1 Equations

The equations solved by `Mosquito23` are based on the following

$$
\begin{aligned}
\frac{\partial X(a,s,g,m)}{\partial t} &= -d_a X + b_{s,g,m}\left[\overbrace{X(a-1,s,g,m)}^{a>0} - \overbrace{X}^{a<N-1}\right] + \overbrace{\nabla\cdot(D_{s,g,m}\nabla X - \mathbf{V}_{s,g,m}X)}^{a=N-1} + \\
a = 0 \quad & \begin{cases} \left(\dfrac{K - \sum_{m^*}\alpha_{m,m^*}\sum_{s,g}\sum_{i<\max(N,1)} X(i,s,g,m^*)}{K}\right)\times \\ \displaystyle\sum_{\substack{g_M,g_F,\\ m_M,m_F}} h(m_M,m_F,m)\ \lambda(g_F,m_F)\ i(g_M,g_F,g)\ \frac{w(m_M,m_F)X(N-1,M,g_M,m_M)}{\sum_{g^*,m^*} w(m^*,m_F)X(N-1,M,g^*,m^*)}\times \\ \quad p(g_M,g_F,m_M,m_F,s)X(N-1,F,g_F,m_F) \end{cases}
\end{aligned}
$$

where a = age (0 = newborn, $N-1$ = adult, $[1, N-2]$ = intermediate stages),
s = sex (M or F),
g = genotype (ww wildtype, Gw heterozygous GM or GG homozygous GM),
m = mosquito species (C = *An. coluzzii*, G = *An. gambiae*)
and $X(a,s,g,m)$ is abbreviated to X.

2 Parameters

Parameter name	Explanation	Degrees of freedom
d_a	Death rate $\begin{cases} d_{\text{adult}} \text{ for } a = N-1 \\ d_{\text{larvae}} \text{ for } a < N-1 \end{cases}$	2
b	Larval emergence rate has distribution $\Gamma(k = N, \theta = b/N)$	1
D	Diffusion rate	1
$\mathbf{V}$	Advection vector field	Distribution of flight times
K	Carrying capacity for species (spatially explicit, dependent on rainfall)	1 (for now)
$h(m_M, m_F, m)$	Hybridisation rate (following Beeton et al. 2019) $= \begin{cases} 1 & \text{if } m = m_M = m_F \\ 0 & \text{otherwise} \end{cases}$	0 (may be set in code)
λ	Larvae per female	1
$i(g_M, g_F, g)$	Inheritance of genotype where $g = \{ww, Gw, GG\}$ $\begin{array}{c\|c\|c\|c} & ww & Gw & GG \\ \hline ww & \{1,0,0\} & \{\frac{1}{2},\frac{1}{2},0\} & \{0,1,0\} \\ Gw & \{\frac{1}{2},\frac{1}{2},0\} & \{\frac{1}{4},\frac{1}{2},\frac{1}{4}\} & \{0,\frac{1}{2},\frac{1}{2}\} \\ GG & \{0,1,0\} & \{0,\frac{1}{2},\frac{1}{2}\} & \{0,0,1\} \end{array}$	0
$p(g_M, g_F, s)$	Proportion of offspring of given sex given genotypes of parents $= \begin{cases} p(Gw,g_F,M) = p(GG,g_F,M) & = a \\ p(Gw,g_F,F) = p(GG,g_F,F) & = 1-a \\ p(ww,Gw,F) = p(ww,GG,F) & = f \\ p(ww,Gw,M) = p(ww,GG,M) & = 1-f \\ 0.5 & \text{elsewhere} \end{cases}$	1 (accuracy a)
$w(m_M, m_F)$	Relative probability of female of species m_F mating with male of species m_M $= \begin{cases} w(C,C) = w(G,G) = 1 \\ w(C,G) = w(G,C) = w \end{cases}$	1 (w) (defaults to $w = 0$)
$\alpha(m, m')$	Lotka-Volterra competition between species	Defaults to $\alpha = I$ (may be set in code)

3 `Mosquito23`

`Mosquito23` simplifies the above equations, by assuming that the diffusion and advection is handled by other parts of the code, so that the above equations reduce to a system of ODEs. To interface with `Mosquito23`, you need to know the ordering of its vector X. For species m, genotype g, sex s and age a, this is

$$X\left(m + gN_{\text{species}} + sN_{\text{species}}N_{\text{genotypes}} + aN_{\text{species}}N_{\text{genotypes}}N_{\text{sexes}}\right) \ , \tag{1}$$

where

- N_{species} is the number of species,
- $N_{\text{genotypes}} = 3$ is the number of genotypes (with ordering $ww = 0$, $Gw = 1$, and $GG = 2$)
- $N_{\text{sexes}} = 2$ is the number of sexes (with order male$= 0$ and female$= 1$)
- N_{ages} (denoted by N in the above sections) is the number of ages (with ordering newborn$= 0$ and adult$=N_{\text{ages}} - 1$, with intermediate stages in between these).

The next sections write the equations explicitly and add some explanation.

3.1 Adults

All adult populations are goverend by

$$\frac{\mathrm{d}X(N-1,s,g,m)}{\mathrm{d}t} = -d_{\text{adult}}X(N-1,s,g,m) + bX(N-2,s,g,m) \ . \tag{2}$$

Here $N-1$ indicates the adult age bracket, and the $N-2$ is the eldest juvenile age bracket. The first term on the right-hand side describes the mortality of adults, while the second term desribes aging from the eldest juveniles. If $N = 1$ there are no adults, and all populations are governed by the "Newborn larvae" equations, below.

3.2 Intermediate juveniles

For $0 < a < N-1$, the populations are governed by

$$\frac{\mathrm{d}X(a,s,g,m)}{\mathrm{d}t} = -d_{\text{larvae}}X(a,s,g,m) + b\left(X(a-1,s,g,m) - X(a,s,g,m)\right) \ . \tag{3}$$

For $N \leq 2$ there are no such intermediate juveniles. The first term on the right-hand side describes the mortality of this age-bracket of juveniles, while the term involving b describes aging to/from older/younger age brackets

3.3 Newborn larvae

For $a = 0$, the populations are govened by

$$\frac{\mathrm{d}X(0,s,g,m)}{\mathrm{d}t} = -d_{\text{larvae}}X(0,s,g,m) - bX(0,s,g,m) + B(s,g,m) \ . \tag{4}$$

The first term describes mortality of newborns, while the second describes aging into the next age-bracket of juveniles. The final term describes the birth of newborn larvae. It is

$$B(s,g,m) = L\left(1 - \frac{C(m)}{K}\right) \sum_{g_M,g_F,m_M,m_F} P_{\text{offspring}}(s,g,m|g_M,g_F,m_M,m_F)P_{\text{mating}}(g_M,m_M,m_F)\lambda X(N-1,F,g_F,m_F) \tag{5}$$

This equation deserves explanation.

- $C(m)$ is the competition that a newborn feels from the rest of the larval populations. It is

$$C(m) = \sum_{a=0}^{N-2}\sum_{s=0}^{N_{\text{sexes}}-1}\sum_{g=0}^{N_{\text{genotypes}}-1}\sum_{m'=0}^{N_{\text{species}}-1} \alpha_{m,m'}X(a,s,g,m') \ . \tag{6}$$

  Notice that this does not include adults $a = N-1$. If $N = 1$, it is assumed that the carrying-capacity still applies, and the sum over a runs from 0 to 0. The Lotka-Voltera matrix α accounts for inter-specific competition. It defaults to $a = I$, that is, newborns only feel competition from their own species. There is one further caveat: if $K < K_{\text{min}}$ for user-defined K_{min} (which defaults to 10^{-6}) then $B = 0$ for all s, g and m. This helps with numerical stability in the case when K is time-dependent.

- The function $L(x) = 0$ if $x \leq 0$, while $L(x) = x$ for $x > 0$. This is to ensure that if $C(m) > K$ no newborns are produced.

- $X(N-1, F, g_F, m_F)$ is the number of adult ($a = N-1$), females of genotype g_F and species m_F. So $\lambda X(N-1, F, g_F, m_F)$ is the number of newborns produced by these female per timestep.

- $P_{\text{mating}}(g_M, m_M, m_F)$ is the probability that a male adult of genogype g_M and species m_M successfully mates with a female adult of species m_F to produce newborn. It is

$$P_{\text{mating}}(g_M, m_M, m_F) = \frac{w(m_M, m_F)X(N-1, M, g_M, m_M)}{\sum_{g'=0}^{N_{\text{genotypes}}}\sum_{m'=0}^{N_{\text{species}}} w(m', m_F)X(N-1, M, g', m')} \ . \tag{7}$$

  The numerator is the number of matings between male of species m_M and genotype g_M and the female, while the denominator normalises the probability. The matrix w defaults to the identity.

- $P_{\text{offspring}}(s, g, m|g_M, g_F, m_M, m_F)$ is the probability the offspring will have sex s, genotype g and species m, given the genotypes and species of its parents. This is

$$P_{\text{offspring}}(s, g, m|g_M, g_F, m_M, m_F) = h(m_M, m_F, m)i(g_M, g_F, g)p(g_M, g_F, m_M, m_F, s) \ . \tag{8}$$

  The first term, h, determines the hybridisation between species, the second determines the inheritance of genotypes, while the final term describes any sex bias in the offspring. The hybridisation defaults to $h = 1$ if $m_M = m_F = m$ and zero otherwise.

- Finally, these expressions are summed over all possible parental genotypes and species using $\sum_{g_M, g_F, m_M, m_F}$.

3.4 Time integration

The ODEs in `Mosquito23` may be integrated in time using one of the following methods.

1. Explicit-Euler, where $X(t + \Delta t) = \Delta t f(X(t))$. This is fast, but results in the greatest error.
2. Runge-Kutta4, where $X(t+\Delta t)$ is given by the fourth-order Runge-Kutta formula. This is approximately 4 times slower than explicit-Euler.
3. Scipy's `solve_ivp` method. This is over 100 times slower than explicit-Euler, but is the most accurate.

In addition, adaptive time-stepping is the default. Here, the user defines Δt, and if the algorithm detects that any $X(t + \Delta t) < 0$, the time-step is solved using a number of smaller sub-time-steps, chosen to guarantee that all X remain non-negative. This type of behaviour occurs when the time-dependent carrying capacity suddenly reduces, and the explicit-Euler or Runge-Kutta4 methods produce large negative changes in population numbers, which, if allowed, would result in $X < 0$. Solving the problem using smaller sub-time-steps overcomes this problem. In this algorithm, there is a minimum Δt allowed, which defaults to 10^{-12}, below which the algorithm exits with an error.

Finally, a user-defined cutoff, c, is placed on $X(t+\Delta t)$. If $X(t+\Delta t) < c$ (at the end of a time step) then $X(t+\Delta t)$ is set to zero. This prevents anomalous round-off and precision errors from accumulating. The default value of c is 10^{-6}.

4 `Mosquito23F`

4.1 Fecundity limiting (old version)

Female-sexed eggs of either Gw or GG fathers are assumed to become mostly inviable after fertilization, such that the sex ratio is skewed male with proportion a. The number of male-sexed eggs is assumed to stay the same as for wildtype mosquitoes.

$$p(g_M, g_F, s) = \begin{cases} p(Gw, g_F, F) = p(GG, g_F, F) & = \frac{1}{2}\left(\frac{1}{a} - 1\right) \\ 0.5 & \text{elsewhere} \end{cases} \tag{9}$$

4.2 Fecundity preserving (current version)

Female-sexed sperm of either Gw or GG fathers are assumed to become mostly inviable before implantation in eggs. In this case, the *total* number of eggs remains the same as for wildtype mosquitoes (as the eggs are not affected by the construct), but the sex ratio is skewed male with proportion $a > 0.5$.

We also include a corresponding female bias $b > 0.5$ in offspring of female Gw or GG "survivors" with wildtype males as demonstrated in Galizi et al. (2014) (Supp Table 6) (TODO: there is probably also an overall decrease in fecundity in this case that we should possibly also model, with 66.0 ± 3.8 eggs hatching versus 79.4 ± 2.2 for the control).

$$p(g_M, g_F, s) = \begin{cases} p(Gw, g_F, M) = p(GG, g_F, M) & = a \\ p(Gw, g_F, F) = p(GG, g_F, F) & = 1 - a \\ p(ww, Gw, F) = p(ww, GG, F) & = f \\ p(ww, Gw, M) = p(ww, GG, M) & = 1 - f \\ 0.5 & \text{elsewhere} \end{cases} \tag{10}$$

5 `Mosquito23G`

We revisit the equations solved by `Mosquito23`, but discretise and make some of the variables random:

$$\begin{aligned} X_t(a,s,g,m) &= X_{t-1}(a,s,g,m) - d'_a + b'_{s,g,m} + D'_{s,g,m} + V'_{s,g,m} + \\ a = 0 & \quad \left\{ \sum_{\substack{g_M, g_F, \\ m_M, m_F}} \lambda'_{s,g,m,g_M,g_F,m_M,m_F} \right. \end{aligned}$$

where:

$$d'_a \sim \text{Binom}\left(n = X_{t-1},\ p = d_a \Delta t\right) \tag{11}$$

$$b'_{s,g,m} \sim \text{Binom}\left(n = \left[\overbrace{X_{t-1}(a-1,s,g,m)}^{a>0} - \overbrace{X_{t-1}}^{a<N-1}\right],\ p = b_{s,g,m}\Delta t\right) \tag{12}$$

$$D'_{s,g,m} \sim \text{Binom}\left(n = X_{t-1},\ p = \left|\frac{\Delta t}{X_{t-1}} \overbrace{\nabla \cdot (D_{s,g,m} \nabla X_{t-1})}^{a=N-1}\right|\right) \text{sign}(p) \tag{13}$$

$$V'_{s,g,m} \sim \text{Binom}\left(n = X_{t-1},\ p = \left|\frac{\Delta t}{X_{t-1}} \overbrace{\nabla \cdot (-\mathbf{V}_{s,g,m} X_{t-1})}^{a=N-1}\right|\right) \text{sign}(p) \tag{14}$$

$$\lambda'_{s,g,m,g_M,g_F,m_M,m_F} \sim \text{Pois}\left(\left[\frac{K - \sum_{m^*} \alpha_{m,m^*} \sum_{s,g} \sum_{i<\max(N,1)} X(i,s,g,m^*)}{K}\right] \times \right. \tag{15}$$

$$h(m_M, m_F, m)\ \lambda(g_F, m_F)\ i(g_M, g_F, g)\ \frac{w(m_M, m_F) X(N-1, M, g_M, m_M)}{\sum_{g^*,m^*} w(m^*, m_F) X(N-1, M, g^*, m^*)} \times \tag{16}$$

$$\left. p(g_M, g_F, m_M, m_F, s) X(N-1, F, g_F, m_F) \Delta t \right) \tag{17}$$

following North and Godfray (2018)'s use of constant probabilities of survival, mortality and dispersal but Poisson-distributed egg laying. Their model tracks the age of each individual juvenile — this is not feasible in our case with such huge numbers of mosquitoes, so we instead assume constant probability of ageing as per the original ODE model's mean field assumption.