

Gene drive through a landscape: Reaction–diffusion models of population suppression and elimination by a sex ratio distorter



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ABSTRACT

Some genes or gene complexes are transmitted from parents to offspring at a greater-than-Mendelian rate, and can spread and persist in populations even if they cause some harm to the individuals carrying them. Such genes may be useful for controlling populations or species that are harmful. Driving-Y chromosomes may be particularly potent in this regard, as they produce a male-biased sex ratio that, if sufficiently extreme, can lead to population elimination. To better understand the potential of such genes to spread over a landscape, we have developed a series of reaction–diffusion models of a driving-Y chromosome in 1-D and radially-symmetric 2-D unbounded domains. The wild-type system at carrying capacity is found to be unstable to the introduction of driving-Y males for all models investigated. Numerical solutions exhibit travelling wave pulses and fronts, and analytical and semi-analytical solutions for the asymptotic wave speed under bounded initial conditions are derived. The driving-Y male invades the wild-type equilibrium state at the front of the wave and completely replaces the wild-type males, leaving behind, at the tail of the wave, a reduced- or zero-population state of females and driving-Y males only. In our simplest model of a population with one life stage and density-dependent mortality, wave speed depends on the strength of drive and the diffusion rate of Y-drive males, and is independent of the population dynamic consequences (suppression or elimination). Incorporating an immobile juvenile stage of fixed duration into the model reduces wave speed approximately in proportion to the relative time spent as a juvenile. If females mate just once in their life, storing sperm for subsequent reproduction, then wave speed depends on the movement of mated females as well as Y-drive males, and may be faster or slower than in the multiple-mating model, depending on the relative duration of juvenile and adult life stages. Numerical solutions are shown for parameter values that may in part be representative for *Anopheles gambiae*, the primary vector of malaria in sub-Saharan Africa.

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1. Introduction

Many selfish genetic elements are able to spread and persist in populations not because they increase the survival or reproduction of individuals carrying them, but because they contrive to bias their transmission from parents to offspring above the Mendelian norm (Burt and Trivers, 2006; Werren, 2011). This phenomenon is often called gene drive, and examples of such genes include gamete killers, meiotic drivers, B chromosomes, transposable elements, and homing endonuclease genes. Because they can spread through populations even if they cause some harm to the organism, gene drive systems may be useful as tools to help control pest populations (Sinkins and Gould, 2006; Alphey, 2014; Burt, 2014).

Amongst the first selfish genes to be investigated for population control was the driving-Y chromosome (or, more precisely, male determining region) found naturally in some *Aedes aegypti* mosquito populations, which in some crosses is transmitted to more than 90% of progeny, the vast majority being sons (Craig et al., 1960; Hickey and Craig, 1966a,b). Such a gene might be expected to increase in frequency, rendering the entire population male-biased, which in turn could lead to suppression or even elimination (Hamilton, 1967). It turned out that most populations with the driving-Y also have resistant alleles, and sex ratios in nature are not severely biased (Wood and Newton, 1991). A similar phenomenon has been observed in *Culex pipiens* mosquitoes (Sweeny and Barr, 1978), but otherwise Y drive has rarely been reported from nature (Helleu et al., 2015). In mosquitoes, Y drive occurs because the development of X-bearing sperm is somehow disrupted; the molecular details are currently unknown, but cytological observations show that it is associated with breakage of the X chromosome during male meiosis (Newton et al., 1976). Recently, it

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has been demonstrated in *Anopheles gambiae* mosquitoes that a synthetic gene construct that expresses an enzyme that specifically cleaves the X chromosome during male meiosis results in the Y chromosome being transmitted to up to 95% of progeny (Galizi et al., 2014). In principle, inserting such a construct onto the Y chromosome could result in a synthetic driving-Y.

Models of random-mating populations have shown that a driving-Y chromosome can invade a population from an arbitrarily low frequency (i.e., there is no invasion threshold); that if it increases from low frequency it will go to fixation, replacing the non-driving-Y (i.e., simple models do not allow a stable intermediate equilibrium frequency); and that the population will be eliminated if the male bias is sufficiently extreme (Hamilton, 1967; Clark, 1987; Deredec et al., 2008, 2011). The dynamics of a driving-Y in spatially structured populations has been much less studied (Hamilton, 1967). North et al. (2013) used individual-based simulations of mosquitoes, each with an explicit location on a landscape, and showed it was still possible to get population elimination with a driving-Y.

Reaction–diffusion equations have been widely used to model biological invasions, both for beneficial mutations replacing a wild-type allele and for species invading a landscape (Fisher, 1937; Kolmogorov et al., 1937; Skellam, 1951; Andow et al., 1990; Shigesada and Kawasaki, 1997; Hastings et al., 2005). In these models a sufficiently localized initial condition can evolve into a travelling waveform that propagates with an asymptotically constant velocity. The wave connects a stable equilibrium state (at the tail of the wave, where the mutant gene has completely replaced the wild-type gene, or species abundance has gone to its carrying capacity) with an unstable state (at the tip of the wave, with the mutation or species absent). These methods have also been used to model the spread of maternally inherited *Wolbachia* bacteria that cause cytoplasmic incompatibility, in which case complex dynamics such as bifurcation, threshold, and Bartonian waves have been identified (Turelli and Hoffmann, 1991; Schofield, 2002; Barton and Turelli, 2011). Reaction–diffusion equations have also been used to model the sterile insect release method and exhibit travelling extinction waves (Lewis and van den Driessche, 1993).

In this paper, we apply reaction–diffusion equations to model the spatial spread of a driving-Y chromosome causing a population crash, and investigate how its spread through the population is affected by the dynamics of population suppression or extinction. In Section 2, we describe the mathematical approach that we use to analyse our systems of partial differential equations and delay PDEs. A series of models is then presented with successively more complex life histories: a one life-stage basic model (Section 3.1); a two life-stage model with immobile juveniles (Section 3.2); and the most complex model for which females mate once only at a male density-dependent rate (Section 3.3). These enhancements add significantly more complexity compared to the Fisher–KPP equation: time delay, up to seven dependent variables, differences in dispersal rate for different types, and an Allee effect. For each model, we calculate travelling waveform solutions and the linear spreading velocity of the travelling waves under bounded initial conditions. In Section 4, we extend the most complex model to two dimensions and apply it to the spatial spread of a driving-Y chromosome in *An. gambiae* mosquito populations, calculating wave speed and other characteristics that are useful in designing release strategies for disease control. In Section 5, we compare results for different models and implications for pest eradication strategies and discuss model assumptions and possible extensions.

2. Mathematical approach

We model the release of driving-Y males into a wild-type population using a series of deterministic, nonlinear reaction–diffusion

PDEs and delay PDEs of the form:

$$\frac{\partial \mathbf{U}(x, t)}{\partial t} = \mathbf{D} \cdot \frac{\partial^2 \mathbf{U}(x, t)}{\partial x^2} + \mathbf{f}(\mathbf{U}(x, t), \mathbf{U}(x, t - T_j)) \quad (1)$$

where the vector $\mathbf{U}(x, t)$ represents the population densities and other dependent variables. Dispersal is based on a local random movement of individuals through space, with the population density flux governed by Fick's first law. We allow different diffusivities for the various types (driving-Y and wild-type males, females) so that we can investigate the role of each in dispersal, where $\mathbf{D} = \text{diag}[D_i]$ is the diagonal diffusivity matrix with D_i denoting the diffusivity for type i . We model an unbounded, homogeneous domain in one spatial dimension for simplicity, although the results are extended to two spatial dimensions (radially-symmetric) in Section 4. The vector function $\mathbf{f}(\mathbf{U}(x, t), \mathbf{U}(x, t - T_j))$ represents the non-linear growth and death terms, and models with two life stages include a time delay T_j due to the immobile juvenile stage. The homogeneous equilibrium states of (1), $\mathbf{U}_{eq}$, are the non-negative solutions of $\mathbf{f}(\mathbf{U}(x, t) = \mathbf{U}_{eq}, \mathbf{U}(x, t - T_j) = \mathbf{U}_{eq}) = 0$, equivalent to setting the spatial and time derivatives in (1) to zero.

We introduce the driving-Y male into the homogeneous wild-type equilibrium state $\mathbf{U}_0 = \{U_{01}, \dots, U_{0n}\}$, where n is the number of different types or dependent variables (up to seven). For each model, we calculate the full numerical solution of the non-linear PDEs (1) using the Method of Lines, combined with the Method of Steps for models with time delay (Bellen and Zennaro, 2003). We show that travelling population density waves are established that connect $\mathbf{U}_0$ at the tip of the wave with an equilibrium state $\mathbf{U}_1 = \{U_{11}, \dots, U_{1n}\}$ behind the wave.

We now describe how we calculate the linear stability of the equilibrium states and derive analytical and semi-analytical expressions for the asymptotic wave speed by linearizing (1) around the relevant equilibrium state. We consider bounded perturbations of the dependent variables $\mathbf{U}(x, t)$ around $\mathbf{U}_0 = \{U_{01}, \dots, U_{0n}\}$. For models with time delay $T_j \neq 0$, we need to consider displacements from equilibrium that persist over an interval of at least the longest time delay, which in our system is T_j . We thus introduce localized (bounded in space) perturbations of $\mathbf{U}(x, t)$ from its equilibrium value $\mathbf{U}_0$ both at times t and $t - T_j$:

$$\delta \mathbf{U}(x, t) = \mathbf{U}(x, t) - \mathbf{U}_0 \quad \text{and} \quad \delta \mathbf{U}(x, t - T_j) = \mathbf{U}(x, t - T_j) - \mathbf{U}_0.$$

We then linearize the system of Eqs. (1), recognizing that $\mathbf{f}(\mathbf{U}_0) = 0$ (since at equilibrium the growth and death terms are balanced), to obtain:

$$\frac{\partial \delta \mathbf{U}(x, t)}{\partial t} = \mathbf{D} \cdot \frac{\partial^2 \delta \mathbf{U}(x, t)}{\partial x^2} + \mathbf{J}^0 \cdot \delta \mathbf{U}(x, t) + \mathbf{J}^1 \cdot \delta \mathbf{U}(x, t - T_j) \quad (2)$$

where the two Jacobian matrices $\mathbf{J}^0 = \left[\frac{\partial f_i}{\partial U_j(x, t)} \right]$ and $\mathbf{J}^1 = \left[\frac{\partial f_i}{\partial U_j(x, t - T_j)} \right]$ are both calculated at the equilibrium point $\mathbf{U}_0$.

We now introduce the spatial Fourier transform and temporal Laplace transform of the dependent variables, with $\widehat{\delta \mathbf{U}}(k, \omega)$ representing the spatial Fourier transformed variables and $\delta \mathbf{U}(k, \omega)$ representing the doubly-transformed variables, defined below for $k \in \mathbb{C}$ and $\omega \in \mathbb{C}$:

$$\begin{aligned} \widehat{\delta \mathbf{U}}(k, \omega) &= \int_0^\infty e^{i\omega t} \widehat{\delta \mathbf{U}}(k, t) dt \\ &= \frac{1}{\sqrt{2\pi}} \int_0^\infty \int_{-\infty}^\infty e^{-ikx + i\omega t} \delta \mathbf{U}(x, t) dx dt. \end{aligned}$$

By performing the double Fourier and Laplace transform on the linearized PDEs (2) we obtain:

$$\begin{aligned} \mathbf{S}(k, \omega) \cdot \widehat{\delta \mathbf{U}}(k, \omega) &= \widehat{\delta \mathbf{U}}(k, t = 0) \\ \implies \widehat{\delta \mathbf{U}}(k, \omega) &= \mathbf{S}^{-1}(k, \omega) \cdot \widehat{\delta \mathbf{U}}(k, t = 0) \\ &= \frac{\text{adj}[\mathbf{S}(k, \omega)]}{|\mathbf{S}(k, \omega)|} \cdot \widehat{\delta \mathbf{U}}(k, t = 0) \end{aligned}$$

with

$$\mathbf{S}(k, \omega) = -i \text{diag}[\omega] + k^2 \mathbf{D} - \mathbf{J}^0 - \mathbf{J}^T \cdot \text{diag}[e^{i\omega T_j}]$$

being the dispersion matrix of the linearized equations and $\mathbf{S}^{-1}(k, \omega)$, $\text{adj}[\mathbf{S}(k, \omega)]$, and $|\mathbf{S}(k, \omega)| = \det[\mathbf{S}(k, \omega)]$ its inverse, adjugate and determinant, respectively.

The last term in the expression for $\mathbf{S}(k, \omega)$, containing the exponential $e^{i\omega T_j}$ that arises from the Laplace transform of the time delay terms, is only present in our models with more than one life stage ($T_j > 0$).

We then take the inverse Fourier and Laplace transforms of $\widehat{\delta \mathbf{U}}(k, \omega)$:

$$\begin{aligned} \delta \mathbf{U}(x, t) &= \frac{1}{(2\pi)^{\frac{3}{2}}} \int_{-\infty}^{\infty} dk e^{ikx} \int_{i\sigma-\infty}^{i\sigma+\infty} d\omega e^{-i\omega t} \\ &\quad \times \frac{\text{adj}[\mathbf{S}(k, \omega)]}{|\mathbf{S}(k, \omega)|} \cdot \widehat{\delta \mathbf{U}}(k, t = 0) \end{aligned} \quad (3)$$

where σ is large enough to ensure that the ω contour of integration is in the region of convergence.

2.1. Linear temporal stability

We now consider the long-time asymptotic response of our system at equilibrium to (spatially bounded) initial perturbations. For an equilibrium state to be temporally unstable, the perturbations must grow with time. At long times, the exponential factor $e^{-i\omega t}$ dominates the integrand in (3), and unless $\text{Im } \omega > 0$ (since the integrand grows as $e^{(\text{Im } \omega)t}$), the integral will disappear. The integral in (3) will also vanish unless there exist pairs (k, ω) for which the integrand is singular. Singularities only arise from values of $\omega = \omega(k)$ that satisfy the dispersion relation $|\mathbf{S}(k, \omega(k))| = 0$, assuming that initial perturbations are spatially bounded (and thus their Fourier transform $\widehat{\delta \mathbf{U}}(k, t = 0)$ is an entire function in k -space). Therefore, for perturbations to persist at long times, we require solutions $\omega(k)$ of the dispersion equation which satisfy $\text{Im } \omega(k) > 0$.

For all our models, we investigate the stability of the invaded equilibrium state $\mathbf{U}_0$ (or the new equilibrium state $\mathbf{U}_1$ in the back of the wave). If a range of k values exists for which the solutions $\omega = \omega(k)$ of the relevant dispersion relation have positive imaginary parts ($\text{Im } \omega(k) > 0$), the equilibrium is linearly temporally unstable to perturbations. If not, it is linearly temporally stable.

2.2. Asymptotic wave speed

We obtain analytical or semi-analytical expressions for the asymptotic spreading speed of the driving-Y wave by extending the linearization analysis above. For a waveform solution travelling at a constant asymptotic speed v , there must exist a coordinate system moving at a speed v in which the perturbations do not grow or decay exponentially in time. We introduce such a moving frame of reference $z = x - vt$ (concentrating on the wave moving in the $+x$ direction) and (3) now becomes:

$$\begin{aligned} \delta \mathbf{U}(z, t) &= \frac{1}{(2\pi)^{\frac{3}{2}}} \int_{-\infty}^{\infty} dk e^{ik(z+vt)} \int_{i\sigma-\infty}^{i\sigma+\infty} d\omega e^{-i\omega t} \\ &\quad \times \frac{\text{adj}[\mathbf{S}(k, \omega)]}{|\mathbf{S}(k, \omega)|} \cdot \widehat{\delta \mathbf{U}}(k, t = 0). \end{aligned} \quad (4)$$

If the double integral in the inverse Laplace–Fourier transform in (4) can be calculated analytically, as for our one life-stage model, we may then directly find the travelling wave velocity v for which the perturbation neither grows nor decays asymptotically at long times (see Section 3.1.2). For more complex models for which the integral in (4) cannot be calculated analytically, we follow the method introduced by Ebert and van Saarloos (2000) and van Saarloos (2003). This method involves deforming the ω and k contours of integration around the singularity of $|\mathbf{S}(k, \omega)|^{-1}$ and a saddle point in the k -plane, respectively, to calculate the asymptotic wave speed.

We first deal with the ω -integral that corresponds to the inversion of the Laplace transform. Since the only singularities in the integrand arise from the denominator, the integral can be evaluated by closing the contour of integration around the roots $\omega(k)$ of the determinant $|\mathbf{S}(k, \omega)|$. We choose σ so that the integrand is analytic along the ω -contour of integration and apply Cauchy's Residue Theorem:

$$\begin{aligned} \int_{i\sigma-\infty}^{i\sigma+\infty} d\omega e^{-i\omega t} \frac{\text{adj}[\mathbf{S}(k, \omega)]}{|\mathbf{S}(k, \omega)|} \cdot \widehat{\delta \mathbf{U}}(k, t = 0) \\ = 2\pi i \sum_j R_j(k, \omega(k)) \end{aligned} \quad (5)$$

where $R_j(k, \omega(k))$ represents the residue of the integrand at the j th root of $|\mathbf{S}(k, \omega(k))|$.

As mentioned earlier, we are only interested in the long-time asymptotics and thus $\text{Im } \omega(k) > 0$. All our models share the property that among all solutions $\omega = \omega(k)$ of the dispersion relation $|\mathbf{S}(k, \omega(k))| = 0$, only one satisfies $\text{Im } \omega(k) > 0$ for some k s. This unique root $\omega(k)$ is a simple pole with a residue:

$$\begin{aligned} R(k, \omega(k)) &= \lim_{\omega \rightarrow \omega(k)} (\omega - \omega(k)) e^{-i\omega t} \frac{\text{adj}[\mathbf{S}(k, \omega)]}{|\mathbf{S}(k, \omega)|} \cdot \widehat{\delta \mathbf{U}}(k, t = 0) \\ &= \frac{e^{-i\omega(k)t} \text{adj}[\mathbf{S}(k, \omega(k))]}{\left. \frac{\partial |\mathbf{S}(k, \omega)|}{\partial \omega} \right|_{\omega=\omega(k)}} \cdot \widehat{\delta \mathbf{U}}(k, t = 0). \end{aligned} \quad (6)$$

At long times only this residue survives, with the sum in the RHS of (5) asymptotically reducing to $2\pi i R(k, \omega(k))$.

Incorporating (5) and (6) in (4) then yields

$$\begin{aligned} \delta \mathbf{U}(z, t) &= \frac{i}{\sqrt{2\pi}} \int_{-\infty}^{\infty} dk e^{-i[\omega(k)-vk]t} \\ &\quad \times \left[e^{ikz} \frac{\text{adj}[\mathbf{S}(k, \omega(k))]}{\left. \frac{\partial |\mathbf{S}(k, \omega)|}{\partial \omega} \right|_{\omega=\omega(k)}} \cdot \widehat{\delta \mathbf{U}}(k, t = 0) \right]. \end{aligned} \quad (7)$$

The k -integral in (7), representing the inverse Fourier transform, cannot in general be evaluated analytically (for finite t). However, as Ebert and van Saarloos (2000) and van Saarloos (2003) have pointed out, the integral can be evaluated at the asymptotic limit of $t \rightarrow \infty$ (i.e. when the waveforms are travelling at their asymptotic speed v) via a saddle point approximation (or method of steepest descent) approach. This involves a deformation of the k -contour of integration so that the only t -dependent term in the integrand, $e^{-i[\omega(k)-vk]t}$, is asymptotically dominated by the contribution of a single saddle point $k = k^*$ as $t \rightarrow \infty$. The saddle point, $k = k^*$, is where the t -dependent term has a maximum:

$$\left. \frac{\partial [-i[\omega(k) - vk]t]}{\partial k} \right|_{k=k^*} = 0 \implies \left. \frac{\partial \omega(k)}{\partial k} \right|_{k=k^*} = v$$

and the integral is dominated by the term $e^{i\text{Im}[\omega(k^*)-vk^*]t}$ as $t \rightarrow \infty$. The asymptotic spreading velocity v is selected so that

$|e^{Im[\omega(k^*) - \nu k^*]t}|$ does not grow or decay exponentially with time in the moving coordinate frame advancing with velocity ν :

$$\begin{aligned} Im[\omega(k^*) - \nu k^*] = 0 &\implies Im \omega(k^*) - \nu Im k^* = 0 \\ &\implies \nu = \frac{Im \omega(k^*)}{Im k^*}. \end{aligned}$$

Additionally, k^* and $\omega(k^*)$ satisfy the dispersion relation relevant to each model. To derive analytical or semi-analytical expressions for the asymptotic spreading velocity ν for our more advanced models, we solve the following system of equations with complex variables k^* and $\omega(k^*)$ and real variable ν :

$$\nu = \frac{Im \omega(k^*)}{Im k^*} = \frac{\partial \omega(k)}{\partial k} \bigg|_{k=k^*} \quad \text{and} \quad |S(k^*, \omega(k^*))| = 0. \quad (8)$$

3. Models

Below, we present PDE and delay-PDE models of increasing complexity for the spatial spread of the driving-Y males. For each model, we find the complete solution numerically and derive an analytical or semi-analytical expression for the wave speed using the mathematical approach above.

3.1. Basic model: one life stage

Before modelling the release of the driving-Y, we begin with a basic model for a diffusing species with one life stage, modified to track males and females separately. Individual females reproduce at a constant, density-independent rate:

$$\begin{aligned} \frac{\partial F(x, t)}{\partial t} &= D_F \frac{\partial^2 F(x, t)}{\partial x^2} + \lambda F(x, t) - (\mu + \gamma N(x, t))F(x, t) \\ \frac{\partial M(x, t)}{\partial t} &= D_M \frac{\partial^2 M(x, t)}{\partial x^2} + \lambda F(x, t) - (\mu + \gamma N(x, t))M(x, t) \end{aligned}$$

$F(x, t)$ and $M(x, t)$ are the population densities of females and males at position x and time t , with the total density given by $N(x, t) = F(x, t) + M(x, t)$. λ is the birth rate (females born per female, per unit time) and μ and γ represent density-independent and density-dependent mortality rates. Using the method outlined in Section 2.1, we find that the zero population state (empty landscape) of the system above is linearly unstable, while the state with the population at carrying capacity, $N_0 = (\lambda - \mu)/\gamma$, $F_0 = M_0 = N_0/2$, is linearly stable (details in Appendix B). If any mix of both males and females are introduced in a bounded area around the origin ($x = 0$) in an otherwise empty landscape, both male and female populations spread through the landscape and reach an asymptotic male/female ratio of 50:50.

The asymptotic speed of the travelling waves is:

$$\nu = 2\sqrt{D_F(\lambda - \mu)}.$$

In this Fisherian result for invasion of a species into an empty landscape, $(\lambda - \mu)$ represents the intrinsic rate of increase of the species at low density (see also Shigesada and Kawasaki, 1997).

3.1.1. Introduction of the driving-Y

We then model the introduction of driving-Y males, denoted by $H(x, t)$. In all models, the driving-Y male transmits the driving-Y chromosome to a fraction m ($0.5 < m \leq 1$) of its progeny, and all those inheriting the chromosome are male. The pre-release state is the wild-type equilibrium without the driving-Y present, $\mathbf{U}_0 = \{H_0, F_0, M_0\} = \{0, N_0/2, N_0/2\}$ with total population density $N_0 = (\lambda - \mu)/\gamma$. For all models, our initial condition corresponds

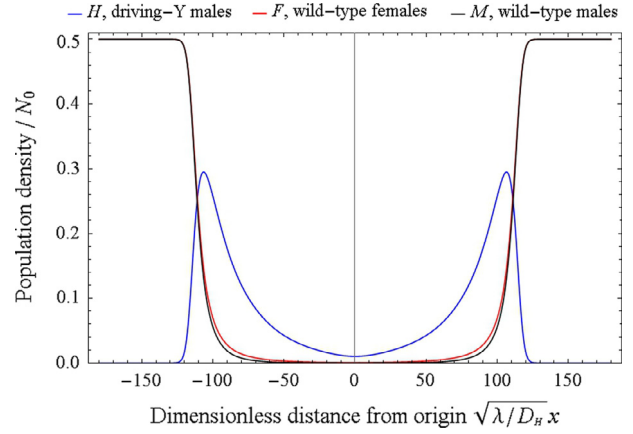


Fig. 1. Population densities $U(x, t)/N_0$ for the basic model, for $\lambda t = t/T_C = 90$ generations, intrinsic rate of increase $R_m = \lambda/\mu = 6$ and $m = 0.95$ for extinction behind the wave ($m_{crit} = 0.917$). Initial release population of driving-Y males is $h/N_0 = 0.01$ within $|x| \leq \sqrt{\lambda/D_H}x$.

to release of the driving-Y at $t = 0$ in a confined area ($-a \leq x \leq a$) of constant density h :

$$H(x, 0) = \begin{cases} h, & \text{if } -a \leq x \leq a \\ 0, & \text{if } x > |a|. \end{cases}$$

In this model, each birth is immediately preceded by a female mating with a driving-Y or wild-type male chosen randomly according to the local (in time and space) proportion of each in the total male population:

$$\begin{aligned} \frac{\partial H}{\partial t} &= D_H \frac{\partial^2 H}{\partial x^2} + 2\lambda F \left[\frac{mH}{M+H} \right] - (\mu + \gamma N)H \\ \frac{\partial F}{\partial t} &= D_F \frac{\partial^2 F}{\partial x^2} + 2\lambda F \left[\frac{(1/2)M}{M+H} + \frac{(1-m)H}{M+H} \right] - (\mu + \gamma N)F \\ \frac{\partial M}{\partial t} &= D_M \frac{\partial^2 M}{\partial x^2} + 2\lambda F \left[\frac{(1/2)M}{M+H} \right] - (\mu + \gamma N)M. \end{aligned} \quad (9)$$

The total number of adults is $N(x, t) = H(x, t) + F(x, t) + M(x, t)$. Note that if $m = 0.5$, $H(x, t)$ and $M(x, t)$ are indistinguishable and the model reduces to the one above for wild-types only.

The homogeneous equilibrium state with driving-Y males is $\mathbf{U}_1 = \{H_1, F_1, M_1\}$ and depends on the value of m and the growth parameters:

$$\mathbf{U}_1 = \begin{cases} \left\{ \frac{m[2\lambda(1-m) - \mu]}{\gamma}, \frac{(1-m)[2\lambda(1-m) - \mu]}{\gamma}, 0 \right\} & \text{if } \frac{1}{2} < m < 1 - \frac{\mu}{2\lambda} \\ \{0, 0, 0\} & \text{if } 1 - \frac{\mu}{2\lambda} \leq m \leq 1. \end{cases}$$

Above a critical value of m , $m_{crit} = 1 - \mu/(2\lambda)$, total population extinction occurs. Below this value only males with the driving-Y chromosome and females exist (at a ratio of $m/(1-m)$). This state is shown in Appendix B to be linearly stable for all m . We apply the Method of Lines to solve the full set of PDEs numerically for release of the driving-Y into the wild-type equilibrium $\mathbf{U}_0$ according to our initial conditions above. Two symmetric sets of waveforms for the female and male populations travelling in the $\pm x$ -direction at the same speed are established, connecting states $\mathbf{U}_0$ (front of the wave) and $\mathbf{U}_1$ (behind the wave). Fig. 1 shows driving-Y wave pulses invading the wild-type state (with a supercritical value of m chosen to cause population extinction behind the wave).

3.1.2. Wave speed analysis and results

We now seek the asymptotic speed of the travelling waveforms according to the method described in Section 2.2 (with $\mathbf{J}^T = \mathbf{0}$, since $T_j = 0$ for this one life-stage model), whereby we introduce a localized perturbation $\delta \mathbf{U}(x, t)$ and linearize the system of equations (9) around the equilibrium state $\mathbf{U}_0$ at the front of the wave. For this model, we find that in the set of linearized equations (2), the equation for the perturbation of the driving-Y population density, $\delta H(x, t)$, is uncoupled from the rest:

$$\frac{\partial \delta H}{\partial t} = D_H \frac{\partial^2 \delta H}{\partial x^2} + [2m\lambda - (\mu + \gamma N_0)] \delta H.$$

Due to this uncoupling, the determinant of the dispersion matrix $\mathbf{S}(k, \omega)$ corresponding to the linearized set of equations for $\delta \mathbf{U}(x, t)$ can be written as (see Appendix B):

$$|\mathbf{S}(k, \omega)| = |\mathbf{Z}^Y(k, \omega)| |\mathbf{Z}^0(k, \omega)|.$$

Here, the submatrix $\mathbf{Z}^Y$ represents the driving-Y males, and the submatrix $\mathbf{Z}^0$ represents the dispersion matrix for the wild-type system before the release of driving-Ys. This general form of the dispersion relation $|\mathbf{S}(k, \omega)|$ holds for all of the models in this paper, with $\mathbf{Z}^Y$ representing the uncoupled equation(s) of the driving population(s), in this case driving-Y males only.

For this model, with the total population density given by $N_0 = (\lambda - \mu)/\gamma$, we have:

$$|\mathbf{Z}^Y(k, \omega)| = i\omega - D_H k^2 + 2m\lambda - \mu - \gamma N_0$$

and

$$|\mathbf{Z}^0(k, \omega)| = \frac{1}{4} [\gamma N_0 (2\lambda - \gamma N_0) + (-2D_M k^2 - 2\mu - 3\gamma N_0 + 2i\omega) \times (-2D_F k^2 + 2\lambda - 2\mu - 3\gamma N_0 + 2i\omega)].$$

As discussed in Section 2.1, for travelling waves we are only interested in solutions of $|\mathbf{S}(k, \omega(k))| = 0$ with $\text{Im } \omega(k) > 0$, otherwise the population density perturbations will be damped and the equilibrium state will be linearly stable. We can see from the dispersion relation above corresponding to the driving-Y perturbation, $|\mathbf{Z}^Y(k, \omega(k))| = 0$, that the linear instability condition $\text{Im } \omega(k) > 0$ for the invaded state $\mathbf{U}_0$ is satisfied for all $|k| < \sqrt{(2m\lambda - \mu - \gamma N_0)/D_H}$. We show in Appendix B that $|\mathbf{Z}^0(k, \omega(k))| = 0$ does not have solutions with $\text{Im } \omega(k) > 0$ for any k , so the wild-type system of males and females is linearly stable to perturbations in the non-driving-Y population densities (wild-types F and M). Unstable modes appear only with the introduction of driving-Y males and are shared by all the sub-populations; thus the perturbations in all the wild-type population densities are entrained by that of the invading driving-Y males.

To find the asymptotic wave speed, as described in Section 2.2, we must compute the long-time value of the inverse Laplace–Fourier transform (4). For this one life-stage model, due to the quadratic dependence of $\omega(k)$ on k in $|\mathbf{Z}^Y(k, \omega)| = 0$, the integral in (4) can be evaluated analytically. We assume an initial perturbation to the equilibrium state $\mathbf{U}_0$ in the form of a rectangular function, $\delta \mathbf{U}(x, 0) = \{\delta H(x, 0), \delta F(x, 0), \delta M(x, 0)\} = \{h \text{rect}(\frac{x}{2a}), 0, 0\}$, that corresponds to our initial condition of localized release of driving-Y males into the wild-type equilibrium state.

For the initial condition above, we obtain for $\delta H(z, t)$ from (4)

$$\begin{aligned} \delta H(z, t) &= \frac{1}{(2\pi)^{\frac{3}{2}}} \int_{-\infty}^{\infty} dk \int_{i\sigma-\infty}^{i\sigma+\infty} d\omega e^{ikz-i[\omega-vk]t} \frac{\delta H(k, t=0)}{|\mathbf{Z}^Y(k, \omega(k))|} \\ &= \frac{ah}{2\pi^2} \int_{-\infty}^{\infty} dk \int_{i\sigma-\infty}^{i\sigma+\infty} d\omega \\ &\quad \times \frac{\text{sinc}[ak] e^{ikz-i[\omega-vk]t}}{i\omega - D_H k^2 + 2m\lambda - (\mu + \gamma N_0)} \end{aligned} \quad (10)$$

where the Fourier transform of the initial perturbation is $\widehat{\delta H}(k, t=0) = \sqrt{\frac{2}{\pi}} a h \text{sinc}[ak]$ ($\text{sinc}[x]$ is the cardinal sine function).

In the double integral in (10), the ω integral, representing the inverse Laplace transform, is a simple exponential function of k . The k integral can then be evaluated using the convolution property of the inverse Fourier transform:

$$\begin{aligned} \delta H(z, t) &= \frac{h\sqrt{\pi}}{2\sqrt{2}} e^{(2m\lambda - \mu - \gamma N_0)t} \\ &\quad \times \left(\text{erf} \left[\frac{z+a+vt}{2\sqrt{D_H t}} \right] - \text{erf} \left[\frac{z-a+vt}{2\sqrt{D_H t}} \right] \right). \end{aligned}$$

We are interested in the asymptotic wave speed v at large times and finite z , so we utilize the asymptotic series expansion of the error function for large values of its argument (Weisstein, n.d.). For large times it suffices to retain only the leading order term of the series:

$$\begin{aligned} \delta H(z, t) &\approx \frac{h}{v} \sqrt{\frac{D_H}{2t}} \left(\exp \left[-\frac{(z+a)^2}{4tD_H} - \frac{v(z+a)}{2D_H} \right] \right. \\ &\quad \left. - \left(-2m\lambda + \mu + \gamma N_0 + \frac{v^2}{4D_H} \right) t \right) \\ &\quad - \exp \left[-\frac{(z-a)^2}{4tD_H} - \frac{v(z-a)}{2D_H} \right] \\ &\quad \left. - \left(-2m\lambda + \mu + \gamma N_0 + \frac{v^2}{4D_H} \right) t \right). \end{aligned} \quad (11)$$

For a travelling wave solution with a constant asymptotic speed v , we require that the perturbation in the population density neither grows nor decays exponentially for a fixed z in the moving coordinate frame as $t \rightarrow \infty$ (Ebert and van Saarloos, 2000; van Saarloos, 2003). There is a unique value for v in (11) that satisfies this requirement:

$$v = 2\sqrt{D_H(2m\lambda - (\mu + \gamma N_0))}.$$

The speed is dependent on the diffusivity of the driving-Y males only (D_H). The factor in large parentheses is the driving-Y net growth rate at the tip of the wave, where the wild-type population is at its equilibrium carrying capacity N_0 (total birth rate λ equals the death rate $(\mu + \gamma N_0)$).¹ By contrast, the speed of the wild-type males and females spreading into an empty landscape is determined by their low-density growth rate, $(\lambda - \mu)$. For a population at carrying capacity, the average generation time equals the average lifetime, $T_G = 1/\lambda = 1/(\mu + \gamma N_0)$, so we may write the speed in the form that we will use henceforth for all models, for ease of comparison:

$$v = 2\sqrt{D_H(2m-1)/T_G}.$$

While we have assumed a density-dependent mortality rate of the form $\gamma N(x, t)$, this expression also holds for more general forms $g_A(N(x, t))$, for which $T_G = 1/\lambda = 1/[\mu + g_A(N_0)]$. The distance travelled per generation is

$$v_G = 2\sqrt{D'_H(2m-1)}$$

where $D'_H = D_H T_G$ is the diffusivity per generation. This corresponds to Fisherian spatial spread of an advantageous gene (Fisher, 1937), with $(2m-1)$ corresponding to a selection coefficient. Thus we conclude that the population suppression

¹ So we could rewrite either as $v = 2\sqrt{D_H \lambda (2m-1)}$ or $v = 2\sqrt{D_H (\mu + \gamma N_0) (2m-1)}$.

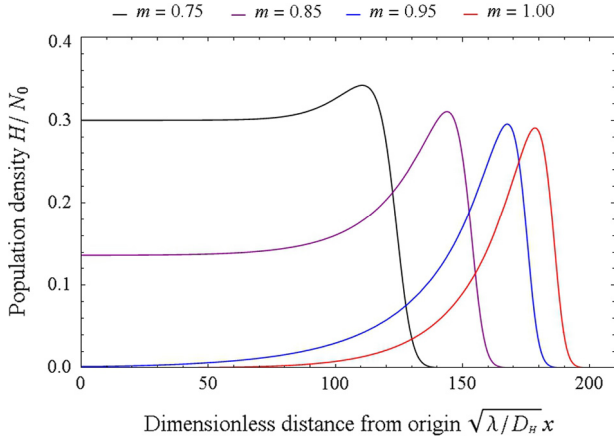


Fig. 2. Population density of driving-Y males for the basic model at time $\lambda t = t/T_C = 90$ generations and intrinsic rate of increase $R_m = \lambda/\mu = 6$, as a function of m . Values of m are sub-critical ($m = 0.75, 0.85$) and super-critical ($m = 0.95, 1$). Initial release conditions are $h/N_0 = 0.01$ within $|x| \leq \sqrt{D_H/\lambda}$.

and extinction caused by the driving-Y male sex bias does not impact the asymptotic speed of the driving-Y invasion. This is because for our system and localized initial conditions, the speed is solely determined by the conditions at the tip of the wave (pulled wave) where wild-type female and male populations are at their equilibrium values. We confirmed this (not shown) by changing (9) so that the birth rate depends on the total population density N (in which case the driving-Y has no effect on population size) or on the density of males M (in which case the driving-Y increases population density). The asymptotic speed in each case remains the same.

However, behind the wave front, the behaviour deviates from classic Fisherian spread, since the population suppression/extinction effect of the driving-Y kicks in and increasingly dominates the dynamics. Moving away from the wave tip towards the tail, the female (and total wild-type) population decreases due to the sex bias created by the driving-Y. The decreasing female population eventually inhibits the driving-Y growth rate such that the driving-Y population density peaks and then falls, leading to the non-monotonic pulse shape (Fig. 2). However, the percentage of driving-Y genes in the male population increases monotonically from tip to tail of the wave, completely replacing the wild-type gene behind the wave pulse. Both processes are mediated by the spatial dispersal dynamics.

The fate of the total population density behind the wave, $N_1 = H_1 + F_1 + M_1$, will depend on the growth parameters and sex ratio distortion m , as shown in Fig. 2. Below $m_{crit} = 1 - \mu/(2\lambda)$, the population behind the wave persists at a somewhat lower abundance with the wild-type Y-chromosome lost. Alternatively, we may write the condition for extinction behind the wave as $R_m(1 - L) < 1$, where $R_m = \lambda/\mu$ represents the intrinsic growth rate (i.e., average lifetime number of daughters produced at low density), and $L = 2m - 1$ is the load imposed on the wild-type population by the driving-Y (Deredec et al., 2011).

3.2. Two life-stage model: addition of immobile juveniles

An implicit assumption of the basic model is that individuals are able to reproduce as soon as they are born. We now consider the effect of introducing a juvenile stage during which individuals cannot reproduce. We further assume, as is true for many insects and other species, that the juvenile stage does not move to any great extent and that all movement is restricted to adults.

We introduce a juvenile stage as $J(x, t)$ with a fixed time of T_J before emerging into adults (although one could include separate

egg, larval and pupal stages). $J(x, t)$ is the total population density of juveniles, consisting of male (driving-Y and wild-type) and female juveniles. The density-dependent death rate for juveniles is given by $g_J(J(x, t))$. We keep this form general for derivations of wave speed, and make a suitable choice for numerical calculations. The density-independent mortality rate is μ_J for juveniles and μ_A for adults. To incorporate the growth dynamics of the juvenile stage into our model, we employ the lumped age class method used for population growth models (Gurney and Nisbet, 1998; Hancock and Godfray, 2007). We denote θ and $W(x, t)$ as the density-independent and density-dependent probabilities of survival through the juvenile stage, which are given by:

$$\theta = \exp(-\mu_J T_J)$$

$$W(x, t) = \exp\left(-\int_{t-T_J}^t g_J(J(x, \tau)) d\tau\right).$$

For a homogeneous equilibrium state, this reduces to $W_{eq} = \exp(-g_J(J_{eq})T_J)$.

We obtain the following delay partial-differential equations for the adult and juvenile populations:

$$\begin{aligned} \frac{\partial H}{\partial t} &= D_H \frac{\partial^2 H}{\partial x^2} + 2\lambda\theta WF^* \left[\frac{mH^*}{M^* + H^*} \right] - (\mu_A + \gamma N)H \\ \frac{\partial F}{\partial t} &= D_F \frac{\partial^2 F}{\partial x^2} + 2\lambda\theta WF^* \left[\frac{\frac{1}{2}M^* + (1-m)H^*}{M^* + H^*} \right] \\ &\quad - (\mu_A + \gamma N)F \\ \frac{\partial M}{\partial t} &= D_M \frac{\partial^2 M}{\partial x^2} + 2\lambda\theta WF^* \left[\frac{\frac{1}{2}M^*}{M^* + H^*} \right] - (\mu_A + \gamma N)M \\ \frac{\partial J}{\partial t} &= 2\lambda F - 2\lambda\theta WF^* - (\mu_J + g_J(J))J \\ \frac{\partial W}{\partial t} &= W(g_J(J^*) - g_J(J)) \end{aligned} \quad (12)$$

where the asterisks indicate time-delayed population density functions, e.g. $F^*(x, t) = F(x, t - T_J)$, etc. Here, $N(x, t) = H(x, t) + F(x, t) + M(x, t)$ is the total adult population density. If the functional form of the density-dependent juvenile mortality, $g_J(J(x, t))$, is chosen so that the density-dependent probability of survival through the juvenile stage $W(x, t) \rightarrow 1$ as $T_J \rightarrow 0$, then $\theta \rightarrow 1$ and $J(x, t) \rightarrow 0$ as $T_J \rightarrow 0$, and we recover the model with only one life stage.

For a given choice of juvenile density-dependent mortality $g_J(J(x, t))$, one may solve for the homogeneous wild-type equilibrium $\mathbf{U}_0 = \{0, F_0, M_0, J_0, W_0\}$ (Appendix C) by setting the time and spatial derivatives and $H(x, t)$ in (12) to zero as discussed in Section 2. Note that for a nonzero total adult population density N_0 , it is required that growth parameters satisfy $\lambda e^{-\mu_J T_J} / \mu_A > 1$. The limit on T_J for a given set of growth parameters that will allow for a non-zero adult population is therefore $T_J < \ln(\lambda/\mu_A)/\mu_J$.

As in the one life-stage model with the driving-Y present ($m > 0.5$), the equations have a ‘subcritical’ equilibrium state for which m is insufficient for population elimination and the driving-Y gene is present in all males, and a ‘supercritical’ state for which the population is eliminated:

$$\mathbf{U}_1 = \begin{cases} \{H_1, F_1, 0, J_1, W_1\} & m < 1 - \mu_A/(2\lambda\theta) \\ \{0, 0, 0, 0, 1\} & m \geq 1 - \mu_A/(2\lambda\theta) \end{cases}$$

$\mathbf{U}_1$, calculated for a particular $g_J(J(x, t))$ from (12), is the homogeneous steady state with the driving-Y present (Appendix C). Again using the method of Section 2.1, we find that this state is linearly stable.

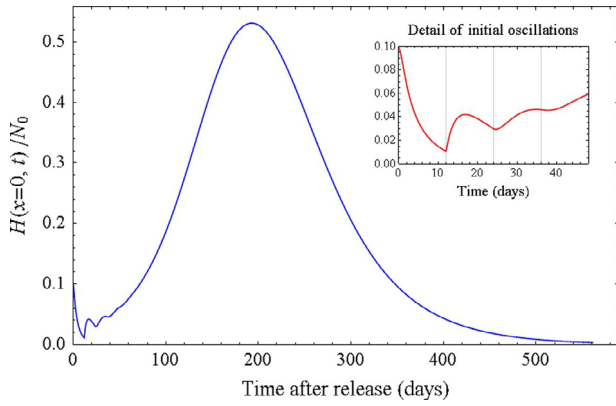


Fig. 3. Population density of driving-Y males at the origin ($x = 0$) for the basic model with juveniles (Section 3.2). Representative *An. gambiae* mosquito parameters are used (see Appendix A) with $m = 0.95$ (total extinction of population behind the wave). Initial release conditions are $h/N_0 = 0.1$ within $|x| \leq 1$ km.

We combine the Method of Steps with the Method of Lines to solve the delay PDEs (12) numerically, with our rectangular function initial condition, for introduction of the driving-Y into the wild-type landscape at $\mathbf{U}_0$. We use parameters representative of *An. gambiae* mosquitoes, a species with an immobile juvenile stage (with $T_J \approx 12$ days, adult average lifetime $T_A \approx 8$ days), and use an appropriate (logarithmic) form of $g_J(J(x, t))$ (given in Appendix A). Because of the time delay due to the juvenile stage, we must also now specify initial population densities for all times $-T_J \leq t < 0$:

$$\mathbf{U}(x, -T_J \leq t < 0) = \{0, F_0, M_0, J_0, W_0\}.$$

After the introduction of the driving-Y, we observe initial temporal oscillations of the population densities with a period of T_J , as shown for $H(0, t)$ in Fig. 3. This is because the newly-introduced driving-Y adult population density immediately begins to decrease due to adult mortality, but must wait T_J days before its number is replenished by the hatching of juveniles. Oscillations eventually dissipate and travelling waveforms moving at asymptotically constant speed are established, with populations completely eradicated in their wake for $m > m_{crit}$.

3.2.1. Wave speed analysis and results

As with the previous model, the driving-Y equation uncouples from the rest in (12) when linearized around $\mathbf{U}_0$, and again the determinant of the dispersion equation takes the form $|\mathbf{S}(k, \omega)| = |\mathbf{Z}^Y(k, \omega)| |\mathbf{Z}^0(k, \omega)|$, where $\mathbf{Z}^Y$ represents the driving-Y males, and $\mathbf{Z}^0$ represents the dispersion submatrix for the wild-type system before the release of driving-Ys. For this model with time delay we have:

$$|\mathbf{Z}^Y(k, \omega(k))| = i\omega(k) - D_H k^2 + (2me^{i\omega(k)T_J} - 1)(\mu_A + \gamma N_0) = 0.$$

There are no solutions of $|\mathbf{Z}^0(k, \omega(k))| = 0$ with $\text{Im } \omega(k) > 0$ for any k , so the wild-type system of males and females for this model is again stable to perturbations in the non-driving-Y population densities. As shown in Appendix B, there exists a finite range of k -values for which $|\mathbf{Z}^Y(k, \omega(k))| = 0$ has solutions with $\text{Im } \omega(k) > 0$. The equilibrium state $\mathbf{U}_0$ is therefore linearly unstable to release of driving-Y males, and the density perturbations $\delta F(x, t)$, $\delta M(x, t)$, and $\delta J(x, t)$ are entrained to move along with that of the driving-Y population $\delta H(x, t)$.

To derive the asymptotic wave speed, we apply the method described in Section 2.2. Because of the exponential term in the dispersion relationship (due to the time delay introduced by the juvenile stage), the resulting double integral in (4) cannot be evaluated analytically as for the one life-stage model. We instead use (8), with the dispersion relation reducing to $|\mathbf{Z}^Y(k^*, \omega(k^*))| =$

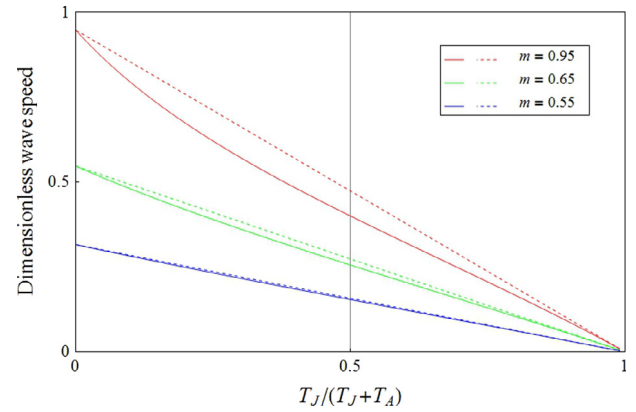


Fig. 4. Effect on wave speed of an immobile juvenile period T_J for the basic model with juveniles (Section 3.2) and same diffusivity D for all types. The dotted straight line represents the expression $\sqrt{(2m-1)[1 - T_J/(T_A + T_J)]}$, and the difference from the dimensionless speed $v(\sqrt{T_A/(4D)})$ (solid line) shows the slowing effect of the nonlinear ‘correction’ term, $[1 - f_1(2m-1, T_J/T_A)]$. The maximum percentage decrease in the speed due to the nonlinear correction term occurs when $T_J = T_A$, $T_J/(T_J + T_A) = 1/2$.

0, to derive two equations for $\omega(k^*)$ and k^* (details of the derivation are shown in Appendix D):

$$e^{-\text{Im } \omega(k^*)T_J} = \frac{2(\mu_A + \gamma N_0) + \text{Im } \omega(k^*)}{2m(\mu_A + \gamma N_0)(2 + \text{Im } \omega(k^*)T_J)}$$

$$\text{Im } k^* = \sqrt{\frac{(\mu_A + \gamma N_0)(1 - 2m e^{-\text{Im } \omega(k^*)T_J}) + \text{Im } \omega(k^*)}{D_H}}.$$

We show in Appendix D that the first equation above has a unique positive solution $\text{Im } \omega(k^*)$. We obtain a transcendental equation for the asymptotic speed by combining $v = \text{Im } \omega(k^*)/\text{Im } k^*$ with the two equations above:

$$v^2[2mT_J^2(\mu_A + \gamma N_0)] = S \exp\left(\frac{T_J v^2 + S}{2D_H}\right) \quad (13)$$

where

$$S \equiv -2D_H + \sqrt{4D_H^2 + T_J^2 v^2[v^2 + 4D_H(\mu_A + \gamma N_0)]}.$$

We can rewrite (13) in dimensionless form as:

$$4mT^2V^2 = (-1 + \sqrt{1 + 4T^2(V^2 + V^4)}) \times \exp(2TV^2 - 1 + \sqrt{1 + 4T^2(V^2 + V^4)}) \quad (14)$$

where $V = v\sqrt{T_A/(4D_H)}$ represents the dimensionless velocity, $T = T_J/T_A$, and $T_A = 1/(\mu_A + \gamma N_0)$ is the average time to reproduction after emerging into the adult stage for the wild-type state $\mathbf{U}_0$ at the tip of the wave (equal to the average adult lifetime). Note that $\mu_A + \gamma N_0 = \lambda\theta W_0$, the equilibrium emergence rate of adults from the juvenile stage. The total generation time of the species is now given by $T_G = T_J + T_A$.

Eq. (14) may be solved numerically for the speed, as shown in Fig. 4 (solid lines), and we find that the longer that the species is immobile during its total lifetime, the slower the speed. We verify these results through numerical solution of the full delay PDEs.

For $T \rightarrow 0$, (14) reduces to $V_{T \rightarrow 0} = \sqrt{2m-1}$ (or, in dimensional form, $v_{T \rightarrow 0} = 2\sqrt{D_H(2m-1)/T_A}$), which is the speed with no immobile juvenile stage. We are thus motivated to rewrite (13) for the speed v :

$$v = \frac{2\sqrt{D_H(2m-1)/T_A}}{1 + T_J/T_A} \left[1 - f_1(2m-1, T_J/T_A)\right] \quad (15)$$

where $v_{T \rightarrow 0}$, the speed at $T_j/T_A = 0$, is multiplied by two slowing factors for $T_j > 0$ that only depend on $T = T_j/T_A$ and m (as can be seen in (14)). The first slowing factor in (15), $1/(1 + T_j/T_A) = T_A/T_G$, represents the fraction of an individual's lifetime spent as a dispersing adult. In Fig. 4, the dotted lines represent the speed at $T_j = 0$ multiplied by only this slowing factor, T_A/T_G . Comparison with the actual speed (solid lines) shows that to a good first order approximation, the reduction in wave speed caused by an immobile juvenile stage of duration T_j is $T_j/(T_A + T_j) = T_j/T_G$, the relative time spent as an immobile juvenile. The second nonlinear slowing factor in (15), $[1 - f_1(2m - 1, T_j/T_A)]$, has only a fairly insignificant second-order effect. We find that $f_1(2m - 1, T_j/T_A)$ lies between zero and $1 - \sqrt{\ln[2m]/(2m - 1)}$ for all parameters. The largest (although still modest) contribution of the nonlinear factor $[1 - f_1(2m - 1, T_j/T_A)]$ occurs when $T_j = T_A$ and $m = 1$ (adding a further speed reduction of 16.7%).

As in our one life-stage model, the velocity depends on the diffusivity of the driving-Y male only. We note that again there is no explicit dependence of the speed on the functional form of the juvenile density-dependent death rate $g_j(J)$; the latter only affects T_A , which is a property of the pre-release wild-type system.

We may also write the distance travelled per generation time, where $D'_H T_A$ is the diffusivity per adult lifetime, as:

$$v_G = 2\sqrt{D'_H(2m - 1)} \left[1 - f_1(2m - 1, T_j/T_A) \right].$$

For the special case of $T_j = T_A$, we have derived an exact analytical solution for the asymptotic wave speed:

$$v = \sqrt{D_H \ln[2m]/T_A} \quad \text{for } T_j = T_A = T_G/2.$$

3.3. Single mating with females also dispersing Y chromosome

An implicit assumption of the basic model is that every newborn is the result of a separate and independent mating event between a male and a female that occurs immediately before birth. In this case the only movement that determines the rate of spread of the driving-Y is the dispersal of the driving-Y male adult. However, for some species, individuals mate only once in their life, storing the sperm from that mating in their spermatheca and carrying it with them as they disperse. We now model this mating system explicitly, such that newly-emerged adult unmated females disperse, then mate once with a local male, then continue to disperse but do not mate again. In this model, if we track a Y chromosome from zygote to zygote, it starts in a male, which develops into an adult that disperses it, then transfers it to an adult female that continues to disperse it, until a new zygote is deposited.

We thus differentiate the females into three types: unmated, mated to wild-type male, and mated to driving-Y male: $F_U(x, t)$, $F_H(x, t)$ and $F_M(x, t)$. We further increase the generality and realism of the model by allowing the mating rate to depend on the local total density of males (i.e., allowing for an Allee effect, Lewis and Kareiva, 1993; McCarthy, 1997; Li, 2008). We use Holling-II density-dependence for the mating rate, for which the mating rate is reduced at low density of males. The mating rate for the total female population is:

$$\eta F_U(x, t) \left(\frac{M(x, t) + H(x, t)}{M(x, t) + H(x, t) + \rho} \right) \quad (16)$$

where ρ is a searching constant that represents the ability of females to find males for mating (higher ρ , greater difficulty), and η is the density-independent mating rate constant. This form is chosen for convenience because when $\rho = 0$, the model reduces to a case of no density dependence of mating rate on male population. When $\eta \rightarrow \infty$, then mating is instantaneous and $F_U(x, t) \rightarrow 0$.

The delay PDEs in this case are:

$$\begin{aligned} \frac{\partial H}{\partial t} &= D_H \frac{\partial^2 H}{\partial x^2} + 2\lambda\theta m W F_H^* - (\mu_A + \gamma N)H \\ \frac{\partial F_H}{\partial t} &= D_{FH} \frac{\partial^2 F_H}{\partial x^2} + \eta F_U \left[\frac{H}{M + H + \rho} \right] - (\mu_A + \gamma N)F_H \\ \frac{\partial F_M}{\partial t} &= D_{FM} \frac{\partial^2 F_M}{\partial x^2} + \eta F_U \left[\frac{M}{M + H + \rho} \right] - (\mu_A + \gamma N)F_M \\ \frac{\partial F_U}{\partial t} &= D_{FU} \frac{\partial^2 F_U}{\partial x^2} + 2\lambda\theta W \left[(1 - m)F_H^* + \frac{F_M^*}{2} \right] \\ &\quad - \eta F_U \left[\frac{M + H}{M + H + \rho} \right] - (\mu_A + \gamma N)F_U \\ \frac{\partial M}{\partial t} &= D_M \frac{\partial^2 M}{\partial x^2} + 2\lambda\theta W \left[\frac{F_M^*}{2} \right] - (\mu_A + \gamma N)M \\ \frac{\partial J}{\partial t} &= 2\lambda(F_H + F_M) - 2\lambda\theta W(F_H^* + F_M^*) - [\mu_J + g_J(J)]J \\ \frac{\partial W}{\partial t} &= W[g_J(J^*) - g_J(J)]. \end{aligned} \quad (17)$$

The asterisks indicate time-delayed functions, e.g., $F_H^*(x, t) = F_H(x, t - T_j)$. We now have seven dependent variables: $\mathbf{U} = \{H, F_H, F_M, F_U, M, J, W\}$. The total population density of adults is:

$$N(x, t) = H(x, t) + F_H(x, t) + F_M(x, t) + F_U(x, t) + M(x, t).$$

The pre-release wild-type equilibria are more complex than those of previous models due to the Holling-II density-dependent mating rate with $\rho > 0$, which introduces an Allee effect. For our representative mosquito parameters and a specific choice of $g_J(J(x, t))$ (see Appendix A), we now obtain a homogeneous pre-release equilibrium $\mathbf{U}_0 = \{0, 0, F_{M0}, F_{U0}, M_0, J_0, W_0\}$ that is stable to perturbations in the wild-type populations, a (pre-release) stable zero state $\mathbf{U}_0^- = \{0, 0, 0, 0, 0, 0, 1\}$, as well as a (pre-release) unstable state $\mathbf{U}_0^+ = \{0, 0, F_{M0}^+, F_{U0}^+, M_0^+, J_0^+, W_0^+\}$ that lies between the other two. Expressions for the equilibria are shown in Appendix C; the stability/instability of each state was determined as for previous models using the approach of Section 2.1.

Comparing to previous models, the pre-release zero state is now stable to perturbations in the wild-type populations due to the Allee effect: when a sufficiently low initial population of wild-types is introduced into an empty landscape, the non-zero equilibrium $\mathbf{U}_0$ will not establish. For driving-Y release, we assume that non-zero wild-type equilibrium $\mathbf{U}_0$ (stable to non-driving-Y perturbations, unstable to driving-Y) has been achieved everywhere.

With the driving-Y present ($m > 0.5$) and $\rho > 0$, we may also have more complex homogeneous equilibria (Appendix C). For $m < m_{crit}$ with the driving-Y gene present in all males, we obtain a non-zero stable 'subcritical' state $\mathbf{U}_1 = \{H_1, F_{H1}, 0, F_{U1}, 0, J_1, W_1\}$ as well as an unstable 'subcritical' state $\mathbf{U}_1^+$. For $m > m_{crit}$ there is a stable 'supercritical' zero state for which all populations are eliminated: $\mathbf{U}_1 = \{0, 0, 0, 0, 0, 0, 1\}$.

We expect travelling waveforms to connect $\mathbf{U}_0$ to the stable $\mathbf{U}_1$ state (with non-zero or extinct populations, depending on the value of m), and this is the case for numerical solutions of (17) carried out for representative *An. gambiae* mosquito parameters. A wave pulse of driving-Y males spreads through the wild-type population, with the fate of the population (persistence or elimination) determined by whether m is below or above the critical value (m_{crit} can be calculated as shown in Appendix C). We denote females mated by driving-Y males as Y^D -mated. Contrasting with the previous model, the Y^D -mated female population density F_H forms a wave pulse similar to that of the driving-Y male density H , although with an asymptotically different shape and peaking/falling before the driving-Y wave peak (Fig. 5). This is

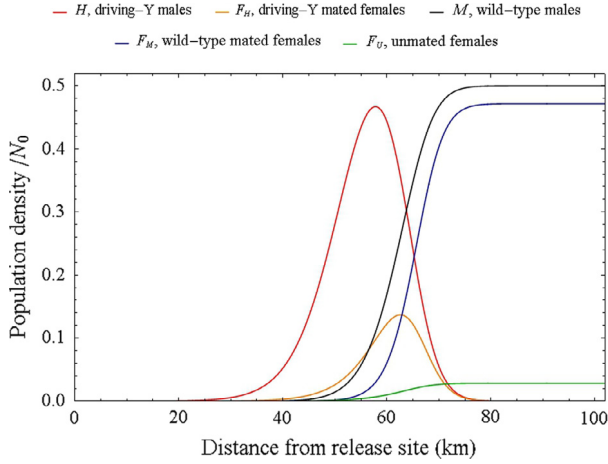


Fig. 5. Population density waveforms for model with single mating and juvenile stage (Section 3.3), 1200 days after release. For representative *An. gambiae* mosquito parameters (Appendix A) and extinction behind the wave, $m = 0.95 > m_{crit}$. Initial release population of driving-Y males is $h/N_0 = 0.1$ with $|x| \leq 0.25$ km.

because behind the tip of the wave, the ratio of Y^D -mated female to male population is continually falling due to the sex bias introduced by the driving-Y, converging to $(1 - m)/m$ at the tail of the wave, irrespectively of whether m is above or below m_{crit} .

3.3.1. Wave speed analysis and results

For a wild-type population spreading into an empty landscape, the introduction of an Allee effect (16), by which the mating rate is reduced at the low densities present at the wave tip, has the result that linearization of the equations cannot be used to determine wave speed (the wave is pushed). However, as discussed in further detail in Section 3.3.4, for invasion of the driving-Y into a landscape with wild-types at carrying capacity, it is only the driving-Y that is at low density at the front of the wave; therefore we may linearize (17) around $\mathbf{U}_0$ using the method described in Section 2 (the wave is pulled). In contrast to previous models (see Sections 3.1.2 and 3.2.1), the set of linearized equations (2) for this model contains two, rather than one, coupled equations for the driving-Y males and Y^D -mated females that are uncoupled from all the other dependent variables:

$$\begin{aligned} \frac{\partial \delta H}{\partial t} &= D_H \frac{\partial^2 \delta H}{\partial x^2} + 2m(\mu_A + \gamma N_0)S_1 \delta F_H^* - (\mu_A + \gamma N_0)\delta H, \\ \frac{\partial \delta F_H}{\partial t} &= D_{FH} \frac{\partial^2 \delta F_H}{\partial x^2} + \frac{(\mu_A + \gamma N_0)}{S_1} \delta H - (\mu_A + \gamma N_0)\delta F_H \end{aligned} \quad (18)$$

where

$$S_1 \equiv \frac{\gamma N_0^2 + N_0(2\rho\gamma + \eta + \mu_A) + 2\rho\mu_A}{\eta N_0}$$

and $\delta F_H^*(x, t) = \delta F_H(x, t - T_j)$ is a time-delayed function. Thus, $\mathbf{Z}^Y$ is now a two-dimensional matrix involving both driving-Y males and Y^D -mated females as the species driving the wave, rather than driving-Y males only. The dispersion relation $|\mathbf{Z}^Y(k, \omega(k))| = 0$ for the driving types again determines the linear instability of the equilibrium state $\mathbf{U}_0$ to introduction of driving-Ys (the other population densities will be entrained due to the stability of the pre-release wild-type state). The dispersion relation $|\mathbf{Z}^Y(k, \omega(k))| = 0$ can be written as:

$$\sqrt{2m}(\mu_A + \gamma N_0)e^{i\omega(k)T_j/2} = \sqrt{S_2}$$

where

$$\begin{aligned} S_2 &= (D_{avg}^2 - D_{dif}^2)k^4 + 2D_{avg}[(\mu_A + \gamma N_0) - i\omega(k)]k^2 \\ &\quad + (\mu_A + \gamma N_0)^2 - 2i(\mu_A + \gamma N_0)\omega(k) - \omega^2(k) \end{aligned}$$

with $D_{avg} = (D_H + D_{FH})/2$ and $D_{dif} = |D_H - D_{FH}|/2$ being the average and the absolute value of the half-difference of D_H and D_{FH} , respectively.

In Appendix B, we prove that for a range of k -values the dispersion relationship is satisfied by $\omega(k)$ with $\text{Im } \omega(k) > 0$ and the equilibrium state $\mathbf{U}_0$ is unstable to introduction of driving-Ys. We then again use (8) from Section 2.2 to determine the asymptotic wave speed, with the dispersion relation reducing to $|\mathbf{Z}^Y(k^*, \omega(k^*))| = 0$. This yields a system of transcendental equations for $\text{Im } \omega(k^*)$ and $\text{Im } k^*$:

$$\begin{aligned} \sqrt{2m}e^{-\Omega/2} &= \frac{\sqrt{2(2T + \Omega)[S_3 - R_D(\Omega + 4)(T + \Omega) + 2T + \Omega]}}{T(\Omega + 4)\sqrt{1 - R_D}} \end{aligned} \quad (19)$$

$$K = \sqrt{\frac{S_3 - T(\Omega + 2) - \Omega(\Omega + 3)}{T(\Omega + 4)(1 - R_D)}}$$

where

$$S_3 \equiv \sqrt{R_D\Omega(\Omega + 4)[T^2 + 2T(\Omega + 1) + \Omega(\Omega + 2)] + (2T + \Omega)^2}.$$

Above, $\Omega = T_j \text{Im } \omega(k^*)$, $K = \sqrt{D_{avg}T_A \text{Im } k^*}$, $R_D = D_{dif}^2/D_{avg}^2$, and $T = T_j/T_A$, where the adult lifetime is given by $T_A = 1/(\mu_A + \gamma N_0)$. Note that $\mu_A + \gamma N_0 = \eta\lambda\theta W_0/(\mu_A[\eta + \mu_A(1 + 2\rho/N_0)])$, the equilibrium emergence rate of adults from the juvenile stage. Eqs. (19) for Ω and K are solved numerically and the dimensionless velocity $V = v\sqrt{T_A/(4D_{avg})}$ is then given by the first equation in (8):

$$V = \frac{\Omega}{2KT}. \quad (20)$$

We have verified these results through numerical solution of the full delay PDEs (17).

One can see from (19) and (20) that the dimensionless velocity V is only a function of the parameters $\sqrt{m}$, $T = T_j/T_A$, and $R_D = D_{dif}^2/D_{avg}^2$, and as with the previous model, this enables us to write an expression for the wave speed as the speed at $T_j = 0$ multiplied by two slowing factors:

$$\begin{aligned} v &= \frac{2\sqrt{D_{avg}(\sqrt{2m} - 1)}/T_A}{1 + T_j/(2T_A)} \\ &\quad \times \left[1 - f_2\left(\sqrt{2m} - 1, \frac{T_j}{2T_A}, \frac{D_{dif}^2}{D_{avg}^2}\right) \right]. \end{aligned} \quad (21)$$

The nonlinear slowing factor in brackets in (21), for which no analytic expression is possible, is again a second-order correction only, and we can show that f_2 varies between zero and 1 – $\sqrt{\ln(\sqrt{2m})/(\sqrt{2m} - 1)}$ with the maximum (modest) slowing at $T_j = 2T_A$, $m = 1$, and $D_{dif} = 0$ (adding a further reduction in speed of up to 8.5%).

Three differences from the previous model in Section 3.2, for which each zygote is derived from an independent mating event, are worth noting. Firstly, we find that the wave speed now depends on the diffusivity of the Y^D -mated females as well as the diffusivity of driving-Y males. Secondly, wherever $2m$ appears in the speed for the previous model, it now appears as $\sqrt{2m}$. Thirdly, the term corresponding to juvenile stage time delay, T_j/T_A , in the previous model is replaced by $T_j/(2T_A)$ in the current model.

These differences arise because there are now two invading types, driving-Y males and Y^D -mated females, and they interact in a nonlinear way to determine wave speed. Since Y^D -mated females can also disperse the gene through their movement, to first order, the speed depends upon the average of the diffusivities, $D_{avg} =$

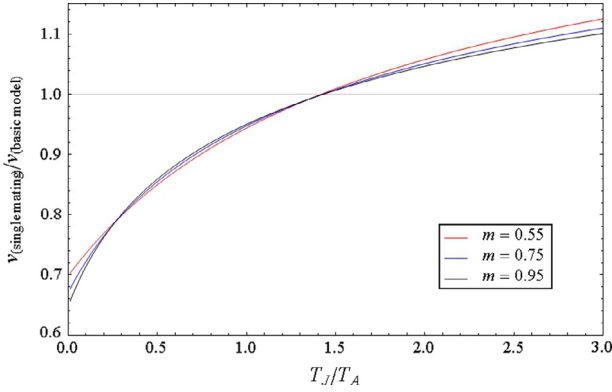


Fig. 6. Ratio of asymptotic wave speed for the single mating model (Section 3.3) vs. the basic model with juveniles (Section 3.2) as a function of the ratio of the duration of the juvenile stage, T_J , to the average adult lifetime at wild-type equilibrium, T_A . For same diffusivity D for all types.

$(D_H + D_{FH})/2$ rather than only on the diffusivity D_H of the driving-Y males. The decrease from $2m$ to $\sqrt{2m}$ in the selection coefficient arises because the effective creation rate at the tip of the wave is now the geometric average of the rates for driving-Y males and Y^D -mated females in the linearized coupled equations (18), and the driving-Y chromosome has a transmission advantage while in a male, but no extra advantage once in a mated female. Moreover, since males move the driving-Y with a time delay equal to the length of the juvenile period T_J , but the Y^D -mated females move it without any delay (i.e., they can begin dispersing the driving-Y the moment they are mated), the effective time delay is $T_J/2$.

Fig. 6 compares wave speed for this single mating model vs. the basic model with juveniles (Section 3.2), for the same diffusivity for both types ($D_{FH} = D_H$). For short juvenile stages, the spatial spread of the driving-Y is slower for this model than the previous one, because the dispersing Y^D -mated female brings down the effective selection constant at the tip of the wave. However, as the length of the juvenile stage increases, the Y^D -mated female makes up for this by her ability to disperse the driving-Y chromosome with no delay, and the wave moves faster than in the previous model.

It is useful to think of the adult lifetime as an average of that for the driving-Y males and Y^D -mated females as:

$$\frac{(T_A + T_J) + (T_A)}{2} = \frac{T_G + T_A}{2}.$$

If we calculate the distance moved per this average generation, we get a similar per-generation form as for the previous model, with $\sqrt{2m} - 1$ as the ‘average’ selection coefficient:

$$v_G = 2\sqrt{D'_{avg}(\sqrt{2m} - 1)} \left[1 - f_2\left(\sqrt{2m} - 1, \frac{T_J}{2T_A}, \frac{D_{diff}^2}{D_{avg}^2}\right) \right]$$

where $D'_{avg} = D_{avg}(T_G + T_A)/2$.

We conclude that the presence of an immobile juvenile stage, as a good first approximation, causes a fractional reduction of $(T_J/2)/(T_A + T_J/2)$ in the speed of spatial spread of the driving-Y.

3.3.2. Same diffusivities for all types

In the special case of equal diffusivities for driving-Y males and Y^D -mated females, we have $D_{FH} = D_H = D$, $R_D = 0$ and (19) reduces to:

$$\sqrt{2m} e^{-\Omega/2} = \frac{2(2T + \Omega)}{T(4 + \Omega)} \quad \text{and} \quad K = \sqrt{\frac{\Omega(2 + T + \Omega)}{T(4 + \Omega)}}.$$

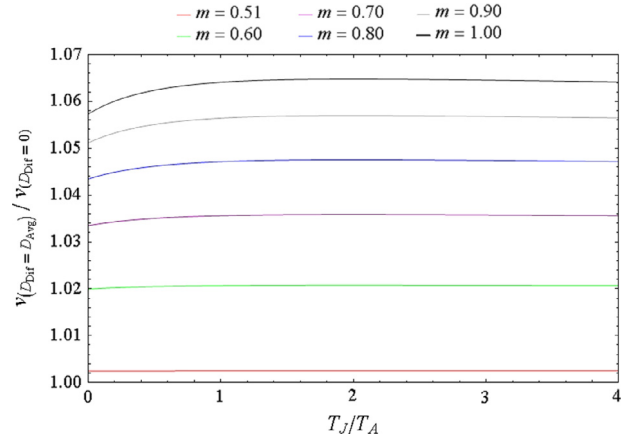


Fig. 7. Effect of sex differences in diffusivity at constant $D_{avg} = (D_H + D_{FH})/2$, for model with single mating (Section 3.3). Ratio of asymptotic speeds at maximum sex difference ($D_{diff} = |D_H - D_{FH}|/2 = D_{avg}$) vs. no sex differences ($D_{diff} = 0$) is shown as a function of the ratio of the duration of the juvenile stage, T_J , to the average adult lifetime at wild-type equilibrium, T_A .

In this case, combining the equations above with (20) yields a single transcendental equation for the dimensionless velocity:

$$\sqrt{2m} T^2 V^2 = 2(-1 + \sqrt{1 + T^2(V^2 + V^4)}) \times \exp(TV^2 - 1 + \sqrt{1 + T^2(V^2 + V^4)}).$$

We observe that the equation above is analogous to that of the one life-stage model (14) with $D_H = D$, if in (14) we replace $2m$ with $\sqrt{2m}$ and T with $T/2$ everywhere.

There are two special cases for which we derive an analytical solution for the speed when the diffusivities are the same:

(a) for a juvenile stage with $T_J = 2T_A$:

$$v = \sqrt{D \ln(\sqrt{2m})/T_A}$$

(b) when $T_J = 0$ (one life stage only):

$$v = 2\sqrt{D(\sqrt{2m} - 1)/T_A}.$$

This can be compared to that of the basic model in Section 3.1:

$$v = 2\sqrt{D(2m - 1)/T_A}.$$

With no sex difference in diffusivity and one life stage only (no delay), the only effect of the dispersing Y^D -mated female on speed is to decrease the effective selection coefficient at the tip of the wave.

We also can show that the asymptotic wave width is proportional to $\sqrt{D}$ when $D_H = D_{FH} = D$.

3.3.3. Effect of different diffusivities

We consider the effect on the wave speed of sex differences on dispersal, $D_{diff} > 0$. Keeping the average diffusivity D_{avg} constant, the maximum possible half-difference between the diffusivities of the driving-Y male and Y^D -mated female is $D_{diff} = D_{avg}$ (which occurs at the limit when either the driving-Y male or the Y^D -mated female are immobile). In Fig. 7, we plot the ratio of velocities $v(D_{diff} = D_{avg})/v(D_{diff} = 0)$ for different m and T_J/T_A . We see that for a constant D_{avg} , the speed increases monotonically as a function of D_{diff} (from a minimum at $D_{diff} = 0$), but this dependence on D_{diff} is rather insignificant for all parameters (the maximum possible increase in speed is 6.5% at $T_J = 2T_A$, $m = 1$). Thus we conclude that wave speed can be well approximated using the average of the diffusivities of driving-Y males and Y^D -mated females.

We also find that to first order, the asymptotic wave width is proportional to $\sqrt{D_{avg}}$ if diffusivities are different. There is a second-order weak dependence of wave width on D_{diff} as well as the diffusivities of all the other types.

3.3.4. Density-dependent mating (Allee effect)

For wild-types invading an empty landscape, the males (along with females) are at low densities at the tip of the wave. The male density-dependent factor in parenthesis in the Holling-II mating rate (16) becomes $M/(M + \rho) \approx M/\rho$; thus males have a first-order effect on the mating rate. Due to this Allee effect, the speed cannot be obtained by linearization at the tip of the wave as for pulled waves, and the wave is pushed at a different speed. Numerical solution of our PDEs for introduction of wild-types only (and $\rho > 0$) into an empty landscape gives a reduced speed as ρ increases (stronger Allee effect), with no population establishment at all below a certain critical limit of localized initial population.

By contrast, the expression for wave speed for the driving-Y into a wild-type equilibrium (21) holds equally for male density-dependence on mating ($\rho \neq 0$) or no density-dependence on mating ($\rho = 0$), with the wave speed in both cases given by linearization at the tip of the wave. Like other growth parameters, ρ only enters the wave speed through T_A , which characterizes the wild-type equilibrium. This is because to leading order, the presence of a small amount of driving-Y invaders does not change the total dependence on male densities in the mating rate (16) at the tip of the wave, where wild-type males are at carrying capacity ($M \gg H$):

$$\frac{(H + M)}{H + M + \rho} \approx \frac{1}{1 + \rho/M_0}.$$

Furthermore, we find that our expression for the speed (as a function of m , T_A , T_J , D_H , and D_{FH}) is a general result that holds for any mating function that is dependent on the total male population density, not just a Holling-II function.

However, at the trailing edge of the driving-Y invasion wave, both driving-Y and wild-type males are at low densities with a correspondingly low mating rate. Numerical solution shows that larger ρ will result in greater suppression of the equilibrium population behind the wave. Also, with male density-dependent mating ($\rho > 0$), there can be a forbidden range of total population densities N_1 behind the wave that is analogous to the Allee threshold for establishment of wild-types into an empty landscape (although the driving-Y wave will always be established). For example, for our choice of $g_J(J(x, t))$ (see Appendix A) and for $\rho > 0$ corresponding to density-dependent mating, as m increases from 0.5 to m_{crit} , the total adult equilibrium population density N_1 behind the wave falls monotonically from N_0 to a (nonzero) value where N_1 and N_1^+ (the unstable, smaller equilibrium adult population density) converge. However, for all values of $m > m_{crit}$, the density there will be zero (i.e., a discontinuity at m_{crit}). This contrasts with the case of no Allee effect ($\rho = 0$), for which the total population density behind the wave falls from N_0 to zero with no forbidden values by increasing m from 0.5 to m_{crit} (i.e., the value of the total subcritical population N_1 converges to 0 as $m \rightarrow m_{crit}$ from below).

4. Application to mosquitoes

Thus far we have presented three models of increasing complexity for the spread of a driving-Y chromosome that causes population suppression. To illustrate how the models could be used, we now apply the most complex model (Section 3.3) to genetically-modified mosquitoes using parameter estimates for *An. gambiae* from the literature (see Appendix A). Unfortunately, little information is currently available for the diffusion rate D in this species, so our calculations should be seen as illustrative only. For greater realism, we extend our model to two spatial dimensions x and y , where diffusion of population densities represents a mean-field limit of individual mosquito dispersal via a

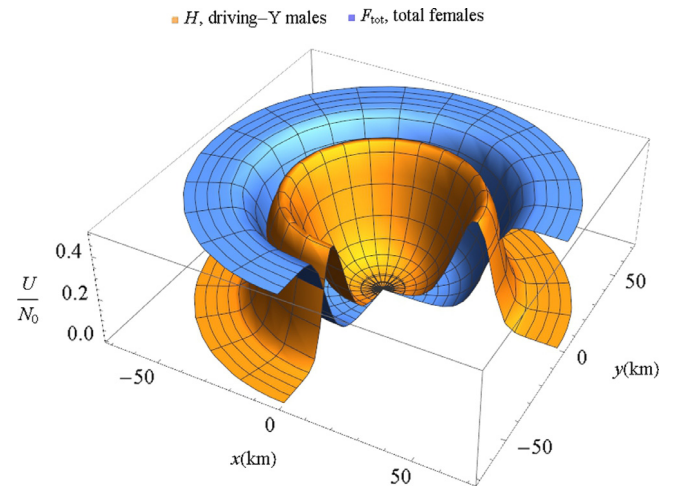


Fig. 8. Population density waveforms for driving-Y males and total population of females, 900 days after release of driving-Y males at the origin (0,0) (to reveal detail, one quarter of the waveforms are not shown). For *An. gambiae* mosquitoes (parameters in Appendix A) with extinction behind the wave, $m = 0.95 > m_{crit}$. Results obtained by numerical solution of single mating model (Section 3.3) extended to two dimensions (Section 4). Initial release population of driving-Y males is $h/N_0 = 0.1$ within $|r| \leq 0.25$ km.

random walk on the x, y plane. For initial release of driving-Y males in a circular area around the origin into a homogeneous landscape, the solution for population densities is radially symmetric. Thus, after we transform from (x, y) to polar coordinates (r, ϕ) , the ϕ -dependence drops out due to rotational symmetry. Net population density flux will be in the radial direction only, and the diffusion term for each type U_i reduces to:

$$D_i \left[\frac{\partial^2 U_i(r, t)}{\partial r^2} + \frac{1}{r} \frac{\partial U_i(r, t)}{\partial r} \right].$$

All results for asymptotic speed from the analysis for one dimension in Section 2.2 are directly applicable to speed in the radial direction, since the second term in the expression above vanishes as $r \rightarrow \infty$. Initial conditions for the driving-Y population released in a circular area at the origin become:

$$H(r, t = 0) = \begin{cases} h, & r \leq a \\ 0, & r > a. \end{cases}$$

With time, the introduced driving-Y population establishes and propagates as a circular travelling pulse, radiating outwards from the origin (see Fig. 8 for a plot and <http://dx.doi.org/10.1016/j.tpb.2015.11.005> for an animation of numerical solution of the equations). Taking into account that there is significant uncertainty in life history parameters and that the PDE model is idealized and rests on certain simplifying assumptions (discussed below in Section 5.3), we can calculate the asymptotic pulse velocity. If we assume $D = 0.1$ km²/day, $m = 0.95$ (greater than m_{crit} for population extinction behind the wave), $T_A = 8.3$ days, and $T_J = 12$ days, we obtain an asymptotic wave speed of $v \approx 72$ m/day ≈ 26 km/year. The speed is proportional to $\sqrt{D}$, so if instead $D = 0.01$ km²/day, then we get $v \approx 8$ km/year.

For release strategies, it is useful to predict not only the asymptotic wave speed, but also how long it will take for the driving-Y population to establish a wave. We model release of driving-Y male mosquitoes at density $h = 0.1 N_0$ in a circular area of radius $a = 0.25$ km. Fig. 9 tracks, with time, the expanding radius of habitat for which driving-Y males represent more than 10% of the total male population, $H/(M + H) > 0.1$ (starting at the origin, then moving outwards). Also of interest for malaria eradication strategies is the time taken to reduce the total (biting) female population. In Fig. 9, we plot the spreading radius of habitat

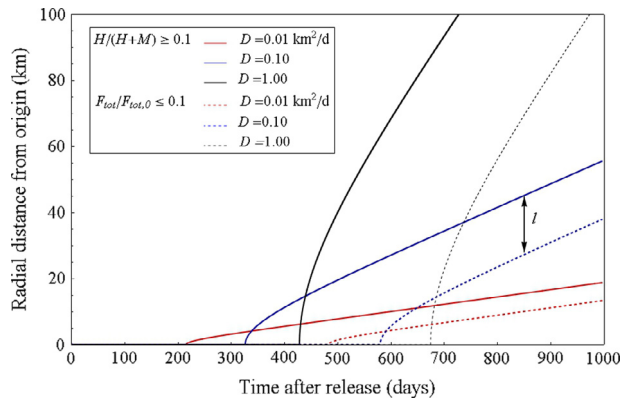


Fig. 9. Radii of habitat for 2D spatial spread of the driving-Y in a wild-type population of *An. gambiae* mosquitoes, for which (a) the fraction of driving-Ys in the total male population is $H/(H+M) \geq 0.1$ and (b) for which the total female population $F_{tot} \leq 0.1F_{tot,0}$, where $F_{tot} = F_U + F_H + F_M$ and $F_{tot,0} = F_{U0} + F_{M0}$. A measure of the width of the travelling waveforms is denoted on the plot by l . Results are obtained using the single mating model (Section 3.3) extended to two dimensions (Section 4), $m = 0.95 > m_{crit}$ (for extinction behind the wave), and representative *An. gambiae* parameters (Appendix A). Initial release population of driving-Y males is $h/N_0 = 0.1$ within $|r| \leq 0.25$ km.

for which the total wild-type female density $F_{tot} = (F_H + F_M + F_U)$ has been suppressed to less than 10% of its initial pre-release equilibrium value. As can be seen, for this particular release size and $D = 0.1$ km²/day, it takes roughly 325 days (≈ 16 mosquito generations) for the driving-Y population density to become easily detectable (greater than 10% of the total male population) at the origin, and roughly 575 days (≈ 28 mosquito generations) to suppress the total female population density at the point of release to less than 10% of its pre-release density.

Results for varying the diffusivity D indicate that for a given driving-Y release range a and density h (i.e., for a given total number of released mosquitoes), the driving-Y male population takes longer to establish at the origin for higher diffusivities, since individuals disperse away from the point of initial release more quickly. However, once the wave is established and spreading, faster dispersal (larger D) corresponds to higher wave speeds (the latter proportional to $\sqrt{D}$). Alternatively, making the release area πa^2 proportional to D (and thus making the number of released mosquitoes also proportional to D) results in a time for establishing the driving-Y male population at the origin that is independent of D . For a given time and diffusivity D , a measure of the width of the travelling set of waveforms is given in Fig. 9 by the vertical distance l between the solid line (front of the driving-Y wave) and the dotted line (back of the female total population wave). For $D = 0.1$ km²/day, this asymptotic waveform width is on the order of 18 km. Again this varies proportionally with $\sqrt{D}$, so $D = 0.01$ km²/day gives a width of about 6 km.

The initial dynamics depend upon the total number of driving-Y males released, unlike the asymptotic wave speed and shape. Releasing larger initial concentrations, or the same number over a larger area, results in shorter times to wave establishment.

5. Discussion

An understanding of the dynamics of spatial spread of genes with greater-than-Mendelian drive is key to the design of pest/vector control strategies that introduce genetically-modified individuals into a wild-type population. In this paper, the reaction–diffusion approach is used to analyse the spatial spread of a selfish gene, in this case a driving-Y chromosome that causes population suppression or extinction by creating a male sex bias. Our systems of equations combine the super-Mendelian spread of a

driving-Y through a wild-type population with complex dynamics similar to that of a multi-species model, due to the interaction of different types (driving-Y and wild-type males and females) with potentially different diffusivities. While we have used representative *An. gambiae* mosquitoes for numerical solutions, the equations are sufficiently general to allow life histories that could be applicable to a range of species. The inclusion of an immobile juvenile stage is particularly suitable for insects.

5.1. Travelling wave solutions

In all models investigated, the wild-type system at carrying capacity is stable to perturbations in the wild-type population densities, but unstable to the introduction of driving-Y males in a bounded region at the origin. For both 1-D and radially-symmetric 2-D models, numerical solutions converge asymptotically to waveforms of unchanging shape and constant speed. The driving-Y male invades the wild-type equilibrium state at the front of the wave and completely replaces the wild-type males, leaving behind, at the tail of the wave, either a new stable but reduced population state of driving-Y males and females at a density ratio $m/(1-m)$ (if $m < m_{crit}$) or a new stable extinction state of zero total population (if $m \geq m_{crit}$). The transition along the waveforms from U_0 (wild-types only) to U_1 (driving-Y males and females only at reduced or zero total population) is different to that for Fisher invasion of a single species or advantageous gene, for which the transition from tip to tail of the wave is driven purely by logistic growth interacting with dispersal. For spread of a driving-Y, we have shown that it is the effect of population suppression/extinction on female-dependent growth rates caused by the driving-Y's bias towards male offspring that increasingly dominates behind the wave tip. The pulse wave dynamics for driving-Y spread therefore can be compared to a reaction–diffusion model of a forest fire, for which consumption of fuel propels the fire forward, but depletion of the fuel resource causes the reaction rate to drop towards the trailing end of the travelling combustion wave (Campos et al., 2004; Mandel et al., 2009; Kim, 2011). Similarly, the driving-Y's spatial spread through the wild-type population reduces the 'fuel' of females it needs to reproduce, thus extinguishing itself and, more importantly, the entire population.

Clearly this property is fortuitous for strategies designed to use the driving-Y for suppression/elimination of pest populations. A finite (and in mathematical terms, at least, arbitrarily small) number of driving-Y males introduced at the origin will develop into a propagating wave adequate to clear or suppress populations in their wake. For the 1-D case, this consists of two pulses each of an asymptotically constant amount of total driving-Ys travelling in opposite directions, and for the 2-D case, a circular pulse of driving-Ys of increasing total amount (asymptotically linear increase with time, or distance from the origin). For control of pest populations, the 'in-situ' continuous self-production of driving-Y males at ever-increasing distances from the release site has a distinct advantage over sterile insect release strategies, as it theoretically eliminates the need for continual re-introductions of lab-produced individuals.

5.2. Wave speed

For all our models, due to the bounded initial conditions that apply to localized releases of driving-Ys into a territory otherwise solely occupied by wild-types, the travelling waveforms are all pulled by the tip of the driving-Y travelling pulse. The asymptotic wave speed can be derived by linearizing the equations at the front of the wave for a broad class of density-dependent adult/juvenile

mortality and mating rate values and functional forms,² since all such rates are evaluated at carrying capacity and thus only enter the wave speed through T_A , which characterizes the pre-release wild-type equilibrium. The travelling waveform solutions behind the tip of the wave, calculated numerically, will, of course, depend upon the specific choices for the form of these rates.

The transparency of the analytical and semi-analytical expressions for asymptotic wave speeds obtained for our PDE models reveal the mechanisms that affect spatial spread of the driving-Y through the wild-type population. For the most basic one life-stage model, we obtain an expression for wave speed per generation analogous to Fisher advantageous gene spread, $v_G = 2\sqrt{D_H'(2m-1)}$. For more complex models, we derive a similar form with an effective selection constant dependent on m and an average diffusivity, and which is further modified by various (slowing) factors depending on the model. All other life history parameters enter the speed only through T_J , the length of the juvenile stage, and T_A , the average adult lifetime at wild-type carrying capacity. Speed for all models is determined solely by the invading types that can spread the driving-Y gene through their movement: driving-Y males and, in relevant models, Y^D -mated females. The shape of the waveforms will depend in a more complex way on the various life history parameters and on diffusivities of all of the different types, including wild-types who do not carry the gene.

We find that whether the female of a species undergoes single or multiple mating is an important factor in spatial spread of the driving-Y gene. When females are mated once only, vs. giving birth immediately upon each mating, they also may disperse the gene, and we additionally allow for their diffusivity to be different to that of the male. Thus for the model with single mating, non-Mendelian inheritance driving the increase in frequency of a driving-Y chromosome occurs only in males, but the spatial dispersal of a driving-Y occurs in both male and female adults. We show that wave speed is determined by the effective averages of diffusivities and growth and delay rates (at the tip of the wave) of the driving-Y males and Y^D -mated females. The contribution of the female towards spatially spreading the gene (wave slowing or speeding) depends upon the particular life history of the species (one or two life stages and duration of immobile stage) as well as sex differences in dispersivity. To first order, the asymptotic speed is proportional to the average of the diffusivities of the driving-Y male and Y^D -mated female, leading to the conclusion that Y^D -mated females could, in theory, spatially spread the gene even if adult driving-Y males were immobile.

Our analysis also shows that in modelling the spatial spread of a selfish gene, presence of an immobile juvenile stage in the life history of the species has a first-order effect on wave speed. The addition of an immobile stage of duration T_J to the one life-stage model reduces the asymptotic wave speed approximately in proportion to $T_J/(T_A + T_J)$, the ratio of time driving-Y males spend as immobile juveniles to the total generation time. If the species exhibits single mating, after which Y^D -mated females may also disperse the gene, then the first-order reduction will be smaller, $(T_J/2)/(T_A + T_J/2)$, since these females can immediately disperse after mating instead of being delayed in the immobile juvenile stage.

Finally, unlike the case for wild-types invading an empty landscape, we find that a mating rate that is dependent on total male population densities does not hinder wave establishment or change the functional form of the asymptotic wave speed (21) into a carrying capacity population. Under the model assumptions, there is therefore no threshold for establishment of the driving-Y in the wild-type population (unlike the Allee effect that occurs for wild-types invading an empty landscape). For species that have a

marked density-dependence on male population density for mating, these results have implications for control strategies in terms of re-invasion of wild-types into a previously-cleared area. For this model there exists a range of sufficiently low initial population densities of wild-types (i.e., below a critical propagule size) for which the wild-types do not establish a population wave in a cleared landscape. However, no such threshold exists for the driving-Y invading an equilibrium population of wild-types, and travelling waves are established for any non-zero release amount of driving-Y invaders. Thus mating that depends on the total male population density is an important factor to be considered when studying a system with both driving-Y invasion into areas populated with wild-types and re-invasion (by wild-types) of cleared areas, although beyond the scope of this work.

5.3. Assumptions and extensions

The results and timescales obtained from applying our model to *An. gambiae* mosquito population control and elimination suggest that release of genetically-modified driving-Y males is a promising approach for disease control. It must be kept in mind, however, that in our idealized formulation we assume that the driving-Y spreads into a spatially homogeneous, unbounded landscape with no seasonal or spatial variation in life-history parameters. Shigesada et al. (1986) and Shigesada and Kawasaki (1997) use PDEs to model spatial spread of a single species in a heterogeneous landscape by representing favourable and unfavourable environments as alternating, periodic or random patches with different growth and dispersal parameters; Seo and Lutscher (2011) use an idealized two-compartment reaction–diffusion system to model seasonal variability, and in certain cases obtain an analytical lower bound for invasion speed. Spatial heterogeneity and seasonality could in future be incorporated into our reaction–diffusion models, although it is likely that only numerical solutions would be possible for wave speed. We have also assumed that wild-type populations are spatially continuous, which is reasonable for some species and landscapes, but less so for others, in which case stepping-stone models may provide an alternative framework (Hancock and Godfray, 2012; Hartfield, 2012).

Implicit in reaction–diffusion models is the assumption of random walk and normally-distributed dispersal distances when applied to biological invasions. However, when the distribution of measured dispersal distances is strongly leptokurtic, integro-difference equations with fat-tail distribution kernels are commonly used (Kot et al., 1996). They show that the wave speed is sensitive to the shape of the fat-tail and generally higher than that predicted by the (implicitly ‘non-fat-tail’) reaction–diffusion models. Another approach that combines short- and long-range diffusion was introduced by Shigesada et al. (1995), in which a fraction of the short-range diffusing population can make long leaps and form new colonies, which either coalesce or grow independently of each other. These stratified diffusion models also produce invasion speeds that are higher than those predicted by short-range diffusion only.

Another implicit assumption of reaction–diffusion equations with continuous population densities is that these can become arbitrarily small. This assumption is valid at a large-scale or mean-field limit of physical situations that are discrete at the microscopic level (e.g. particles, lattice models, etc.). However, when modelling biological populations consisting of discrete individuals, there is an implicit lower bound on the population densities imposed by the fact that the number of individuals must be an integer. This is especially pertinent in the case of an invading population where isolated individuals will be the first to arrive at previously uninvaded territory. The population density of the invader must jump from zero to at least a small number ϵ that

² As long as they are dependent on total population densities of adults, juveniles, or total males respectively and lead to stable wild-type-only and driving-Y-only equilibria.

Table A.1
Parameters for *An. gambiae* mosquitoes.

Symbol	Definition	Estimate	Source
D_i	Diffusion coefficient of adult type U_i	0.01 & 0.1 km ² da ⁻¹	Example values
m	Fraction of progeny of driving-Y males that inherit the driving-Y	0.95	Galizi et al. (2014)
λ	Fecundity (female eggs per female)	16 da ⁻¹	Deredec et al. (2011)
η	Adult density-independent mating coefficient	2 da ⁻¹	Equivalent to $e^{-2} = 14\%$ of females remaining unmated after 1 day
μ_A	Adult density-independent mortality coefficient	0.12 da ⁻¹	Deredec et al. (2011)
γ	Adult density-dependent mortality coefficient (linear density dependence)	0	For <i>An. gambiae</i> , density-dependent death occurs mainly in juvenile stage (Hancock and Godfray, 2007)
ρ	Adult density-dependent mating coefficient	0	No information available
μ_J	Juvenile density-independent mortality coefficient	0.25 da ⁻¹	Recalculated from Molineaux and Gramiccia (1980), following Deredec et al. (2011) using $T_J = 12$ da
T_J	Duration of juvenile period (from oviposition to emergence of adults)	12 da	Depinay et al. (2004)
T_A	Average adult lifetime	8.3 da	$1/\mu_A$ ($\gamma = 0$)
θ	Probability of survival through juvenile stage due to density-independent mortality	0.05	$\theta = \exp(-\mu_J T_J)$
$g_J(J(x, t))$	Juvenile density-dependent mortality function	$\alpha_1 = 1/T_J = 0.083$ da ⁻¹ , $\alpha_2 = 7.06N_0$	Continuous-time analogue of discrete-time function of Deredec et al. (2011) (logarithmic form avoids over-compensation), Eq. (A.1)

represents the presence of one individual. Brunet and Derrida (1997) have modelled this effect by introducing a population density cut-off at the tip of the wave front in certain types of reaction–diffusion equations, and it results in a slowing effect on the wave speed.

The spatially explicit individual-based modelling framework of North et al. (2013) is particularly well suited to analysing the dynamics of a driving-Y when populations are sparse and stochastic effects can predominate. In such environments, the driving-Y can eliminate a small sub-population into which it has been released, and itself disappear, before dispersing to neighbouring sub-populations. In such cases, increasing the number of release sites, even at the expense of releasing fewer mosquitoes per site, can greatly increase the probability of successful population suppression or extinction. These models can also be used to explore the effects of environmental heterogeneity (North et al., 2013).

In conclusion, we have proposed a series of reaction–diffusion models as a way to study spatial spread of a particular type of selfish gene, and our results suggest that this approach could be a useful starting point for planning strategies that use the driving-Y to eliminate pest populations. The strength of delay PDE models for spatial spread lies in their generality and ability to reveal underlying diffusion/growth mechanisms, even if mean-field and other assumptions may mean some loss of realistic detail. The reaction–diffusion approach should therefore be viewed as complementary to discrete-individual and meta-population models. In future, we will explore enhancements to our model framework such as seasonal variation of life-history parameters and stochastic effects.

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Appendix A

Parameters for *An. gambiae* mosquitoes is given in Table A.1.

$$g_J(J(x, t)) = \alpha_1 \ln \left(\frac{\alpha_2 + J(x, t)}{\alpha_2} \right). \quad (\text{A.1})$$

Appendix B

Below, we show proofs and details of calculations of linear temporal stability for all equilibrium states for the one life-stage model and selected cases of interest for the other models. We use the method outlined in Section 2.1 (i.e., the existence of a range of values of k yielding a positive imaginary root(s) $\omega_i = \text{Im } \omega(k)$ in the relevant dispersion relation of the linearized equations for a particular equilibrium state proves that the state is unstable to perturbations; if no such root exists, the state is stable).

B.1. Basic model: one life stage

B.1.1. Stability of wild-type states before driving-Y invasion

We first consider the zero state, $\{F = 0, M = 0\}$, corresponding to wild-type males and females invading an empty landscape. We linearize the wild-type-only equations in Section 3.1 around the zero state to obtain the dispersion relation:

$$k^4 D_F D_M + k^2 (\mu D_F + \omega_i D_F - \lambda D_M + \mu D_M + \omega_i D_M) - \lambda \mu + \mu^2 - \lambda \omega_i + 2\mu \omega_i + \omega_i^2 = 0.$$

Solutions for ω_i are:

$$\omega_{i1} = \lambda - \mu - k^2 D_F, \quad \omega_{i2} = -\mu - k^2 D_M.$$

Since $D_F > 0$ and $\lambda > \mu > 0$, the first root ω_{i1} is positive for $|k| \leq \sqrt{(\lambda - \mu)/D_F}$. The second root ω_{i2} is always negative for all (real) k . Thus, this state is temporally linearly unstable to perturbations that include F .

We now consider the carrying-capacity equilibrium state

$$\{F = N_0/2 = (\lambda - \mu)/(2\gamma), M = N_0/2 = (\lambda - \mu)/(2\gamma)\}.$$

The dispersion relation given by linearization of the equations around this state is:

$$(-2D_M k^2 - 2\mu - 3\gamma N_0 - 2i\omega_i) (-2D_F k^2 + 2\lambda - 2\mu - 3\gamma N_0 - 2i\omega_i) + \gamma N_0 (2\lambda - \gamma N_0) = 0.$$

The roots for ω_i are (substituting $N_0 = (\lambda - \mu)/\gamma$):

$$\omega_{i1} = \frac{1}{2} \left(-2\lambda + \mu - k^2 D_F - k^2 D_M - \sqrt{\mu^2 + k^4 D_F^2 + 2k^2 \lambda D_M + k^4 D_M^2 - 2k^2 D_F (\lambda + k^2 D_M)} \right)$$

$$\begin{bmatrix} -D_H k^2 + 2m\lambda - \mu - \gamma N_0 - \omega_i & 0 & 0 \\ \lambda(1-2m) - \frac{\gamma N_0}{2} & -D_F k^2 + \lambda - \mu - \frac{3\gamma N_0}{2} - \omega_i & -\frac{\gamma N_0}{2} \\ -\frac{\gamma N_0}{2} - \lambda & \lambda - \frac{\gamma N_0}{2} & -D_M k^2 - \mu - \frac{3\gamma N_0}{2} - \omega_i \end{bmatrix}.$$

Box 1.

$$\omega_{i2} = \frac{1}{2} \left(-2\lambda + \mu - k^2 D_F - k^2 D_M + \sqrt{\mu^2 + k^4 D_F^2 + 2k^2 \lambda D_M + k^4 D_M^2 - 2k^2 D_F (\lambda + k^2 D_M)} \right).$$

The first root ω_{i1} is always negative for all (real) k , since $\mu < \lambda$. Using Wolfram Mathematica *Reduce* with the conditions $D_F > 0$, $D_M > 0$, $\lambda > \mu > 0$, we find that there is no value of k (real) for which the second root ω_{i2} is positive. The system is therefore temporally linearly stable to perturbations in F and M .

B.1.2. Dispersion matrix and stability for $\mathbf{U}_0$ (introduction of driving-Y)

We linearize (9) around $\mathbf{U}_0 = \{H, F, M\} = \{0, N_0/2, N_0/2\}$, where $N_0 = (\lambda - \mu)/\gamma$, to obtain the dispersion matrix as given in Box 1. We see that the matrix $\mathbf{S}$ is of the form:

$$\mathbf{S} = \begin{bmatrix} \mathbf{Z}^Y & 0 \\ \dots & \mathbf{Z}^0 \end{bmatrix}$$

where the 1×1 submatrix $\mathbf{Z}^Y$ and 2×2 submatrix $\mathbf{Z}^0$ are given by

$$\mathbf{Z}^Y = [-D_H k^2 + 2m\lambda - \mu - \gamma N_0 - \omega_i]$$

$$\mathbf{Z}^0 = \begin{bmatrix} -D_F k^2 + \lambda - \mu - \frac{3\gamma N_0}{2} - \omega_i & -\frac{\gamma N_0}{2} \\ \lambda - \frac{\gamma N_0}{2} & -D_M k^2 - \mu - \frac{3\gamma N_0}{2} - \omega_i \end{bmatrix}.$$

For all such matrices $\mathbf{S}$, the determinant is the product of the determinants of the two submatrices, i.e. $|\mathbf{S}| = |\mathbf{Z}^Y| |\mathbf{Z}^0|$. The dispersion relation $|\mathbf{S}| = 0$ is thus:

$$(-D_H k^2 + 2\lambda m - \mu - \gamma N_0 - \omega_i) \left((-2D_M k^2 - 2\mu - 3\gamma N_0 - i\omega_i) \times (-2D_F k^2 + 2\lambda - 2\mu - 3\gamma N_0 - 2\omega_i) + \gamma N_0 (2\lambda - \gamma N_0) \right) = 0.$$

The root of the first factor is $\omega_{i1} = 2m\lambda - \mu - \gamma N_0 - k^2 D_H$. We see that for all $|k| < \sqrt{(2m\lambda - \mu - \gamma N_0)/D_H}$, the first factor returns positive $\omega_i(k)$. The system is therefore unstable to perturbations in the driving-Y. The second factor, $|\mathbf{Z}^0|$, is the same as in the dispersion relation for the carrying-capacity equilibrium state of the system before the release of the driving-Y (Appendix B.1.1). As shown there, there are no positive roots ω_i for the second factor. The important consequence of this is that the wild-type population densities will be entrained by perturbations in the driving-Y, at the speed calculated by using only the dispersion relation for the driving-Ys, i.e. $|\mathbf{Z}^Y| = 0$.

B.1.3. Stability of the equilibrium state $\mathbf{U}_1$ (behind the wave)

We consider whether perturbations to $\mathbf{U}_1$ grow or decay. First, we consider the case of $1/2 < m \leq m_{crit}$. Linearizing (9) around $\mathbf{U}_1 = \{H_1 = m[2\lambda(1-m) - \mu]/\gamma$,

$$F_1 = (1-m)[2\lambda(1-m) - \mu]/\gamma, M_1 = 0\}$$

we obtain the dispersion relation:

$$\left(k^2 D_M - \frac{\lambda}{m} - 2\lambda m + 3\lambda + \omega_i \right) [k^4 D_F D_H + k^2 (D_F (2\lambda (1-m)^2 - \mu m + \omega_i) + D_H (2\lambda (1-m)^2 - \mu (1-m) + \omega_i)) + (2\lambda (1-m) + \omega_i) (-\mu + 2\lambda (1-m) + \omega_i)] = 0.$$

The roots for ω_i are:

$$\omega_{i1} = \left(-3 + \frac{1}{m} + 2m \right) \lambda - k^2 D_M$$

$$\omega_{i2} = \frac{1}{2} \left(-4\lambda + 4m\lambda + \mu - k^2 D_F - k^2 D_H - [\mu^2 + k^4 D_F^2 + 2k^2 (4m\lambda - 4m^2\lambda + \mu - 2m\mu) D_H + k^4 D_H^2 - 2k^2 D_F (4m\lambda (1-m) + \mu - 2m\mu + k^2 D_H)]^{1/2} \right)$$

$$\omega_{i3} = \frac{1}{2} \left(-4\lambda + 4m\lambda + \mu - k^2 D_F - k^2 D_H + [\mu^2 + k^4 D_F^2 + 2k^2 (4m\lambda - 4m^2\lambda + \mu - 2m\mu) D_H + k^4 D_H^2 - 2k^2 D_F (4m\lambda (1-m) + \mu - 2m\mu + k^2 D_H)]^{1/2} \right).$$

Since $(-3 + \frac{1}{m} + 2m) \leq 0$ for $\frac{1}{2} < m \leq 1$, and $D_M > 0$, the first root ω_{i1} can never be positive. For the second and third roots ω_{i2} and ω_{i3} , it can be shown using Wolfram Mathematica *Reduce* with conditions $\omega_i > 0$, $D_F > 0$, $D_M > 0$, $\lambda > \mu > 0$, $m > 1/2$, $m \leq m_{crit}$ that there is no value of k (real) for which either ω_{i2} or ω_{i3} is positive. The system overall is therefore temporally linearly stable to all perturbations in H , F and M .

Now we consider the case of $m_{crit} < m \leq 1$, corresponding to the extinction state. To investigate the system of Eqs. (9) linearized at $\mathbf{U}_1 = \{H_1 = 0, F_1 = 0, M_1 = 0\}$, we need to evaluate the ratio F/H at the limit where both F and H are 0. However, we find that this ratio converges to $F/H = (1-m)/m$ independently of whether m is above or below m_{crit} . We can thus use this relation to evaluate the linearized matrix for $m_{crit} < m \leq 1$ even in the limit of the individual population densities going to zero to obtain the dispersion relation:

$$2(-1+m)\lambda + \mu + \omega_i + k^2 D_F (\mu + \omega_i + k^2 D_H) \times \left(\frac{(-1+m)\lambda}{m} + \mu + \omega_i + k^2 D_M \right) = 0.$$

The roots are:

$$\omega_{i1} = \left(-1 + \frac{1}{m} \right) \lambda - \mu - k^2 D_M$$

$$\omega_{i2} = -\mu - k^2 D_H$$

$$\omega_{i3} = 2(1-m)\lambda - \mu - k^2 D_F.$$

Since $m > m_{crit} = 1 - \mu/(2\lambda)$ and $\lambda > \mu > 0$, it follows that

$$\left(-1 + \frac{1}{m} \right) \lambda - \mu < -\lambda + \frac{2\lambda^2}{2\lambda - \mu} - \mu = -\mu \frac{\lambda - \mu}{2\lambda - \mu} < 0$$

and

$$2(1-m)\lambda - \mu < 2\left(\frac{\mu}{2\lambda} \right) \lambda - \mu = 0$$

and thus ω_{i1} and ω_{i3} can never be positive. It can also be seen by inspection that ω_{i2} can never be positive. Since there is no value of k (real) for which any of the three roots are positive, the system is temporally linearly stable to perturbations in H .

B.2. Model with immobile juvenile stage

We now consider the stability of $\mathbf{U}_0$ for our model with an immobile juvenile stage (Section 3.2). As above, due to the form of

the dispersion matrix for this system, for a linear stability analysis we focus on the factor in the dispersion relation relating to the driving-Ys:

$$|\mathbf{Z}^Y(k, \omega(k))| = i\omega(k) - D_H k^2 + (2m e^{i T_J \omega(k)} - 1) \times (\mu_A + \gamma N_0) = 0.$$

This can be rearranged as:

$$2m(\mu_A + \gamma N_0) e^{i T_J \omega(k)} = -i\omega(k) + D_H k^2 + \mu_A + \gamma N_0.$$

Multiplying both sides by

$$T_J e^{-i T_J \omega(k) + (\mu_A + \gamma N_0 + D_H k^2) T_J}$$

gives $X = Y e^Y$ where

$$X = 2m(\mu_A + \gamma N_0) T_J e^{(\mu_A + \gamma N_0 + D_H k^2) T_J}$$

and

$$Y = (-i\omega(k) + D_H k^2 + \mu_A + \gamma N_0) T_J.$$

From $X = Y e^Y$, it follows that $W[X] = W[Y e^Y]$, where $W[\cdot]$ is the Lambert W function. For its properties see [Corless et al. \(1996\)](#). Since the Lambert W function is defined as $W[Y e^Y] = Y$, we obtain $Y = W[X]$. After substituting in $Y = W[X]$ the expressions for X and Y and rearranging, we obtain an explicit expression for $\omega(k)$:

$$\omega(k) = i \left(-\mu_A - \gamma N_0 - D_H k^2 + \frac{W \left[2m(\mu_A + \gamma N_0) T_J e^{(\mu_A + \gamma N_0 + D_H k^2) T_J} \right]}{T_J} \right)$$

$W[y]$ is real and single-valued for real and non-negative y , so since the argument of the Lambert W function in the equation above is positive for all real k values, $\omega(k)$ is thus single-valued and imaginary and given by:

$$\text{Im}(\omega(k)) = -\mu_A - \gamma N_0 - D_H k^2 + \frac{W \left[2m(\mu_A + \gamma N_0) T_J e^{(\mu_A + \gamma N_0 + D_H k^2) T_J} \right]}{T_J}.$$

In concise form, the equation above can be written as:

$$\Omega(K) = W \left[2m T e^{K^2 + T} \right] - K^2 - T$$

where $\Omega = T_J \text{Im} \omega(k)$, $T = T_J(\mu_A + \gamma N_0)$, and $K = k\sqrt{T_J D_H}$.

At $K = 0$, $\Omega(0) = W[2m T e^T] - T$. Since $W[y]$ is a monotonically increasing function of $y > 0$, for $T > 0$ and $2m > 1$ we have $\Omega(0) = W[2m T e^T] - T \geq W[T e^T] - T$. From the definition of the Lambert W function, it follows that $\Omega(0) \geq 0$.

Also, since

$$\frac{\partial \Omega(K)}{\partial K} = -\frac{2K}{1 + W[2m T e^{K^2 + T}]}$$

≤ 0 for all $K > 0$, $\Omega(K)$ decays monotonically from the positive value $\Omega(0)$ as K increases from 0. The same type of analysis applies for negative K s, i.e., $\Omega(K)$ decreases monotonically as K decreases from 0. As a result, there is a finite range of K (and k , since $K = k\sqrt{T_J D_H}$) between $K = -K_0$ and $K = K_0$ where $\text{Im} \omega(k) > 0$ and the equilibrium state $\mathbf{U}_0$ is unstable. For this model, K_0 is defined as the solution of $W[2m T e^{K_0^2 + T}] - K_0^2 - T = 0$ and from the definition of the Lambert W function we obtain $2m T = K_0^2 + T \Rightarrow K_0 = \sqrt{(2m - 1)T}$.

We have thus shown that the range

$$|k| \leq \sqrt{\frac{(2m - 1)(\mu_A + \gamma N_0)}{D_H}}$$

yields $\text{Im} \omega(k) > 0$, which is the result also obtained for the basic one life-stage model.

B.3. Model with females also dispersing Y chromosome

The dispersion relation $|\mathbf{Z}^Y(k, \omega(k))| = 0$ for the model in Section 3.3 is:

$$\sqrt{2m}(\mu_A + \gamma N_0) e^{i\omega(k) T_J / 2} = \sqrt{S_2}$$

where

$$S_2 = (D_{\text{avg}}^2 - D_{\text{diff}}^2) k^4 + 2D_{\text{avg}}[(\mu_A + \gamma N_0) - i\omega(k)] k^2 + (\mu_A + \gamma N_0)^2 - 2i(\mu_A + \gamma N_0)\omega(k) - \omega^2(k).$$

For (real) k values, the dispersion relation above reduces to:

$$2m T^2 e^{-\Omega(K)} + (1 - R_D) K^4 + 2K^2[T + \Omega(K)] + [T + \Omega(K)]^2 = 0$$

where $\Omega = T_J \text{Im} \omega(k)$, $T = T_J(\mu_A + \gamma N_0)$, $K = k\sqrt{T_J D_{\text{avg}}}$ and $R_D = D_{\text{diff}}^2 / D_{\text{avg}}^2$ (note that $0 \leq R_D \leq 1$).

For $K = 0$, the equation above gives

$$\Omega(0) = 2 \left(W \left[\sqrt{2m} \frac{T}{2} \exp \left(\frac{T}{2} \right) \right] - \frac{T}{2} \right).$$

Since $\sqrt{2m} \geq 1$ and $T > 0$, we obtain in similar fashion to the previous model:

$$\begin{aligned} \Omega(0) &= 2 \left(W \left[\sqrt{2m} \frac{T}{2} \exp \left(\frac{T}{2} \right) \right] - \frac{T}{2} \right) \\ &\geq 2 \left(W \left[\frac{T}{2} \exp \left(\frac{T}{2} \right) \right] - \frac{T}{2} \right) \end{aligned}$$

and from the definition of the Lambert W function it follows that $\Omega(0) \geq 0$.

Also, since

$$\frac{\partial \Omega(K)}{\partial K} = -\frac{2K(K^2(1 - R_D) + T + \Omega(K))}{K^2 + m T^2 e^{-\Omega(K)} + T + \Omega(K)}$$

is ≤ 0 for all $K \geq 0$ and $\Omega(K) > 0$, it follows that $\Omega(K)$ decays monotonically from the positive value of $\Omega(0)$ as K increases from 0. The derivative is guaranteed to remain negative until $\Omega(K)$ becomes 0 at

$$K = K_0 = \sqrt{\frac{T(\sqrt{2m}(1 - R_D) + R_D - 1)}{1 - R_D}}$$

which is obtained by setting $\Omega(K) = \Omega(K_0) = 0$ in the dispersion relation. The same analysis can be applied for negative K s and as a result, we have shown that there is a finite range of k (since $K = k\sqrt{T_J D_{\text{avg}}}$), given by

$$|k| \leq \sqrt{\frac{(\sqrt{2m}(1 - R_D) + R_D - 1)(\mu_A + \gamma N_0)}{(1 - R_D) D_{\text{avg}}}}$$

for which $\text{Im} \omega(k) > 0$ and the equilibrium state $\mathbf{U}_0$ is unstable.

Appendix C

Below, we show homogeneous equilibria and calculation of m_{crit} for our models with two life stages (Sections 3.2 and 3.3). All results below are for a logarithmic form of the juvenile density-dependent mortality given by (A.1) in Appendix A and no adult density-dependent mortality ($\gamma = 0$), corresponding to the representative mosquito case used for numerical solutions of the full equations.

C.1. Two life-stage model with immobile juveniles

Homogeneous equilibria for the two life-stage model with immobile juveniles ($T_J \neq 0$), (Section 3.2), are calculated as

described in Section 2. The equilibrium populations for the pre-release wild-type equilibrium state, $\mathbf{U}_0 = \{H_0, F_0, M_0, J_0, W_0\}$, are obtained from (12)

$$\begin{aligned} H_0 &= 0 \\ F_0 &= M_0 = \frac{N_0}{2} \\ J_0 &= \frac{\alpha_2 (\lambda \theta - \mu_A)}{\mu_A} \\ W_0 &= \frac{\mu_A}{\lambda \theta} \end{aligned}$$

along with:

$$N_0 = \frac{\alpha_2 (\lambda \theta - \mu_A) \ln \left[\frac{\lambda}{\mu_A} \right]}{(\lambda - \mu_A) \mu_A T_j}.$$

For $\mathbf{U}_1 = \{H_1, F_1, M_1, J_1, W_1\}$, the equilibrium state with the driving-Y present, we obtain from (12)

$$\begin{cases} m < 1 - \frac{\mu_A}{2\lambda\theta} \left\{ \begin{aligned} N_1 &= \frac{\alpha_2 (2(1-m)\theta\lambda - \mu_A) \ln \left[\frac{2\lambda(1-m)}{\mu_A} \right]}{(2(1-m)\lambda - \mu_A) \mu_A T_j} \\ F_1 &= (1-m) N_1 \\ H_1 &= m N_1 \\ M_1 &= 0 \\ J_1 &= \frac{\alpha_2 (2(1-m)\theta\lambda - \mu_A)}{\mu_A} \\ W_1 &= \frac{\mu_A}{2(1-m)\theta\lambda} \end{aligned} \right. \\ m \geq 1 - \frac{\mu_A}{2\lambda\theta} \left\{ \begin{aligned} N_1 &= F_1 = H_1 = M_1 = 0 \\ J_1 &= 0 \\ W_1 &= 1. \end{aligned} \right. \end{cases}$$

Thus, $m_{crit} = 1 - \mu_A/(2\lambda\theta)$.

C.2. Single mating model with Y^D -mated females

Below we treat the two life-stage model ($T_j \neq 0$) with females also dispersing the Y chromosome (Section 3.3).

C.2.1. Homogeneous Equilibria

The homogeneous equilibrium populations for the pre-release wild-type state, $\mathbf{U}_0 = \{H_0, F_{H0}, F_{M0}, F_{U0}, M_0, J_0, W_0\}$, are obtained from (17) at steady state. The following equation must be solved numerically to obtain the adult population density N_0 :

$$\mu_A T_j N_0 (L_0 - 1) - \alpha_2 (\theta L_0 - 1) \ln L_0 = 0 \quad (C.1)$$

where

$$L_0 = \frac{N_0 \eta \lambda}{\mu_A [2\rho\mu_A + N_0 (\eta + \mu_A)]}.$$

For $\rho \neq 0$ (male density-dependent mating), solution of (C.1) gives two equilibrium states with positive real values as well as a zero state. We assume that a non-zero wild-type equilibrium population density has been established before the release of a driving-Y, and thus we select the largest root of (C.1) (in general, which state is reached for wild-types invading a landscape depends upon the initial conditions of release).

For the special case of $\rho = 0$ (no male density-dependent mating) we obtain an analytical solution for the total adult population density:

$$N_0 = \frac{\alpha_2 (\mu_A^2 - \eta (\theta\lambda - \mu_A)) \ln \left[\frac{\eta\lambda}{\mu_A (\eta + \mu_A)} \right]}{\mu_A (\mu_A^2 - \eta (\lambda - \mu_A)) T_j}.$$

The other population densities and values can be written in terms of N_0 :

$$\begin{aligned} H_0 &= F_{H0} = 0 \\ F_{U0} &= \frac{N_0 (N_0 + 2\rho) \mu_A}{2[N_0 (\eta + \mu_A) + 2\rho\mu_A]} \\ F_{M0} &= \frac{N_0^2 \eta}{2[N_0 (\eta + \mu_A) + 2\rho\mu_A]} \\ M_0 &= \frac{N_0}{2} \\ J_0 &= \alpha_2 \left(\frac{N_0 \eta \theta \lambda}{\mu_A [2\rho\mu_A + N_0 (\eta + \mu_A)]} - 1 \right) \\ W_0 &= \frac{\mu_A (2\rho\mu_A + N_0 (\eta + \mu_A))}{N_0 \eta \theta \lambda}. \end{aligned}$$

For $\mathbf{U}_1 = \{H_1, F_{H1}, F_{M1}, F_{U1}, M_1, J_1, W_1\}$, the equilibrium state with the driving-Y present, values depend on m_{crit} . For $m \geq m_{crit}$, we obtain

$$\{H_1, F_{H1}, F_{M1}, F_{U1}, M_1, J_1, W_1\} = \{0, 0, 0, 0, 0, 0, 1\}.$$

For $m < m_{crit}$, the following equation can be solved numerically for the total adult population density N_1 :

$$\mu_A T_j N_1 (L_1 - 1) - \alpha_2 (\theta L_1 - 1) \ln L_1 = 0 \quad (C.2)$$

where

$$L_1 = \frac{2m(1-m)\eta\lambda N_1}{\mu_A [\rho\mu_A + mN_1 (\eta + \mu_A)]}.$$

As above, for $\rho \neq 0$ (male density-dependent mating) there are two positive real roots and a zero state for N_1 . For our travelling wave solutions, numerical solution of (17) shows that the equilibrium state established behind the wave for $m < m_{crit}$ is given by the largest real root of (C.2).

For the special case of $\rho = 0$ (no male density-dependent mating) we have an analytical solution:

$$N_1 = \frac{\alpha_2 (\mu_A^2 + \eta (2(m-1)\theta\lambda + \mu_A)) \ln \left[\frac{2(1-m)\eta\lambda}{\mu_A (\eta + \mu_A)} \right]}{\mu_A [\mu_A^2 + \eta (2(m-1)\lambda + \mu_A)] T_j}.$$

The other population densities and values can be written in terms of N_1 :

$$\begin{aligned} H_1 &= m N_1 \\ F_{H1} &= \frac{(1-m) m N_1^2 \eta}{\rho\mu_A + m N_1 (\eta + \mu_A)} \\ F_{U1} &= \frac{(1-m) N_1 (m N_1 + \rho) \mu_A}{\rho\mu_A + m N_1 (\eta + \mu_A)} \\ F_{M1} &= 0 \\ M_1 &= 0 \\ J_1 &= \alpha_2 \left(\frac{2(1-m) m N_1 \eta \theta \lambda}{\mu_A [\rho\mu_A + m N_1 (\eta + \mu_A)]} - 1 \right) \\ W_1 &= \frac{\mu_A (m N_1 \eta + m N_1 \mu_A + \rho\mu_A)}{2(1-m) m N_1 \eta \theta \lambda}. \end{aligned}$$

C.2.2. Calculation of m_{crit}

For $\rho \neq 0$ (male density-dependent mating), there are two real and positive solutions of the transcendental equation (C.2) for N_1 . These converge to a single solution as $m \rightarrow m_{crit}$. Note that there is a discontinuity in N_1 at m_{crit} : for $m = m_{crit} - \varepsilon$, where ε is a small positive number, we have $N_1 \rightarrow N_{1crit}$ (corresponding to convergence of the two positive roots); when $m = m_{crit} + \varepsilon$, the only real solution is $N_1 = 0$, i.e. total extinction of all populations. At m_{crit} , where the two non-zero solutions converge as $m \rightarrow m_{crit}$ from below, the derivative of N_1 with respect to m will be zero. So,

in order to determine m_{crit} , we differentiate (C.2) with respect to N_1 and set the derivative equal to zero to yield:

$$\begin{aligned} N_1^3 T_J [-2\eta\lambda m^3 (\eta + \mu_A) - m^2 (\eta + \mu_A) (\mu_A^2 + \eta\mu_A - 2\lambda\theta\eta)] \\ - N_1^2 T_J [4m^2 \rho\lambda\eta\mu_A + 2m\rho\mu_A (\mu_A^2 + \eta\mu_A - 2\lambda\theta\eta)] \\ + N_1 \left[2\alpha_2\eta\theta\lambda m (1-m) \rho \ln \left[\frac{\mu_A(\eta m N_1 + \mu_A m N_1 + \mu_A \rho)}{2\eta\lambda m(1-m)N_1} \right] \right. \\ \left. + 2\alpha_2\lambda\theta\eta m^2 \rho + \alpha_2 m \rho (\mu_A^2 + \eta\mu_A - 2\lambda\theta\eta) - \mu_A^3 \rho^2 T_J \right] \\ + \alpha_2 \mu_A^2 \rho^2 = 0. \end{aligned}$$

Simultaneous numerical solution of this equation with (C.2) yields m_{crit} and N_{1crit} (the latter represents the adult population that corresponds to $m \rightarrow m_{crit}$). For the special case of $\rho = 0$ (no male density-dependent mating) we obtain:

$$m_{crit} = 1 - \frac{\mu_A (\eta + \mu_A)}{2\lambda\theta\eta}.$$

Appendix D

In the case of the two life-stage model in Section 3.2, the system of Eqs. (8) gives:

$$i\omega(k^*) - D_H k^{*2} + (2me^{i\omega(k^*)T_J} - 1)(\mu_A + \gamma N_0) = 0 \quad (D.1)$$

$$v = \frac{\text{Im } \omega(k^*)}{\text{Im } k^*} \quad (D.2)$$

$$\frac{\text{Im } \omega(k^*)}{\text{Im } k^*} = \frac{\partial \omega(k)}{\partial k} \Big|_{k=k^*}. \quad (D.3)$$

For uniformly translating wave fronts, as shown in Ebert and van Saarloos (2000), $\text{Re } k^* = 0$ and $\text{Re } \omega(k^*) = 0$. Hence, we can write $\omega(k^*) = i \text{Im } \omega(k^*)$ and $k^* = i \text{Im } k^*$. (D.1) now becomes

$$\begin{aligned} -\text{Im } \omega(k^*) + D_H (\text{Im } k^*)^2 + (2m e^{-\text{Im } \omega(k^*)T_J} - 1) \\ \times (\mu_A + \gamma N_0) = 0. \end{aligned} \quad (D.4)$$

Using implicit differentiation of (D.1), we obtain

$$\frac{\partial \omega(k)}{\partial k} \Big|_{k=k^*} = \frac{2D_H \text{Im } k^*}{2(\mu_A + \gamma N_0)mT_J e^{-\text{Im } \omega(k^*)T_J} + 1}. \quad (D.5)$$

Combining (D.3)–(D.5) yields the equations in Section 3.2.1:

$$e^{-\text{Im } \omega(k^*)T_J} = \frac{2(\mu_A + \gamma N_0) + \text{Im } \omega(k^*)}{2m(\mu_A + \gamma N_0)(2 + \text{Im } \omega(k^*)T_J)} \quad (D.6)$$

$$\text{Im } k^* = \sqrt{\frac{(\mu_A + \gamma N_0)(1 - 2m e^{-\text{Im } \omega(k^*)T_J}) + \text{Im } \omega(k^*)}{D_H}}. \quad (D.7)$$

We will now show that (D.6) has a unique positive solution $\text{Im } \omega(k^*)$. The LHS decreases monotonically from 1 to 0 for $\text{Im } \omega(k^*)$ ranging from 0 to ∞ (and $T_J > 0$). If $T_J(\mu_A + \gamma N_0) > 1$, then the RHS decreases monotonically from $1/(2m)$, where $1/2 \leq 1/(2m) < 1$, to $1/[2mT_J(\mu_A + \gamma N_0)]$ at ∞ . Therefore, at $\text{Im } \omega(k^*) = 0$, the value of the RHS is below the value of the LHS ($=1$), but finishes above it at $\text{Im } \omega(k^*) \rightarrow \infty$ since $1/[2mT_J(\mu_A + \gamma N_0)] > 0$. Thus the LHS and RHS intersect for a unique value of $\text{Im } \omega(k^*) > 0$. If $T_J(\mu_A + \gamma N_0) < 1$, then the RHS increases monotonically from $1/(2m) < 1$ to $1/[2mT_J(\mu_A + \gamma N_0)]$. Again, at $\text{Im } \omega(k^*) = 0$ the value of the RHS is below the value of the LHS ($=1$) and finishes above it at $\text{Im } \omega(k^*) \rightarrow \infty$, and the LHS and RHS intersect for a unique value of $\text{Im } \omega(k^*) > 0$.

Combining (D.2), (D.6) and (D.7) yields (13) for the velocity v . The same type of analysis also applies to the model in Section 3.3.

Appendix E. Supplementary data

Supplementary material related to this article can be found online at <http://dx.doi.org/10.1016/j.tpb.2015.11.005>.

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