has \( n \) males (and the probability of only mating once is \((1 - a)^{n-1}\)). This creates a density-dependent increase in polyandry (Figure S1). Note that males are not limited in their mating (other than by females not always accepting them).

**2.5.3 | Birth**

Each mated female begins her pregnancy with up to six offspring. The number of offspring \( N_v \) at the start of the pregnancy is affected by the local density in relation to the carrying capacity of the patch (reflecting increasingly constrained resources):

\[
N_v = \text{round} \left( \frac{6}{1 + e^{0.1 \cdot (24 + (N_p - K_p))}} \right)
\]

where \( N_v \) is the number of mice on the patch with carrying capacity \( K_p \). This relationship predicts zero offspring if the local population has reached carrying capacity, exactly one offspring at \( N_v = K_p - 1 \) and increasing numbers of offspring (up to 6) when densities fall clearly below the carrying capacity (see Figure S2). This assumption avoids flooding the population with unrealistically large numbers of offspring that would make up almost all of the population in the next turn after mice died due to density (see Mortality below).

Each offspring is assigned sex independently from each other (1:1 primary sex ratio); only viable offspring will be born, at which point they are assigned an age of 0. Embryonic viability is only affected in t/t homozygotes. A t/t will be viable with the probability \( \tau \), set globally for each simulation. The sire for each young is determined independently with the following procedure. For mothers who mated singly, the sire is obvious. For mothers who mated with multiple sires, every t-carrying mate has the probability of being a sire

\[
\frac{c}{c \cdot N_x + N_{a/t}} \]

with the corresponding probability of a +/- mate being the sire

\[
\frac{1}{c \cdot N_x + N_{a/t}} \]

where \( N_v \) is the number of t-carrying (+/t or t/t) males that mated with that female, \( N_{a/t} \) is the corresponding number of +/- males and \( c \) represents the sperm-competitive ability of t-carrying males relative to +/- males. To simplify interpretation of the results, we translated \( c \) into the probability of a t-carrying male being the sire when competing against one +/- male \( P_{t, sperm} \) which is \( P_{t, sperm} = \frac{c}{c + 1} \) and we will refer to \( P_{t, sperm} \) from here. We chose \( P_{t, sperm} = 0.15 \) as the default, following experiments (Manser et al., 2017; Sutter & Lindholm, 2015) that suggest values between 0.11 and 0.19.

If the sire is +/-, the t-carrying chromosome is transmitted with probability \( P_{drift} \) (and the + -carrying chromosome with the complementary probability \( 1 - P_{drift} \)). Females, as well as +/- and t/t males transmit a randomly chosen chromosome. We do not make the chromosomes recombine, thus all loci carried by a chosen chromosome are transmitted to the next generation.

Finally, the dispersal loci \( D_i \) mutate in the offspring with a probability that is initially higher (to allow for efficient searching of the space of possible reaction norms) and gradually diminishes. All dispersal loci mutate independently with a probability of 1.0 (100%) in the beginning, which linearly decreases to \( 10^{-3} \) over the first 10% of the turns, when only +/- are in the simulation and then goes back to 1.0 as \( t \) enters and decreases again to \( 10^{-3} \) over the final 90% of the turns. This temporal variation in mutation frequency is done to allow +/- to find their optimum before \( t \) chromosomes enter and then give both + and \( t \) enough time and mutations to find an optimum for both. We found this approach to be better suited than an unchanging mutation rate, as genetic drift needs to be carefully balanced with mutations in our question due to the different effective population sizes of + and \( t \).

In case a mutation takes place, the new value of the variable will be an addition or subtraction (chosen randomly) of \( 10^{-3} \) in case of the intercept \( D_0 \) or of \( 2 \cdot 10^{-3} \) in case of the slope \( D_3 \). These values differ because of their different impact: a mutation of the slope increases or decreases the dispersal propensity at a density of 50 (mean carrying capacity) by \( 10^{-3} \), just as a mutation of the intercept does at a density of 0. Mutations that move the value outside the parameter space are set to the relevant boundary.

**2.5.4 | Mortality**

We include both density-independent and density-dependent mortality. A focal mouse dies due to density-independent causes with a probability of \( M_{\text{turn}} \) per turn. After applying this mortality to all mice, we further impose patch-specific carrying capacities \( K_p \) on the survivors, causing density-dependent mortality. The number of mice that die is \( N_p - K_p \), that is mice in excess of the carrying capacity are removed. The necessary mortality to achieve this is random with respect to traits or sex of the mice.

**2.6 | Conditions**

We refer to the set of values \( \{\sigma_{K_p} = 15, \, \sigma_{K_p} = 15, \, \alpha = 0.02 \text{ and } \tau = 0\} \) as the ‘natural condition’ as it combines moderate temporal and spatial carrying capacity heterogeneity, common female multiple mating (\( \alpha = 0.02 \) implies that almost half of all females mate with more than one male at average density, see Figure S1) and fully lethal t/t (\( \tau = 0 \)) and leads to the evolution of realistic +/- frequencies, averaging 0.32 (SD = 0.05) in two-locus models, with natural frequencies ranging from 0.14 to 0.31 in populations in which t is not very rare or absent (Ardlie & Silver, 1998). While +/- frequency was on the high end of
naturally occurring frequencies, α values above 0.02 led to unrealistically frequent t extinctions. Below, we describe the deviations from this natural condition that were also analysed to understand the effects of both deleterious t traits on the outcomes of the simulations.

2.6.1 | Female multiple mating

To examine how polyandry impacts the divergence between evolving dispersal propensities in + and t, we varied α, which impacts how likely a female mates with more than one male (see Mating), between 0 and 0.02. The number of t chromosomes in the simulation is influenced by the local density and α, see Figure S3a for this relationship in simulations where all mice disperse with probability 0.1, without any evolution of that trait).

2.6.2 | Homozygous lethality

We also varied r, the probability with which a t/t embryo is viable, to examine the extent to which t’s homozygous lethality is responsible for dispersal evolution. To keep the intended effects operating in our model, r must not be too high as otherwise +/+ will be outcompeted, which eliminates competition between + and t which we envisage to be important for the evolution of dispersal in this system. Given that we assume a dominant effect of t on dispersal in +/t, only +/+ produce the +’s phenotype and their presence is essential for understanding differences between + and t in dispersal. We set r to 0.0, 0.25 or 0.5 (for the resulting t frequencies for the latter two, see Figure S3b & c).

2.6.3 | Infertile t/t males

As described in the introduction, the consequences of t haplotype homozygosity can be either inviability or male sterility. While we focused primarily on inviable t/t (the case for the t variant in which dispersal effects were studied in Runge and Lindholm (2018) & Runge and Lindholm (2021)), we also examined conditions in which t/t were infertile as males, but fully viable (Lewontin (1962); r = 1.0). In this case we assumed that they approach females and mate with them normally, but are completely ignored as potential sires. Some females will, in such a setting, mate with infertile males only and have no offspring. The resulting t frequencies can be seen in Figure S3d.

2.6.4 | Temporal and spatial heterogeneity

We investigated differences in dispersal propensity under varying environmental heterogeneity (in the otherwise natural condition α = 0.02 & r = 0.0) in two-locus simulations. We ran all combinations of spatial heterogeneity σK_x = 0.5, 10, 15, 20, 25 and temporal heterogeneity σK_y = 0.5, 10, 15, 20, 25 and investigated how these impacted dispersal differences and t survival.

2.6.5 | Weak drive and low fitness costs

To understand if meiotic drivers generally lead to increased dispersal, we searched for and analysed combinations of homozygote viability r = 0.5…1 and drive strength P_drive = 0.5…1 in increments of 0.05 that allowed for long-term survival of both + and t, without polyandry, as well as combinations of the proportion of offspring sired by a driver-carrier in a polyandrous mating P_t-sperm = 0.0…0.5 and P-drive = 0.5…1, with r = 0; α = 0.02. All of these combinations were simulated with σK_x = 15; σK_y = 15. We only did this for one-locus models as they provided faster results.

2.7 | Execution and analysis of the simulations

We ran simulations for 100,000 (one-locus models) or 1,000,000 (two-locus) turns for each condition (see S1 for a table of how many times each condition was run). To visualize the evolved dispersal functions, we combined all simulations with the same conditions, randomly selected up to 100,000 chromosomes per haplotype (t or +) in the last 10 turns and extracted each haplotype’s loci. For the one-locus models, we then analysed the distributions of the dispersal propensity D, in the two-locus models, we analysed the dispersal propensities at low and high densities. These were defined as the mean (μ = 50) minus or plus one SD (σK_x) carrying capacity ±1 (low density: μ − σK_x ± 1, high density: μ + σK_x ± 1). These choices allow us to show the variation in dispersal propensity using violin plots.

To quantify the differences in dispersal propensity between t and +, we calculated the mean dispersal difference between the genotypes and a 95% confidence interval of this difference using a t distribution with the degrees of freedom equalling the number of individuals that were used as a basis for the difference. Whether and by how much this confidence interval overlapped 0 was used to understand whether the difference in dispersal was clear. Note that all heatmaps use their own colour-to-value distribution to ensure best visibility. All presented results are based on fully completed simulations, thereby excluding those where coexistence was not achieved (i.e. t or + died out). For an overview of all simulations that were run, including how many did not coexist until the maximum number of turns, see Table S1.

3 | RESULTS

3.1 | Dispersal is increased in +/t due to its deleterious traits

In one-locus models, +/t exhibited an increased dispersal propensity compared to +/+ in the natural condition [σK_x = 15, σK_y = 15, α = 0.02 and r = 0], with an average increase in dispersal propensity of 0.07 (95% CI: −0.01 to 0.15, Figure 2a & c, top left, Figure S4). As seen in Figure 2c, this difference became smaller with decreasing levels of polyandry (decreasing α), and also changed direction as homozygous
t/t became more viable (increasing r) when both deleterious t traits were least pronounced (α = 0 and r = 0.5). This condition made it especially difficult for + to outcompete t locally as sperm competition is absent and t/t individuals are viable, and as a result, +/+ generally dispersed more (−0.07, −0.21 to 0.06, Figure 2 c, bottom right).

### 3.2 The t evolves an increased density-dependent dispersal propensity

The two-locus model allows us to investigate differences in the density-dependence of the dispersal phenotype. In the natural condition, +/t generally evolved to disperse at much higher rates than +/+ in all densities, but more strongly at high densities (mean difference: 0.14, −0.04 to 0.32; low densities: 0.09, −0.03 to 0.2, Figure 2 b & d, top left). This difference was achieved via an increased D₁ (dispersal slope with density), while D₀ (dispersal at 0 density) was essentially identical between t and + (Figures S5 and S6).

The evolution of this difference again depended on both deleterious traits (Figure 2d). However, the results differed from the one-locus models. Higher polyandry probabilities α decreased rather than increased the mean difference in dispersal of t and + (less red colour from bottom to top in Figure 2d), but at high densities, the lower bound of the confidence interval of the difference in dispersal propensity was consistently equal or increasing with

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**Figure 2** Overview of the differences in evolved dispersal propensities between +/+ and +/t. a) Violin plot of the evolved dispersal propensities of +/+ and +/t in the natural condition with one locus. b) Violin plot of the evolved dispersal propensities in two-locus models at different local densities. c) Heatmap showing the mean difference between t and + dispersal propensities in one-locus models in varying polyandry α and t/t viability t. Red indicates increased t dispersal, blue indicates increased + dispersal. The text indicates the 95% confidence interval. The natural condition of a is in the top left corner. d) Heatmap showing the mean difference between t and + dispersal propensities in two-locus models in low and high densities. The natural condition of b is in the top left corner.
increases in $\alpha$. Similarly to the one-locus models, increases in t/t viability $\tau$ changed the direction of the difference in dispersal propensity, with mostly, but not consistently increased confidence intervals. At higher densities, +/- never clearly evolved to disperse more than +/- on average.

When investigating both genotypes separately (Figures S7 and S8), t was found to evolve the largest high-density dispersal when $\alpha > 0 \& \tau = 0$, but once again, a negative relationship between dispersal propensity and $\alpha$ can be observed. In contrast, + dispersal propensity from high densities generally increases with increasing $\alpha$, but not above t’s propensity.

### 3.3 Infertile homozygous males also select for increased dispersal

In the case where t/t males are viable but sterile, the results for the difference in dispersal between t and + were overall qualitatively the same (Figure S9) as in the case of inviable t/t described above. However, confidence intervals were larger for sterile t/t simulations and mean differences were greater (e.g. at $\alpha = 0.02$, the dispersal difference at high densities was 0.19, -0.13 to 0.52 compared to the 0.14, -0.04 to 0.32, mentioned above).

### 3.4 Spatial heterogeneity is important for t survival and dispersal

We also simulated the natural condition in two-locus models under combinations of spatial heterogeneity $\sigma_{K_s} = \{5, 10, 15, 20, 25\}$ and temporal heterogeneity $\sigma_{K_t} = \{0, 5, 10, 15, 20, 25\}$. We found that t could survive under almost all conditions with the exception of very high spatial heterogeneity $\sigma_{K_s} = 25$ and low temporal heterogeneity $\sigma_{K_t} = 5$. The differences between + and t were more pronounced with increasing spatial heterogeneity, but did not have clear pattern with temporal heterogeneity (Figure S10).

### 3.5 Weak drive with some viability costs also promotes dispersal

We found that in 100% ($n = 27$) of all combinations of $\tau$ and $P_{\text{drive}}$ that evolved a clear difference between driver and wildtype dispersal (i.e. survival of wildtype and driver, no overlap with 0 in the 95% CI), the driver had an increased dispersal propensity compared to the wildtype (Figure 3a). This was also the case in 67% ($n = 98$) of simulations without a clear difference. This result was also found in 100% ($n = 26$ for clear differences and $n = 32$ for unclear ones) of the conditions when we varied t’s disadvantage in polyandrous matings, $P_{\text{t-sperm}}$ rather than $\tau$, and $P_{\text{drive}}$ (Figure 3b).

In both cases, visual inspection revealed that the magnitude and direction of the difference was associated with the balance of drive efficacy and costs. The stronger the disadvantage of the driver (lower $P_{\text{drive}}$, lower $\tau$ or lower $P_{\text{t-sperm}}$), the more it increased dispersal. However, this relationship was least clear for changes in $P_{\text{t-sperm}}$ (Figure 3b). The models in Figure 3b were run with $\tau = 0$, which was chosen to explore a broad range of $P_{\text{t-sperm}}$ without driver fixation, but also increases driver dispersal as seen in Figure 3a.

### 4 DISCUSSION

Our results show that the t haplotype evolves a more dispersive phenotype than the wildtype under conditions that mimic natural settings (i.e. with polyandry and full t homozygous lethality), particularly at high densities. By comparing the natural condition of the t haplotype with hypothetical conditions where we varied the female mating rates and the viability and fertility of t/t, we were able to demonstrate that all of t’s known disadvantages are jointly responsible for the elevation in dispersal propensity. However, higher multiple mating frequency did not consistently result in larger dispersal differences in the two-locus models. Moreover, by varying driver efficiency, homozygous costs and polyandrous disadvantages, we showed that driver disadvantages more generally select for increased dispersal.

All of the modelled t disadvantages (polyandry, homozygous lethality and homozygous male infertility) contributed to increased dispersal of +/- or t/t over +/+ , both at high and low densities, in some or all conditions. At full homozygous lethality, no polyandry was needed to produce a clear increase of t over + dispersal in one- or two-locus models. In contrast, at 25% homozygous viability, only models with polyandry showed a conclusive increase in dispersal in one locus models, but no polyandry was needed to show a dispersal difference when density-dependent dispersal was possible. Thus, when t can evolve a density-dependent dispersal propensity, the dispersal rates diverged from + already at smaller t disadvantages. This is likely in part a result of our assumption that polyandry increased with density, a pattern also found in studies in the field (Dean et al., 2006; Firman & Simmons, 2008; Manser et al., 2020). However, polyandry did not increase the differences in dispersal in high densities with low t/t viability; under such settings, +/- individuals, too, increased their high-density dispersal with increasing polyandry. Clearly, +/- also benefit from avoiding polyandrous matings and thus engaging in sperm competition, likely with their kin, but to a lesser degree than t-carriers. Nonetheless, +/- were only as dispersive or more dispersive than t-carriers when at least one negative t trait was reduced.

We also found that t and + could co-exist in a wide range of spatially and temporally heterogeneous (or homogeneous) environments. Yet, moderate spatial heterogeneity was required to elicit a strong differentiation between +/- and +/- dispersal at high densities. No clear impact on dispersal differences could be found for temporal heterogeneity. In nature, house mice are widespread and live in very heterogeneous habitats, from less dense and more temporally heterogeneous feral to dense, more stable commensal populations.
RUNGE ET AL. (Bronson, 1979). Thus, natural habitats of house mice are spatially and temporally heterogeneous and likely fulfil the requirements for the evolution of dispersal differences.

In the alternative setting where both male and female t/t were fully viable, but male t/+ were infertile, t frequencies evolved to be much higher, but the difference in dispersal between t and +
evolved to the same qualitative pattern as in the t/t inviability scenario. Quantitatively, the difference in dispersal was higher with infertile t/t males, especially at high densities, but less convincing due to larger confidence intervals. Both scenarios imply that matings between t-carriers are deleterious and should be avoided, and dispersal helps to achieve this. Similarly, in both cases, remaining philopatric carries an increased risk of local extinction: for inviable t/t this could happen if genetic drift is strong, as t frequency is limited to 0.5 and can only drift to 0, not 1; and for infertile t/t as their fixation would crash their population. Infertile t/t males compete for resources with +/t males, which could lower t fitness, which has been speculated to select for inviable t/t (Silver, 1993). However, we found that t frequency was much higher when t/t were infertile, but viable, with either polyandry or dispersal evolution keeping t frequency at bay. An increased dispersal propensity could alleviate the negative fitness consequences of male infertility by avoiding deleterious matings, which may reduce selection towards inviability, making the latter more likely a by-product of reduced recombination (Sugimoto, 2014) rather than a selected trait when dispersal is high enough.

Finally, we also modelled driver dispersal more generally by investigating evolved dispersal differences between driver-carriers and wildtypes for two types of drivers: drivers with varying viability and drive strength in populations without any polyandry, and drivers with homozygous inviability, but varying drive strength and disadvantage in polyandrous matings. Whenever coexistence of driver and wildtype was possible, that is the driver was neither too weak nor too successful, drivers were generally selected to increase dispersal. Essentially, the less successful the driver, the more it was selected to disperse. Drivers that are not fixed or close to fixation should roughly fit into this category of not being too successful (Price et al., 2019). The wildtype was also selected to disperse when the driver was close to being too successful for coexistence, but in these conditions confidence intervals of the dispersal difference were always overlapping 0, thus our results did not predict a clear difference in dispersal. Based on these results, we predict that meiotic drivers that are genetically linked with increased dispersal should outcompete drivers that are not. Thus, it would be interesting to test other systems for the presence of increased dispersal of driver-carriers, which has so far not been done.

Previous models of the t haplotype’s dispersal phenotype, derived during a time when empirical evidence was unavailable, predicted that dispersal was particularly important for t’s fitness, either because wildtype-fixed populations should be easily infected by t (Lewontin & Dunn, 1960), or because sub-populations carrying the t would go extinct frequently (Lewontin, 1962), or because a reduction in +/t dispersers due to selection between sub-populations would lead to low t frequencies (Nunney & Baker, 1993). These studies, however, could not consider the t’s disadvantage in polyandrous contexts because it was only discovered later (Manser et al., 2011; Olds-Clarke & Peitz, 1985; Sutter & Lindholm, 2015). Ours is the first model that includes the effects of both deleterious traits on the dispersal phenotype. Our results indicate that including these traits is essential for understanding the evolution of dispersal differences between the t haplotype and the wildtype.

We did not include potentially sex-specific dispersal phenotypes in our model; for example, one could speculate that only +/t males should disperse at higher rates because of the problems their sperm encounter in multiple mating contexts. We chose this simplifying assumption primarily because we did not see sex biased effects in our long-term field study (Runge & Lindholm, 2018). Our current results show that a potentially more easily evolvable, sex-independent effect can evolve. It is also conceivable that females, as mothers of some +/t sons, may profit from moving to places where the t haplotype tends to do well. To that end, a study that asked very different questions from ours has found that fitness benefits of dispersal that are reaped a few generations after a dispersing ancestor can still select for dispersal (Travis et al., 2009). Either way, selection towards increased dispersal of +/t females is likely weaker than on +/t males. Our results, with clear differences in dispersal phenotype between +/+ and +/t when dispersal effects were constrained to be identical for both sexes, reflect the result of selection that is averaged over the two sexes.

There is an ongoing effort to create a male-determining-gene carrying t haplotype drive system (t-SRY) to eradicate harmful house mouse populations (Gemell & Tompkins, 2017; Kanavy & Serr, 2017; Piaggio et al., 2017). It is crucial for the safety and success of this project to understand the dynamics of the t in the wild (Manser et al., 2019). In this study, we have provided evidence that t-carrying mice can be expected to have an increased dispersal propensity, which could help them spread a modified t haplotype further than planned. It is therefore important to model the influence of increased dispersal when considering the impact of the t-SRY system in the wild.

Our study provides, to our knowledge, the novel result and explanation of how an intragenomic conflict involving a meiotic driver can select for increased dispersal of driver-carrying individuals. Changes in behaviour of driver-carriers have so far rarely been documented. A comparable phenomenon is found in fire ants where colonies of ants carrying a driving supergene are differently organized than those of non-carriers (Ross & Shoemaker, 2018; Wang et al., 2013). In general, parasites (that are not drives) often benefit from increasing the dispersal rate of their hosts (Lion et al., 2006) or increasing their mating rate (e.g. the increased mating rate of Wolbachia-infected flies (Champion de Crespigny et al., 2006)). In summary, we showed how drivers can evolve an increased dispersal of their carriers. With this, we add another layer to the already complex intragenomic conflict between the driver and the rest of the genome.

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CONFLICT OF INTEREST
The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS
JNR conceived the study, programmed the simulation, and analyzed the data. JNR and HK contributed to simulation design. JNR, HK, and AKL wrote the manuscript.

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This article has been awarded Open Materials, Open Data, Badges. All materials and data are publicly accessible via the Open Science Framework at https://zenodo.org/record/4486286; https://github.com/jnrunge/t-vs-w-dispersal-evolution.

DATA AVAILABILITY STATEMENT
The code of the simulation is available at https://github.com/jnrunge/t-vs-w-dispersal-evolution/. The data is available at https://doi.org/10.5281/zenodo.4486286.

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REFERENCES
Amaral, A., & Herrmann, B. G. (2021). RAC1 controls progressive movement and competitiveness of mammalian spermatocytes. PLOS Genetics, 17, e1009308. https://doi.org/10.1371/journal.pgen.1009308
Ardlie, K. G., & Silver, L. M. (1998). Low frequency of t haplotypes in natural populations of house mice (Mus musculus domesticus). Evolution, 52, 1185–1196. https://doi.org/10.2307/2411247
Bronson, F. H. (1979). The reproductive ecology of the house mouse. The Quarterly Review of Biology, 54, 265–299. https://doi.org/10.1086/411295
Bruck, D. (1957). Male segregation ratio advantage as a factor in maintaining lethal alleles in wild populations of house mice. Proceedings of the National Academy of Sciences, 43, 152–158. https://doi.org/10.1073/pnas.43.1.152
Burt, A., & Trivers, R. L. (2006). Genes in conflict. Harvard University Press.
Champion de Crespigny, F. E., Pitt, T. D., & Wedell, N. (2006). Increased male mating rate in Drosophila is associated with Wolbachia infection. Journal of Evolutionary Biology, 19, 1964–1972. https://doi.org/10.1111/j.1420-9101.2006.01143.x
Charron, Y., Willert, J., Lipkowitz, B., Kusecek, B., Herrmann, B. G., & Bauer, H. (2019). Two isoforms of the RAC-specific guanine nucleotide exchange factor TIA1M2 act oppositely on transmission ratio distortion by the mouse t-haplotype. PLOS Genetics, 15, e1007964. https://doi.org/10.1371/journal.pgen.1007964
Comins, H. N., Hamilton, W. D., & May, R. M. (1980). Evolutionarily stable dispersal strategies. Journal of Theoretical Biology, 82, 205–230. https://doi.org/10.1016/0022-5193(80)90099-5
Dean, M. D., Ardlie, K. G., & Nachman, M. W. (2006). The frequency of multiple paternity suggests that sperm competition is common in house mice (Mus domesticus). Molecular Ecology, 15, 4141–4151. https://doi.org/10.1111/j.1365-294X.2006.02868.x
Dowle, M., & Srivivasan, A. (2019). Data.table: Extension of ‘data.frame’. Retrieved from: https://cran.r-project.org/package=data.table
Dunn, L. C., & Levene, H. (1961). Population dynamics of a variant t-allele in a confined population of wild house mice. Evolution, 15, 385. https://doi.org/10.2307/2406306
Firman, R. C., & Simmons, L. W. (2008). Polanydriad, sperm competition, and reproductive success in mice. Behavioral Ecology, 19, 695–702. https://doi.org/10.1093/beheco/arm158
Fishman, L., & Kelly, J. K. (2015). Centromere-associated meiotic drive and female fitness variation in Mimulus. Evolution, 69, 1208–1218. https://doi.org/10.1111/evo.12661
Gemmell, N. J., & Tompkins, D. M. (2017) Gene drives and rodent control: response to Piaggio et al. Trends in Ecology and Evolution, 32, 314–315. https://doi.org/10.1016/j.tree.2017.03.005
Hamilton, W. D., & May, R. M. (1977). Dispersal in stable habitats. Nature, 269, 578–581. https://doi.org/10.1038/269578a0
Kanavy, D., & Serr, M. (2017). Sry gene drive for rodent control: reply to Gemmell and Tompkins. Trends in Ecology and Evolution, 32, 315–316. https://doi.org/10.1016/j.tree.2017.03.006
Kelemen, R. K., & Vicoso, B. (2018). Complex history and differentiation patterns of the t-haplotype, a mouse meiotic driver. Genetics, 208, 365–375. https://doi.org/10.1534/genetics.117.300513
Klein, J., Sipos, P., & Figueroa, F. (1984). Polymorphism of t-complex genes in European wild mice. Genetic Research, 44, 39–46. https://doi.org/10.1017/S0016672300026239
Larrauente, A. M., & Presgraves, D. C. (2012). The selfish segregation distorter gene complex of Drosophila melanogaster. Genetics, 192, 33–53. https://doi.org/10.1534/genetics.112.141390
Levin, B. R., Petras, M. L., & Rasmussen, D. I. (1969). The effect of migration on the maintenance of a lethal polymorphism in the house mouse. The American Naturalist, 103, 647–661.
Lewontin, R. C. (1962). Interdeme selection controlling a polymorphism in the house mouse. The American Naturalist, 96, 65–78. https://doi.org/10.1086/282208
Lewontin, R. C., & Dunn, L. C. (1960). The evolutionary dynamics of a polymorphism in the house mouse. Genetics, 45, 705–722.
Lindholm, A. K., Musolf, K., Weidt, A., & König, B. (2013). Mate choice for genetic compatibility in the house mouse. Ecology and Evolution, 3, 1231–1247. https://doi.org/10.1002/ece3.534
Lindholm, A. K., Sutter, A., Künzeli, S., Tautz, D., & Rehrauer, H. (2019). Effects of a male meiotic driver on male and female transcriptomes in the house mouse. Proceedings of the Royal Society B: Biological Sciences, 286, 20191927. https://doi.org/10.1098/rspb.2019.1927
Lion, S., van Baalen, M., & Wilson, W. G. (2006). The evolution of parasite manipulation of host dispersal. Proceedings of the Royal Society B: Biological Sciences, 273, 1063–1071. https://doi.org/10.1098/rspb.2005.3412
Lyon, M. F. (1986). Male sterility of the mouse t-complex is due to homozygosity of the distorter genes. Cell, 44, 357–363. https://doi.org/10.1016/0092-8674(86)90770-1
Manser, A., Correll, S. J., Sutter, A., Blondel, D. V., Serr, M., Godwin, J., & Price, T. A. R. (2019). Controlling invasive rodents via synthetic gene drive and the role of polyandry. Proceedings of the Royal Society B: Biological Sciences, 286, 20190852. https://doi.org/10.1098/rspb.2019.0852
Manser, A., König, B., & Lindholm, A. K. (2020). Polyandry blocks gene drive in a wild house mouse population. Nature Communications, 11, 5590. https://doi.org/10.1038/s41467-020-18967-8
Manser, A., Lindholm, A. K., König, B., & Bagheri, H. C. (2011). Polyandry and the decrease of a selfish genetic element in a wild house mouse population. Evolution, 65, 2435–2447. https://doi.org/10.1111/j.1558-5646.2011.01336.x
Manser, A., Lindholm, A. K., Simmons, L. W., & Firman, R. C. (2017). Sperm competition suppresses gene drive among experimentally
evolving populations of house mice. *Molecular Ecology*, 38, 42–49. https://doi.org/10.1111/mec.14215

Núñez, M. A. B., Nuckolls, N. L., & Zanders, S. E. (2018). Genetic villains: killer meiotic drivers. *Trends in Genetics*, 34, 424–433. https://doi.org/10.1016/j.tig.2018.02.003

Nunney, L., & Baker, A. E. M. (1993). The role of deme size, reproductive patterns, and dispersal in the dynamics of t-lethal haplotypes. *Evolution*, 47, 1342–1359. https://doi.org/10.2307/2410152

Olds-Clarke, P., & Peitz, B. (1985). Fertility of sperm from t/+ mice: Evidence that a+-bearing sperm are dysfunctional. *Genetical Research*, 47, 49–52. https://doi.org/10.1017/S0016672300024502

Piaggio, A. J., Segelbacher, G., Seddon, P. J., Alphey, L., Bennett, E. L., Carlson, R. H., Friedman, R. M., Kanavy, D., Phelan, R., Redford, K. H., Rosales, M., Slobodian, L., & Wheeler, K. (2017). Is it time for synthetic biodiversity conservation? *Trends in Ecology and Evolution*, 32, 97–107. https://doi.org/10.1016/j.tree.2016.10.016

Price, T. A. R., Hodgson, D. J., Lewis, Z., Hurst, G. D. D., & Wedell, N. (2008). Selfish genetic elements promote polyandry in a fly. *Science*, 322, 1241–1243. https://doi.org/10.1126/science.1163766

Price, T. A. R., Verspoor, R., & Wedell, N. (2019). Ancient gene drives: An evolutionary paradox. *Proceedings of the Royal Society B: Biological Sciences*, 286, 20192267. https://doi.org/10.1098/rspb.2019.2267

Price, T. A. R., & Wedell, N. (2008). Selfish genetic elements and sexual selection: their impact on male fertility. *Genetica*, 134, 99–111. https://doi.org/10.1007/s10709-008-9253-y

Queller, D. C., & Strassmann, J. E. (2018). Evolutionary conflict. *Annual Review of Ecology, Evolution, and Systematics*, 49, 73–93. https://doi.org/10.1146/annurev-ecolsys-110617-062527

Ross, K. G., & Shoemaker, D. (2018). Unexpected patterns of segregation distortion at a selfish supergene in the fire ant *Solenopsis invicta*. *BMC Genetics*, 19, 101. https://doi.org/10.1186/s12863-018-0685-9

Runge, J.-N., & Lindholm, A. K. (2018). Carrying a selfish genetic element on sperm competitiveness in house mice. *Behavioral Ecology*, 29, 376–383. https://doi.org/10.1016/j.tree.2016.10.016

Taylor, M. L., Price, T. A. R., & Wedell, N. (2014). Polyandry in nature: a global analysis. *Trends in Ecology and Evolution*, 29, 151–158. https://doi.org/10.1016/j.tree.2009.03.008

Wang, J., Wurm, Y., Nipitwattanaphon, M., Riba-Grognuz, O., Huang, Y.-C., Shoemaker, D., & Keller, L. (2013). A Y-like social chromosome causes alternative colony organization in fire ants. *Nature*, 493, 664–668. https://doi.org/10.1038/nature11832

Wickham, H. (2009). ggplot2: Elegant graphics for data analysis. Springer, New York. https://doi.org/10.1007/978-0-387-98141-3

Wickham, H. (2019). *Strings: Simple, consistent wrappers for common string operations*. Retrieved from: https://cran.r-project.org/package=stringr

Wickham, H., François, R., Henry, L., & Müller, K. (2019). *Dplyr: A grammar of data manipulation*. Retrieved from: https://cran.r-project.org/package=dplyr

Wilensky, U. (1999). *NetLogo*. Center for Connected Learning; Computer-Based Modeling, Northwestern University. Retrieved from: http://ccl.northwestern.edu/netlogo/

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