Mathematical Biology

Eradicating vector-borne diseases via age-structured culling

Stephen A. Gourley · Rongsong Liu · Jianhong Wu

Abstract   We derive appropriate mathematical models to assess the effective-ness of culling as a tool to eradicate vector-borne diseases. The model, focused on the culling strategies determined by the stages during the development of the vector, becomes either a system of autonomous delay differential equations with impulses (in the case where the adult vector is subject to culling) or a system of nonautonomous delay differential equations where the time-varying coefficients are determined by the culling times and rates (in the case where only the immature vector is subject to culling). Sufficient conditions are derived to ensure eradication of the disease, and simulations are provided to compare the effectiveness of larvicides and insecticide sprays for the control of West Nile virus. We show that eradication of vector-borne diseases is possible by culling the vector at either the immature or the mature phase, even though the size of the vector is oscillating and above a certain level.

Keywords   Stage-structure · Delay · Impulse · Culling · Vector-borne disease

Mathematics Subject Classification (2000)   34K45 · 34K25 · 34K60 · 92D30

S. A. Gourley (✉)
Department of Mathematics, University of Surrey, Guildford, Surrey GU2 7XH, UK
e-mail: s.gourley@surrey.ac.uk

R. Liu
Department of Mathematics, Purdue University, 150 N. University Street,
West Lafayette, IN 47907-2067, USA

J. Wu
Laboratory for Industrial and Applied Mathematics, Department of Mathematics and Statistics,
York University, Toronto, ON, Canada M3J 1P3

1 Introduction

Culling has been a common method for pest control and ecosystem management. Despite different formats such as shooting, trapping and crop spraying, culling often takes place at certain particular times only. These culling times are regulated by many factors including the maturation status of individuals of the species involved. For example, crop spraying may be exercised at certain times coinciding with critical stages in the insects' development.

Culling has also been a widely adopted tool to control vector-borne diseases in the hope that culling the vector at carefully chosen times may intervene the transmission cycle and reduce the infection. A specific example is larvicides and insecticide sprays as techniques in the war against mosquitoes, the vector for many mosquito-born diseases including West Nile virus (WNv) and Dengue fever.

One purpose of this article is to qualitatively assess the effectiveness of larvicides and insecticide sprays in the control of West Nile virus in North America. The virus was isolated in the West Nile district of Uganda in 1937 [11], and has been maintained in an enzootic cycle involving culicine mosquitoes and birds [3,4] in the eastern hemisphere. In North America, the WNv activities were first recorded in the borough of Queens, New York City, in 1999 [2,7], and the virus has expanded spatially so rapidly within the subsequent 5 years that it has become a permanent fixture of the North America medical landscape [8]. Various techniques have been used in the war against mosquitoes, from the rolled up newspaper to sprayer trucks. But for speed and effectiveness, few techniques compare to larvicides, substances that destroy mosquito larva, the pre-adult insects that breed and mature in standing water. Biological larvicides are made from the bacteria Bacillus thuringiensis israaelensis or Bacillus sphaericus. The bacteria produce a crystal which is poisonous to mosquito larvae, but virtually harmless to other forms of aquatic life. Unfortunately, as with many insect species, the larva can be difficult to find. An alternative to larvicides is insecticide sprays to kill adult mosquitoes. Called adulticides and used in many residential areas, some kill both mosquitoes and "good insects" that eat mosquitoes. Another drawback, in addition to limited effect, is the perceived public health implication. Large numbers of mosquitoes survive adulticide sprays by flying away or finding shelter in gutter downspouts and eaves, under foliage, and other protected areas (http://www.rifleco.org/Parks/mosquitoes.htm). Therefore, it is highly desirable to develop appropriate models so that we can qualitatively examine the effectiveness of larvicides and insecticide sprays.

We start, in Sect. 2, to describe the impact of culling of the immature individuals on the dynamics of the adult population in a single population with two stages: immature and mature. This is important for the later model formulation of the vector-borne disease transmission when the vector also has two stages and when the immature of the vector does not participate in the transmission cycle. We show that the adult population is governed by a certain nonautonomous

delay differential equation. The growth rate of the adult population is the balance of the death rate and the maturation rate. The latter is the birth rate exactly at the maturation length ago, corrected to allow for juvenile mortality. Mortality of juveniles may be attributed either to "natural" mortality, or to culling. The former is accounted for by a factor depending on the per-capita natural death rate of juveniles and the maturation period. Mortality attributable to culling is accounted for by a certain time dependent factor representing the probability that an individual will survive every attempt to kill it before it becomes an adult. Our model is quite general in that it does not require the culls to occur at equally spaced times, nor every cull to remove the same proportion of individuals. Indeed, even if the culls are equally spaced in time, as time t progresses the interval $[t - \tau, t]$ will not always contain the same number of culls. Thus different cohorts of juveniles may be subjected to different numbers of culls. These considerations lead to a nonautonomous delay equation for the total number of adults.

In Sect. 3, we formulate the model equation for the vector-borne disease transmission under the assumption that (i) the vector (thinking of mosquitoes as the vector) involves two stages—immature and mature, and the immature will not get infected through the reservoir species (birds, perhaps) and there is no vertical transmission within the vector; (ii) the total population of the reservoir species remains relatively constant in time. We shall consider culling either the immature and or the mature, and the resulted model is a system of delay differential equations for the susceptible matured vector, the infected matured vector and the infected birds. In the case where culling takes place for immature only, the model becomes a nonautonomous system of delay differential equations; while in the case of culling the mature vector, we end up with an autonomous system of delay differential equations subject to impulses at fixed times. In either case, we derive some sufficient conditions under which the infected vector and reservoir species become extinct.

Section 4 provides the results of some numerical simulations. These simulations show that the analytically obtained sufficient conditions for eradicating the disease are feasible under a wide range of culling strategies, and eradication of the disease can be achieved by culling even when the vector population oscillates periodically with a large amplitude. The simulations also illustrate the relative effectiveness of larvicides and adulticides.

2 Culling of immatures: model derivation

In a recent paper, Simons and Gourley [9] studied a time dependent stage structured population in which the adults (but not juveniles) are subject to culling or trapping which occurs only at certain particular times $t_1, t_2, t_3, \ldots$. Their model equation is

$$u'_m(t) = e^{-\mu\tau} b(u_m(t - \tau)) - d(u_m(t)) - \sum_{j=1}^{\infty} b_j u_m(t_j^-)\delta(t - t_j), \quad t > 0 \quad (2.1)$$

where $\mu > 0$ represents juvenile mortality, $u_m(t)$ is the total number of adults at time t, $u_m(t_j^-)$ is the population just before the impulsive cull at time t_j, τ is the maturation time, b_j is the proportion of the mature species trapped or culled at time t_j and δ denotes the Dirac delta function. In (2.1), $b(u_m(t))$ is a function representing the birth rate of the immature species while $d(u_m(t))$ is the natural death rate of the mature species. The $e^{-\mu\tau}b(u_m(t-\tau))$ term is the rate at which immature individuals become mature. This term incorporates the delay τ and equals the birth rate τ time units ago, corrected to allow for juvenile mortality.

In their derivation of (2.1), Simons and Gourley [9] assumed the immature population was not subject to culling. In some situations this may be a reasonable assumption especially if the immature members are well hidden and protected and therefore difficult to access. However, particularly where it is necessary to eradicate a species completely, it is sometimes as important to find and destroy the immature members as the adults. Indeed, in insect infestations isolated efforts aimed only at destroying the flying adults (e.g., by spraying) might not eliminate the infestation if there remain large numbers of eggs and larvae that are unaffected by the nature of the eradication efforts. In insect species adults typically lay many hundreds of eggs during their (usually short) lives.

In this section we will develop these ideas further by examining a stage-structured model for a single species population in which only the immatures are culled. Even if the adults are not culled, this strategy can result in eradication as long as the adults have some intrinsic death rate. Following Simons and Gourley [9], culling occurs only at certain discrete times t_j. However, in this section it is the immatures that are culled rather than the matures.

Let $u(t,a)$ be the density of individuals of age a at time t. We will assume that

$$\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} = -\mu(a)u - \sum_{j=1}^{\infty} b_j(a)u(t_j^-,a)\delta(t-t_j), \quad 0 < a < \tau \qquad (2.2)$$

where τ is the age at which an individual becomes a mature reproducing adult, $\mu(a)$ is the natural death rate for immatures, $b_j(a) \in [0,1]$ is the fraction of individuals of age a that are removed at the cull at time t_j and δ is the Dirac delta function. The superscript "$-$" on the variable t_j in $u(t_j^-,a)$ denotes the limit of $u(t,a)$ as t approaches t_j from below (in other words, the population just prior to the cull at time t_j). We shall frequently also need the right limit, denoted using a superscript $+$, to refer to the situation immediately after a cull.

We shall assume that

$$u(t,0) = b(u_m(t)) \qquad (2.3)$$

where $b(\cdot)$ is the birth function and $u_m(t)$ is the total number of adults, given by

$$u_m(t) = \int_{\tau}^{\infty} u(t,a)\,\mathrm{d}a. \qquad (2.4)$$

Equation (2.3) states that the birth rate $u(t,0)$ is some function of the total number of adults.

The solution of (2.2) will be continuous in time except for discontinuous jumps at the particular times t_j when culls occur. To see that $b_j(a)$ does indeed have the interpretation of being the fraction of age a removed at time t_j, integrate (2.2) from time t_j^- to t_j^+ to obtain

$$u(t_j^+, a) = (1 - b_j(a))u(t_j^-, a). \tag{2.5}$$

This result will be important later.

In this section we will assume that the adults are not subject to culling and also that their intrinsic death rate is a constant, μ_m. Thus

$$\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} = -\mu_m u, \quad \text{for } a > \tau \tag{2.6}$$

where μ_m is some constant. Recall that $u_m(t)$ is defined by (2.4). Differentiating this expression and assuming that $u(t, \infty) = 0$ gives

$$\frac{du_m(t)}{dt} = \int_\tau^\infty \left(-\frac{\partial u}{\partial a} - \mu_m u(t, a) \right) da = u(t, \tau) - \mu_m u_m(t) \tag{2.7}$$

and thus the aim is to try to find $u(t, \tau)$ in terms of the function u_m. This is a little tricky in that the culls do not have to be equally spaced in time, and so as time progresses the issue is mainly one of keeping track of how many culls have occurred in the previous τ units of time. We will develop the ideas as follows. Fortunately, the intermediate steps can all be interpreted ecologically in terms of probabilities and this aids the understanding.

Let us assume $t > a$ (eventually we shall set $a = \tau$) and define

$$u_\xi(a) = u(\xi + a, a).$$

Then

$$\frac{du_\xi}{da} = \left[\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} \right]_{t=\xi+a}$$

$$= \left[-\mu(a)u(t, a) - \sum_{j=1}^\infty b_j(a)u(t_j^-, a)\delta(t - t_j) \right]_{t=\xi+a}$$

so that

$$\frac{du_\xi}{da} = -\mu(a)u_\xi(a) - \sum_{j=1}^\infty b_j(a)u(t_j^-, a)\delta(a + \xi - t_j). \tag{2.8}$$

We will deal with the culls shortly, but let us first understand something about the evolution of the immatures in the period between the culls at times t_{i-1} and t_i. We will integrate (2.8) for a between $t_{i-1}^+ - \xi$ and $t_i^- - \xi$ [an interval of values of a throughout which the summation term in (2.8) plays no role]. This gives, in terms of the original variable u,

$$u(t_i^-, t_i^- - \xi) = \exp\left(-\int_{t_{i-1}^+ - \xi}^{t_i^- - \xi} \mu(s)\, ds\right) u(t_{i-1}^+, t_{i-1}^+ - \xi) \tag{2.9}$$

or, letting $\xi = t_i - a$ and dropping superscripts on the t_i where they are not needed,

$$u(t_i^-, a) = \exp\left(-\int_{a-(t_i-t_{i-1})}^{a} \mu(s)\, ds\right) u(t_{i-1}^+, a - (t_i - t_{i-1})). \tag{2.10}$$

Using (2.5), this becomes

$$u(t_i^-, a) = \exp\left(-\int_{a-(t_i-t_{i-1})}^{a} \mu(s)\, ds\right)\left(1 - b_{i-1}(a - (t_i - t_{i-1}))\right) u(t_{i-1}^-, a - (t_i - t_{i-1}))$$
$$\tag{2.11}$$

which deals with the cull at time t_{i-1} and can be understood as follows. The term in the left-hand side is those of age a at time t_i^-, so that the cull at time t_i is imminent. The individuals alive at this time have survived the previous cull which occurred at time t_{i-1} (at which time these individuals were of age $a - (t_i - t_{i-1})$) and have also not died naturally. The probability of an age $a - (t_i - t_{i-1})$ individual surviving the cull at time t_{i-1} is precisely $1 - b_{i-1}(a - (t_i - t_{i-1}))$, and the probability of surviving naturally (i.e. not dying a natural death) from age $a - (t_i - t_{i-1})$ to age a is

$$\exp\left(-\int_{a-(t_i-t_{i-1})}^{a} \mu(s)\, ds\right)$$

and the expression in (2.11) arises from multiplying these probabilities.

One can replace i by $i - 1$ and a by $a - (t_i - t_{i-1})$ in (2.11) to give

$$u(t_i^-, a) = \exp\left(-\int_{a-(t_i-t_{i-2})}^{a} \mu(s)\, ds\right) \times \left(1 - b_{i-1}(a - (t_i - t_{i-1}))\right)$$
$$\times \left(1 - b_{i-2}(a - (t_i - t_{i-2}))\right) u(t_{i-2}^-, a - (t_i - t_{i-2})) \tag{2.12}$$

which can be interpreted in a similar probabilistic way. This pattern can of course be continued to include even earlier culls. There will be only a finite number of them over the interval of time of length τ during which an individual is immature, but the actual culls involved and the number of them (they do not have to be equally spaced in time) will vary from cohort to cohort depending on the time of birth.

What is really needed is an expression for $u(t, \tau)$ (with t not necessarily one of the t_i). Such an expression is expected essentially to be the birth rate τ units of time ago, which is $u(t - \tau, 0)$ or $b(u_m(t - \tau))$, corrected for egg to adult survival. The expressions (2.11) and (2.12) suggest how this correction will be achieved, the main changes being adaptation of the arguments of the b_i, and appropriate notation to keep track of how the relevant culls change as time progresses. At a general time t, only culls that occurred between times $t - \tau$ and t are relevant.

For a general time t, we shall let

$$i(t) = \max\{i : \ t_i \le t\} \tag{2.13}$$

and

$$k(t) = \min\{i : \ t_i > t - \tau\}, \tag{2.14}$$

then, for a given t, relevant culls are those at the times t_j with j between $k(t)$ and $i(t)$ inclusive. The expression for $u(t, \tau)$ is then the following, in which the exponential term is the probability of not dying a natural death during the maturation phase from age 0 to τ:

$$
\begin{aligned}
u(t, \tau) &= u(t - \tau, 0) \exp\left(-\int_0^\tau \mu(s)\,ds\right) \prod_{j=k(t)}^{i(t)} \left(1 - b_j(\tau - (t - t_j))\right) \\
&= b(u_m(t - \tau)) \exp\left(-\int_0^\tau \mu(s)\,ds\right) \prod_{j=k(t)}^{i(t)} \left(1 - b_j(\tau - (t - t_j))\right). \tag{2.15}
\end{aligned}
$$

Thus, the delay differential equation (2.7) for the total number of adults $u_m(t)$ becomes

$$\frac{du_m(t)}{dt} = S(t) \exp\left(-\int_0^\tau \mu(s)\,ds\right) b(u_m(t - \tau)) - \mu_m u_m(t) \tag{2.16}$$

where

$$S(t) = \prod_{j=k(t)}^{i(t)} \left(1 - b_j(\tau - (t - t_j))\right) \tag{2.17}$$

with $i(t)$ and $k(t)$ given by (2.13) and (2.14). All information relating to culling is embodied in the function $S(t)$ and features nowhere else. Note that $0 \le S(t) \le 1$ for all $t > \tau$, so that $\limsup_{t \to \infty} S(t)$ exists. The total number of adults evolves according to a nonautonomous delay differential equation (2.16).

3 The West Nile virus

3.1 Culling of immature mosquitoes

In this section we shall formulate a mathematical model for the situation when only immature (larval) mosquitoes are culled. By solving the von Foerster equation for the larval mosquitoes, we can formulate a model involving only three state variables: $M_S(t)$, $M_I(t)$ and $B_I(t)$ which denote respectively the total numbers of susceptible adult mosquitoes, infected adult mosquitoes and infected birds.

Larval mosquitoes $l(t, a)$ are assumed not to interact with the adults or the birds. The larval stage (considered as the only stage prior to adulthood) is of duration τ. Larvae are culled and so, following the modelling described in Sect. 2, their evolution equation is taken to be of the form

$$\frac{\partial l}{\partial t} + \frac{\partial l}{\partial a} = -\mu(a)l - \sum_{j=1}^{\infty} b_j(a)l(t_j^-, a)\delta(t - t_j), \quad 0 < a < \tau, \quad (3.1)$$

where the t_j are the times at which culls happen. Both susceptible and infected mosquitoes may lay eggs but the virus is not passed on to offspring. The birth rate $l(t, 0)$ of mosquitoes is therefore assumed to be a function of the total number of adult mosquitoes $M_S(t) + M_I(t)$, so that

$$l(t, 0) = b(M_S(t) + M_I(t)) \quad (3.2)$$

where $b(\cdot)$ is the birth rate function. Susceptible adult mosquitoes are assumed to satisfy an equation of the form

$$\frac{dM_S}{dt} = l(t, \tau) - \gamma B_I M_S - d_S M_S$$

where $l(t, \tau)$ is the rate at which mosquitoes becomes mature. In this equation, $\gamma B_I M_S$ is the rate at which susceptible mosquitoes becomes infected mosquitoes (a mosquito becomes infected when it bites an infected bird) and $d_S M_S$ is the death rate for susceptible mosquitoes. By analogy with the earlier analysis for a single species,

$$l(t, \tau) = l(t - \tau, 0) \exp\left(-\int_0^\tau \mu(s)\, ds\right) S(t)$$

$$= b(M_S(t - \tau) + M_I(t - \tau)) \exp\left(-\int_0^\tau \mu(s)\, ds\right) S(t)$$

where $S(t)$ is again defined by (2.17). Thus, the equation for the susceptible mosquitoes is

$$\frac{\mathrm{d}M_S}{\mathrm{d}t} = S(t) \exp\left(-\int_0^\tau \mu(s)\,\mathrm{d}s\right) b(M_S(t-\tau)+M_I(t-\tau))-\gamma B_I M_S-d_S M_S, \quad (3.3)$$

which we now couple with the following equations for the infected mosquitoes and the infected birds respectively:

$$\frac{\mathrm{d}M_I}{\mathrm{d}t} = \gamma B_I M_S - d_I M_I, \quad (3.4)$$

$$\frac{\mathrm{d}B_I}{\mathrm{d}t} = \beta(N_B - B_I)M_I - d_B B_I. \quad (3.5)$$

The meaning of the terms in (3.4) is obvious. As regards (3.5), we are assuming that the total number of birds is some constant $N_B > 0$, so that $N_B - B_I$ is the number of susceptible birds. Thus $\beta(N_B - B_I)M_I$ is the rate at which susceptible birds become infected birds, assumed to be given by the law of mass action. A bird becomes infected when it is bitten by an infected mosquito.

Our aim is to understand something about the dynamics of the nonautonomous system consisting of Eqs. (3.3), (3.4) and (3.5) for $t > 0$, where $S(t)$ is given by (2.17). The system is solved subject to the following initial data:

$$M_S(\theta) = M_S^0(\theta) \geq 0, \quad \theta \in [-\tau, 0],$$
$$M_I(\theta) = M_I^0(\theta) \geq 0, \quad \theta \in [-\tau, 0], \quad (3.6)$$
$$B_I(0) = B_I^0 \in [0, N_B]$$

where $M_S^0(\theta)$, $M_I^0(\theta)$ and B_I^0 are prescribed. Note that all the information about the culling of larval mosquitoes is contained within the function $S(t)$, and so, unlike in Sect. 3.2 of this paper where we consider culling of adult mosquitoes, the system is not supplemented by impulse conditions at the times t_j. We will first prove the following proposition on non-negativity of solutions.

Proposition 3.1 *Let the birth function* $b(\cdot)$ *satisfy* $b(0) = 0$ *and* $b(M) > 0$ *for all* $M > 0$. *Then the solution of system* (3.3), (3.4) *and* (3.5) *for* $t > 0$, *subject to* (3.6), *satisfies* $M_S(t) \geq 0$, $M_I(t) \geq 0$, $B_I(t) \in [0, N_B]$ *for all* $t > 0$.

Proof We first prove that $B_I(t)$ never exceeds N_B. If this is false then there exists a first time t_1 (which could in principle be zero) with $B_I(t_1) = N_B$ and $B_I'(t_1) \geq 0$. Evaluation of (3.5) at time t_1 immediately gives a contradiction.

Next we shall prove that $M_S(t) \geq 0$ for all $t > 0$. This is by the method of steps, and the result will first be established for $t \in (0, \tau]$. On this interval, from (3.3),

$$\frac{dM_S}{dt} \geq -\gamma B_I M_S - d_S M_S.$$

Hence

$$M_S(t) \geq M_S^0(0) \exp\left(-\int_0^t (\gamma B_I(\xi) + d_S)\, d\xi\right)$$

and so $M_S(t) \geq 0$ for all $t \in (0, \tau]$. Repeating this analysis shows that $M_S(t) \geq 0$ for all $t \in (\tau, 2\tau]$ and the argument can be continued to include all positive times.

It remains to prove that $M_I(t) \geq 0$ and $B_I(t) \geq 0$ for $t > 0$. But, having shown that $B_I(t) \leq N_B$, the variable $(M_I(t), B_I(t))$ can be interpreted as satisfying a system of the form (3.4), (3.5) in which $M_S(t)$ is now a prescribed non-negative function. The resulting system generates a monotone dynamical system and the results by Smith [10, p. 32] immediately assure us that $(M_I(t), B_I(t))$ cannot leave the closed first quadrant of the (M_I, B_I) plane. The proof is complete.

We will now prove the following theorem which provides conditions sufficient for the eradication of the disease.

Theorem 3.2 *Consider system* (3.3), (3.4) *and* (3.5) *for* $t > 0$, *subject to* (3.6). *Suppose the birth function* $b(\cdot)$ *satisfies* $b(0) = 0$ *and* $b(M) > 0$ *for all* $M > 0$, *and let* $S(t)$ *be defined by* (2.17). *Let* $S^\infty = \limsup_{t\to\infty} S(t)$. *Assume that either*

$$\min(d_I, d_S) > S^\infty b'_{\max} \exp\left(-\int_0^\tau \mu(s)\, ds\right) \qquad (3.7)$$

or

$$d_I d_B > \frac{\gamma \beta N_B b_{\max} S^\infty \exp\left(-\int_0^\tau \mu(s)\, ds\right)}{\min(d_I, d_S)} \qquad (3.8)$$

where $b_{\max} = \sup_{m\geq 0} b(m)$ *and* $b'_{\max} = \sup_{m\geq 0} b'(m)$. *Then* $B_I(t) \to 0$ *and* $M_I(t) \to 0$ *as* $t \to \infty$.

Proof Denote the total number of adult mosquitoes by $M_T(t) = M_S(t) + M_I(t)$. We will establish that $M_I(t) \to 0$ under condition (3.7) by showing that, under this condition, $M_T(t) \to 0$. By adding (3.3) and (3.4) we see that

$$\frac{dM_T}{dt} = S(t) \exp\left(-\int_0^\tau \mu(s)\, ds\right) b(M_T(t-\tau)) - d_I M_I - d_S M_S$$

$$\leq S(t) \exp\left(-\int_0^\tau \mu(s)\, ds\right) b(M_T(t-\tau)) - M_T(t)\min(d_I, d_S). \quad (3.9)$$

Let $\epsilon > 0$ be sufficiently small that

$$\min(d_I, d_S) > (S^\infty + \epsilon)b'_{\max} \exp\left(-\int_0^\tau \mu(s)\,ds\right) \qquad (3.10)$$

and choose $T_1 > 0$ sufficiently large that, when $t \geq T_1$, $S(t) \leq S^\infty + \epsilon$. Applying this bound in (3.9), and also the mean value theorem to find a bound on $b(M_T(t - \tau))$, we have, for $t \geq T_1$,

$$\frac{dM_T}{dt} \leq (S^\infty + \epsilon) \exp\left(-\int_0^\tau \mu(s)\,ds\right) b'_{\max}M_T(t - \tau) - M_T(t)\min(d_I, d_S)$$

which is a linear delay differential inequality from which we can infer from well known results (see [5]) that, by virtue of (3.10), $M_T(t) \to 0$ as $t \to \infty$. Hence also $M_I(t) \to 0$, and this knowledge enables us to conclude from (3.5) that $B_I(t) \to 0$.

Next we prove the conclusion of the theorem under hypothesis (3.8). Let $\epsilon > 0$ be arbitrary. There exists $T_2 > 0$ such that, for all $t \geq T_2$, $S(t) \leq S^\infty + \epsilon$. Then, for $t \geq T_2$,

$$\frac{dM_T}{dt} \leq (S^\infty + \epsilon) \exp\left(-\int_0^\tau \mu(s)\,ds\right) b(M_T(t - \tau)) - d_I M_I - d_S M_S$$

$$\leq (S^\infty + \epsilon) \exp\left(-\int_0^\tau \mu(s)\,ds\right) b_{\max} - M_T(t)\min(d_I, d_S).$$

Hence

$$\limsup_{t \to \infty} M_T(t) \leq \frac{(S^\infty + \epsilon) \exp\left(-\int_0^\tau \mu(s)\,ds\right) b_{\max}}{\min(d_I, d_S)}.$$

This holds for all $\epsilon > 0$. Also $M_S(t) \leq M_T(t)$. Hence

$$\limsup_{t \to \infty} M_S(t) \leq \frac{S^\infty \exp\left(-\int_0^\tau \mu(s)\,ds\right) b_{\max}}{\min(d_I, d_S)}.$$

Let $\epsilon > 0$ be sufficiently small that

$$d_I d_B - \gamma \beta N_B \left(\frac{b_{\max}S^\infty \exp\left(-\int_0^\tau \mu(s)\,ds\right)}{\min(d_I, d_S)} + \epsilon\right) > 0 \qquad (3.11)$$

which is possible by (3.8). There exists $T_3 > 0$ such that, for all $t \geq T_3$,

$$M_S(t) \leq \frac{S^\infty \exp\left(- \int_0^\tau \mu(s)\, ds\right) b_{\max}}{\min(d_I, d_S)} + \epsilon.$$

Then, for $t \geq T_3$,

$$\frac{dM_I}{dt} \leq \gamma B_I \left(\frac{S^\infty \exp\left(- \int_0^\tau \mu(s)\, ds\right) b_{\max}}{\min(d_I, d_S)} + \epsilon \right) - d_I M_I,$$

$$\frac{dB_I}{dt} \leq \beta N_B M_I - d_B B_I.$$

By the theory of monotone systems [10], we conclude from this that $M_I(t) \leq \tilde{M}_I(t)$ and $B_I(t) \leq \tilde{B}_I(t)$ where $\tilde{M}_I$ and $\tilde{B}_I$ satisfy

$$\frac{d\tilde{M}_I}{dt} = \gamma \tilde{B}_I \left(\frac{S^\infty \exp\left(- \int_0^\tau \mu(s)\, ds\right) b_{\max}}{\min(d_I, d_S)} + \epsilon \right) - d_I \tilde{M}_I,$$

$$\frac{d\tilde{B}_I}{dt} = \beta N_B \tilde{M}_I - d_B \tilde{B}_I$$

subject to $\tilde{M}_I(0) = M_I(0)$, $\tilde{B}_I(0) = B_I(0)$. This linear system has solutions with temporal dependence $\exp(\lambda t)$ where λ satisfies

$$\lambda^2 + (d_I + d_B)\lambda + d_I d_B - \gamma \beta N_B \left(\frac{b_{\max} S^\infty \exp\left(- \int_0^\tau \mu(s)\, ds\right)}{\min(d_I, d_S)} + \epsilon \right) = 0.$$

In view of (3.11), the roots of this quadratic both have negative real parts. Hence $M_I(t)$ and $B_I(t)$ approach zero as $t \to \infty$. The proof of the theorem is complete.

3.2 Culling of mature mosquitoes

As in the previous subsection we assume that the total number of birds in an area is some constant N_B. If birds are divided into two classes: uninfected B_S and infected B_I, then $B_S = N_B - B_I$. Then the change rate of infected birds is increased through infection of uninfected birds when they are bitten by infected mosquitoes and reduced by the natural death and disease-induced death (at a rate d_B). Thus,

$$\frac{dB_I}{dt} = \beta(N_B - B_I)M_I - d_B B_I, \tag{3.12}$$

where β is the contact rate between infected mosquitoes and uninfected birds (β equals the multiplication of the biting rate of mosquitoes and the transmission possibility between infected mosquitoes and uninfected birds).

As far as mosquitoes are concerned, in this section we assume that only the adults are subject to culling. Adult mosquitoes are divided into two classes: uninfected M_S and infected M_I. Since it would be difficult in practice to cull only infected ones, culling will be applied equally to both classes. The total number of adult mosquitoes will be denoted by $M_T = M_S + M_I$. Culling occurs only at the particular prescribed times t_j, $j = 1, 2, 3, \ldots$, satisfying the assumptions below. At the cull which occurs at time t_j a proportion c_j of the adult mosquito population is culled, causing a sharp decrease in the population and consequently a discontinuity in the evolution of $M_S(t)$ and $M_I(t)$ at each time t_j. The following assumption is made:

$$0 < t_1 < t_2 < \cdots < t_j < \cdots \text{ with } t_j \to \infty \text{ as } j \to \infty,$$
$$\inf_{j \geq 1} \delta_j > 0, \text{ where } \delta_j = t_j - t_{j-1}, \qquad (3.13)$$
$$c_j \in (0, 1] \text{ for each } j = 1, 2, 3, \ldots.$$

Note that no c_j is allowed to be zero (we can of course eliminate any "null culls" by relabelling the sequence t_j to include only "genuine" culls with $c_j > 0$, and we are assuming that this has been done). The evolution of $B_I(t)$ (infected birds) will remain continuous in time, but its derivative will have discontinuities at the times t_j.

Let $l(t, a)$ be the density of larval mosquitoes at time t of age a, and assume that a mosquito becomes mature on reaching the age τ. In this subsection immature mosquitoes are not subject to culling but only to natural death. Thus

$$\frac{\partial l}{\partial t} + \frac{\partial l}{\partial a} = -d_L l, \quad t > 0, \ 0 < a < \tau \qquad (3.14)$$

with $d_L > 0$ constant. The birth rate $l(t, 0)$ is a function of the total number of adult mosquitoes, so that

$$l(t, 0) = b(M_T(t)). \qquad (3.15)$$

We assume there is no vertical transmission between mosquitoes, so the uninfected mosquitoes population is increased via the maturation rate $l(t, \tau)$. It is diminished by infection, which may be acquired when uninfected mosquitoes feed from the blood of infected birds, by natural death at a rate d_M and by culling at the times t_j, $j = 1, 2, 3, \ldots$. Thus

$$\frac{dM_S}{dt} = l(t, \tau) - \gamma M_S B_I - d_M M_S - \sum_{j=1}^{\infty} c_j M_S(t_j^-) \delta(t - t_j), \qquad (3.16)$$

where γ is the contact rate between uninfected mosquitoes and infected birds (γ equals the multiplication of the biting rate of mosquitoes and the transmission possibility between uninfected mosquitoes and infected birds).

The infected mosquito population is generated via the infection of uninfected mosquitoes by infected birds and diminished by natural death at a rate d_M and

culling at the times $t_j, j = 1, 2, 3, \ldots$. Thus,

$$\frac{dM_I}{dt} = \gamma M_S B_I - d_M M_I - \sum_{j=1}^{\infty} c_j M_I(t_j^-) \delta(t - t_j). \tag{3.17}$$

It is assumed that the uninfected mosquitoes and infected mosquitoes are equally mixed, so that at each cull the proportions of each class removed are the same.

From (3.14) and (3.15),

$$l(t, \tau) = b(M_T(t - \tau)) e^{-d_L \tau}.$$

Our model for culling of adult mosquitoes but not larvae thus takes the form

$$\begin{cases} \dfrac{dB_I}{dt} = \beta(N_B - B_I)M_I - d_B B_I, \\[2mm] \dfrac{dM_S}{dt} = b(M_T(t - \tau))e^{-d_L \tau} - \gamma M_S B_I - d_M M_S - \displaystyle\sum_{j=1}^{\infty} c_j M_S(t_j^-)\delta(t - t_j), \\[2mm] \dfrac{dM_I}{dt} = \gamma M_S B_I - d_M M_I - \displaystyle\sum_{j=1}^{\infty} c_j M_I(t_j^-)\delta(t - t_j) \end{cases} \tag{3.18}$$

to be solved for $t > 0$ subject to initial conditions of the form (3.6). By integrating the second and third equations of (3.18) from t_j^- to t_j^+, we obtain the following alternative version of model (3.18):

$$\begin{cases} \dfrac{dB_I}{dt} = \beta(N_B - B_I)M_I - d_B B_I, \\[2mm] \dfrac{dM_S}{dt} = b(M_T(t - \tau))e^{-d_L \tau} - \gamma M_S B_I - d_M M_S, \quad t \neq t_j, \\[2mm] M_S(t_j^+) = (1 - c_j)M_S(t_j^-), \\[2mm] \dfrac{dM_I}{dt} = \gamma M_S B_I - d_M M_I, \quad t \neq t_j, \\[2mm] M_I(t_j^+) = (1 - c_j)M_I(t_j^-) \end{cases} \tag{3.19}$$

again subject to (3.6). Next, we establish non-negativity of solutions.

Proposition 3.3 *Assume* (3.13) *holds, and let the birth function* $b(\cdot)$ *satisfy* $b(0) = 0$ *and* $b(M) > 0$ *for all* $M > 0$. *Then the solution of system* (3.19) *for* $t > 0$, *subject to* (3.6), *satisfies* $M_S(t) \geq 0$, $M_I(t) \geq 0$, $B_I(t) \in [0, N_B]$ *for all* $t > 0$.

Proof For any time $t \in (0, \tau]$ other than one of the t_i, we have

$$\frac{dM_S}{dt} \geq -\gamma M_S B_I - d_M M_S$$

and this means that, provided $M_S(t)$ is non-negative immediately after a cull, we are assured that $M_S(t)$ remains non-negative until the next cull. We then only have to observe that, since $c_j \in (0, 1]$, the instantaneous effect of a cull is that $M_S(t)$ changes from a non-negative value to a non-negative value. Thus, $M_S(t) \geq 0$ for all $t \in (0, \tau]$. The method of steps is then applied to conclude $M_S(t) \geq 0$ for all $t > 0$.

Proving that $B_I(t) \leq N_B$ is straightforward. It remains to show $M_I(t) \geq 0$ and $B_I(t) \geq 0$. Whenever t is in the open interval between two successive culls we observe, similarly to the proof of Proposition 3.1, that $(M_I(t), B_I(t))$ can be interpreted as satisfying equations which form a monotone system. Therefore, if $(M_I(t), B_I(t))$ is in the closed first quadrant in the (M_I, B_I) plane immediately after a cull, it will still be there when the next cull is imminent. We then only have to observe that, at a cull, $(M_I(t), B_I(t))$ is repositioned from one point to another in the closed first quadrant of the (M_I, B_I) plane. The proof is complete.

In the remainder of the present subsection the following assumptions will be made regarding the birth function:

$$b(0) = 0, \ b(\cdot) \text{ is strictly monotonically increasing, there exists } M_T^* > 0 \text{ such} \\ \text{that } e^{-d_L \tau} b(M) > d_M M \text{ when } M < M_T^* \text{ and } e^{-d_L \tau} b(M) < d_M M \text{ when} \\ M > M_T^*. \tag{3.20}$$

From system (3.19), note that the total number $M_T(t)$ of adult mosquitoes obeys

$$\frac{\mathrm{d}M_T}{\mathrm{d}t} = b(M_T(t - \tau))e^{-d_L \tau} - d_M M_T(t), \\ M_T(t_j^+) = (1 - c_j)M_T(t_j^-). \tag{3.21}$$

In the absence of culling, the quantity $M_T^* > 0$ referred to in (3.20) is an equilibrium of (3.21) and $M_T(t) \to M_T^*$ as $t \to \infty$ (see [5]). Due to the assumptions in (3.20) which imply that the differential equation in (3.21) has the properties of a monotone system, solutions of (3.21) with culling are bounded above by the corresponding solutions without culling. It is therefore easy to appreciate that, with culling, there exists a finite time beyond which $M_T(t) \leq M_T^*$, and hence also $M_S(t) \leq M_T^*$. Our next aim is to generate from this an improved upper bound for $M_S(t)$ which involves the c_j and an upper bound $\delta_{\sup}$ on the amount of time that elapses between two successive culls. This will be important for the later analysis because, as we would anticipate, such quantities will play an important role in the design of culling strategies that result in disease eradication.

Proposition 3.4 *Assume* (3.13) *and* (3.20) *hold, and let*

$$c_{\inf} = \inf_{j \geq 1} c_j, \quad \delta_{\sup} = \sup_{j \geq 1} (t_{j+1} - t_j)$$

and assume $c_{\inf} > 0$ and $\delta_{\sup} < \infty$. Then solutions $M_T(t)$ of (3.21) satisfy

$$M_T(t) \leq M^{**} := M_T^*(1 - c_{\inf}e^{-d_M\delta_{\sup}}) \tag{3.22}$$

for all t sufficiently large. Consequently, $M_S(t) \leq M^{**}$ for t sufficiently large.

Proof As explained above, there exists some finite time T beyond which $M_T(t) \leq M_T^*$. For $t \geq T + \tau$,

$$\frac{dM_T}{dt} \leq b(M_T^*)e^{-d_L\tau} - d_M M_T(t).$$

By integrating this differential inequality over the interval (t_j, t) with $t \in (t_j, t_{j+1}]$, assuming j is large enough that $t_j \geq T + \tau$, we obtain that

$$M_T(t) \leq e^{-d_M(t-t_j)}M_T(t_j^+) + \frac{b(M_T^*)e^{-d_L\tau}}{d_M}\left(1 - e^{-d_M(t-t_j)}\right)$$

for $t \in (t_j, t_{j+1}]$. However, for j sufficiently large,

$$M_T(t_j^+) = (1 - c_j)M_T(t_j^-) \leq (1 - c_j)M_T^*$$

and, from (3.20), $e^{-d_L\tau}b(M_T^*) = d_M M_T^*$. Hence

$$\begin{aligned}
M_T(t) &\leq M_T^*\left(1 - c_j e^{-d_M(t-t_j)}\right) \quad \text{for } t \in (t_j, t_{j+1}] \\
&\leq M_T^*\left(1 - c_j e^{-d_M(t_{j+1}-t_j)}\right)
\end{aligned}$$

giving

$$M_T(t) \leq M_T^*(1 - c_{\inf}e^{-d_M\delta_{\sup}}) \quad \text{for } t \in (t_j, t_{j+1}].$$

This bound is independent of j and holds for all j sufficiently large. The proof of Proposition 3.4 is complete.

Our next theorems give conditions sufficient for disease eradication.

Theorem 3.5 *Suppose* (3.13) *and* (3.20) *hold, and that*

$$d_B d_M > \gamma\beta N_B M^{**} \tag{3.23}$$

where M^{**} is defined by (3.22). *Then $B_I(t) \to 0$ and $M_I(t) \to 0$ as $t \to \infty$, where $B_I(t)$ and $M_I(t)$ satisfy* (3.19) *subject to* (3.6).

Proof By Proposition 3.4 we know that, for sufficiently large times,

$$\frac{\mathrm{d}B_I}{\mathrm{d}t} \leq \beta N_B M_I - d_B B_I,$$
$$\frac{\mathrm{d}M_I}{\mathrm{d}t} \leq \gamma M^{**} B_I - d_M M_I, \quad t \neq t_j, \tag{3.24}$$
$$M_I(t_j^+) = (1 - c_j) M_I(t_j^-).$$

The differential inequalities in (3.24) have the structure of a monotone system. Solutions with culling will be bounded above by the corresponding solutions without. Hence, we can say that $B_I(t) \leq \tilde{B}_I(t)$ and $M_I(t) \leq \tilde{M}_I(t)$, where $\tilde{B}_I(t)$ and $\tilde{M}_I(t)$ satisfy the following linear problem without impulses:

$$\frac{\mathrm{d}\tilde{B}_I}{\mathrm{d}t} = \beta N_B \tilde{M}_I - d_B \tilde{B}_I,$$
$$\frac{\mathrm{d}\tilde{M}_I}{\mathrm{d}t} = \gamma M^{**} \tilde{B}_I - d_M \tilde{M}_I. \tag{3.25}$$

This being a linear system it is trivial to show that, under condition (3.23), $\tilde{B}_I(t)$ and $\tilde{M}_I(t)$ tend to zero, and hence so do $B_I(t)$ and $M_I(t)$, as $t \to \infty$. The proof is complete.

Remarks Condition (3.23) makes sense, in that it predicts disease eradication when death rates are high, contact rates are low, the total number of birds is low, and the quantity M^{**} is low. Recall that this latter quantity, being defined by (3.22), involves information about the culling and is low when large fractions are removed at each cull and the culls are frequent. Thus, even though the above proof apparently does not utilize information about the culling, such information is present in the analysis via M^{**}.

If condition (3.23) is violated then solutions of (3.25) will not decay to zero. Appending the culling condition to (3.25) may of course change things. This makes things algebraically more complicated but yields additional insight.

Theorem 3.6 *Suppose* (3.13) *and* (3.20) *hold, that* $\delta_{\sup} = \sup_{j \geq 1}(t_{j+1} - t_j) < \infty$ *and that* $c_{\inf} > 0$ *where* $c_{\inf} = \inf_{j \geq 1} c_j$. *Suppose also that* $d_B d_M \leq \gamma \beta N_B M^{**}$ *and*

$$\sup_{j \geq 1} \left[(\lambda_2(1 - c_j) - \lambda_1) \mathrm{e}^{\lambda_1 \delta_j} + (\lambda_2 + (c_j - 1)\lambda_1) \mathrm{e}^{\lambda_2 \delta_j} + c_j d_M (\mathrm{e}^{\lambda_2 \delta_j} - \mathrm{e}^{\lambda_1 \delta_j}) \right.$$
$$\left. - (\lambda_2 - \lambda_1)(1 - c_j) \mathrm{e}^{-(d_B + d_M)\delta_j} \right] < \lambda_2 - \lambda_1 \tag{3.26}$$

where $\lambda_1 < 0$ *and* $\lambda_2 \geq 0$ *satisfy*

$$\lambda^2 + (d_B + d_M)\lambda + \left(d_B d_M - \gamma \beta N_B M^{**} \right) = 0. \tag{3.27}$$

Then $B_I(t) \to 0$ *and* $M_I(t) \to 0$ *as* $t \to \infty$, *where* $B_I(t)$ *and* $M_I(t)$ *satisfy* (3.19) *subject to* (3.6).

Proof The proof begins in much the same way as that of Theorem 3.5, but this time we retain the culling conditions in the system for $\tilde{B}_I(t)$ and $\tilde{M}_I(t)$. In other words, we study the system

$$
\begin{aligned}
\frac{d\tilde{B}_I}{dt} &= \beta N_B \tilde{M}_I - d_B \tilde{B}_I, \\
\frac{d\tilde{M}_I}{dt} &= \gamma M^{**} \tilde{B}_I - d_M \tilde{M}_I, \quad t \neq t_j \\
\tilde{M}_I(t_j^+) &= (1 - c_j) \tilde{M}_I(t_j^-).
\end{aligned}
\tag{3.28}
$$

On each interval $t \in (t_j, t_{j+1})$ the solution of (3.28) will be of the form

$$
\tilde{M}_I(t) = A_j e^{\lambda_1(t-t_j)} + B_j e^{\lambda_2(t-t_j)}
\tag{3.29}
$$

$$
\tilde{B}_I(t) = \frac{1}{\gamma M^{**}} \left((\lambda_1 + d_M) A_j e^{\lambda_1(t-t_j)} + (\lambda_2 + d_M) B_j e^{\lambda_2(t-t_j)} \right)
\tag{3.30}
$$

where λ_1 and λ_2 satisfy (3.27). Under the hypotheses these numbers λ_i are either real and of opposite sign, or one is zero and the other negative.

Solving (3.28) therefore involves patching together the solutions for each interval (t_j, t_{j+1}), i.e. expressions (3.29) and (3.30) above, using the culling condition on $\tilde{M}_I$ at each t_j and the fact that $\tilde{B}_I$ is continuous for all t. This procedure yields

$$
\begin{pmatrix} A_j \\ B_j \end{pmatrix} = \mathbf{W}_j \begin{pmatrix} A_{j-1} \\ B_{j-1} \end{pmatrix}
\tag{3.31}
$$

where the matrix $\mathbf{W}_j$ is given by

$$
\begin{aligned}
\mathbf{W}_j = {} & \frac{1}{\lambda_2 - \lambda_1} \\
& \times \begin{pmatrix} ((1-c_j)(\lambda_2+d_M)-(\lambda_1+d_M))e^{\lambda_1 \delta_j} & -c_j(\lambda_2 + d_M)e^{\lambda_2 \delta_j} \\ c_j(\lambda_1 + d_M)e^{\lambda_1 \delta_j} & (\lambda_2+d_M-(1-c_j)(\lambda_1+d_M))e^{\lambda_2 \delta_j} \end{pmatrix}
\end{aligned}
$$

with

$$
\delta_j = t_j - t_{j-1}.
$$

Since $\sup_{j \geq 1}(t_{j+1} - t_j) < \infty$ the exponential terms in (3.29) and (3.30) cannot grow as time proceeds. Therefore to complete the proof of the theorem it is sufficient to show that A_j and B_j tend to zero as $j \to \infty$. A sufficient condition for this is that there exist $j_0 \in \mathbf{N}$ and a real number $\rho^* \in (0, 1)$ such that

$$
\rho(\mathbf{W}_j) \leq \rho^* < 1 \quad \text{for all } j \geq j_0
\tag{3.32}
$$

where $\rho(\mathbf{W}_j)$ is the spectral radius of $\mathbf{W}_j$. The eigenvalues μ_j of $\mathbf{W}_j$ satisfy

$$\mu_j^2 - \left(\frac{(\lambda_2 - \lambda_1 - c_j(\lambda_2 + d_M))e^{\lambda_1\delta_j} + (\lambda_2 - \lambda_1 + c_j(\lambda_1 + d_M))e^{\lambda_2\delta_j}}{\lambda_2 - \lambda_1} \right)\mu_j$$
$$+ (1 - c_j)e^{-(d_B+d_M)\delta_j} = 0$$

where we have used that $\lambda_1 + \lambda_2 = -(d_B + d_M)$.

The Jury conditions state that the eigenvalues μ_j of $\mathbf{W}_j$ will lie strictly in the unit circle for a particular j if

$$|\text{trace } \mathbf{W}_j| < 1 + \det \mathbf{W}_j < 2. \tag{3.33}$$

However, merely lying strictly in the unit circle for each j is not enough, since we must have existence of the number $\rho^* < 1$ in (3.32). It is easy to see that we can achieve this by requiring, instead of (3.33), the stronger condition that there exist real numbers $\rho_1, \rho_2 \in (0, 1)$ such that

$$\det \mathbf{W}_j \leq \rho_1 < 1 \quad \text{for each } j \tag{3.34}$$

and, since trace $\mathbf{W}_j$ can be shown to be non-negative,

$$\text{trace } \mathbf{W}_j - \det \mathbf{W}_j \leq \rho_2 < 1 \quad \text{for each } j. \tag{3.35}$$

Condition (3.34) certainly holds, since

$$\det \mathbf{W}_j = (1 - c_j)e^{-(d_B+d_M)\delta_j} \leq (1 - c_{\text{inf}}) < 1.$$

It is hypothesis (3.26) which guarantees (3.35), the quantity ρ_2 being the left hand side of (3.26) divided by $\lambda_2 - \lambda_1$. The proof is complete.

Remarks One has to address the question of whether the hypotheses of Theorem 3.6 can be satisfied. The quantities involved can be worked out explicitly and conveniently in the particular case when $d_B d_M = \gamma\beta N_B M^{**}$. In this case, $\lambda_1 = -(d_B + d_M)$ and $\lambda_2 = 0$, and condition (3.26) can after some algebra be written in the alternative infimum form:

$$\inf_{j\geq 1} c_j\left(1 - e^{-(d_B+d_M)\delta_j}\right) > 0$$

which holds automatically since $c_{\text{inf}} > 0$ and the δ_j satisfy (3.13). Theorem 3.6 tells us that the disease is eradicated for any culling consistent with $d_B d_M = \gamma\beta N_B M^{**}$, so that the theorem builds on Theorem 3.5.

4 Simulations and discussion

In this section we present the results of some numerical simulations to compare the effectiveness of larval culling versus adult culling. Larval culling is described by system (3.3), (3.4) and (3.5), and let us recall that for larval culling all information about the culling is embodied in the function $S(t)$ defined by (2.17). Culling of adults is described by system (3.19).

In the simulations we take the birth function of mosquitoes as

$$b(M) = bMe^{-aM} \tag{4.36}$$

which we feel to be an ecologically reasonable choice, being linear in M only for small densities M, levelling off as a consequence of intraspecific competition working to reduce per capita fecundity, and then actually dropping at very large densities M due to the available resources in these circumstances being utilized by the adults only for their own physiological maintenance and not reproduction.

Figures 1, 2, 3 and 4 are intended to compare larval culling with adult culling in a variety of culling regimes. Each figure contains nine plots in all; these being the variables $M_S(t)$, $M_I(t)$ and $B_I(t)$ in each of the situations of no culling, culling of adult mosquitoes and culling of larval mosquitoes. Where a simulation is of a variable with adult mosquito culling, the simulation is of model (3.19) with the c_j value shown in the caption. Where larval culling is mentioned the simulation is of system (3.3), (3.4) and (3.5) with the b_j given in the caption. In all simulations the culls are at equally spaced times, although we do examine the effect of different spacings, i.e. different frequencies of culling. The interval between two consecutive culls we shall denote as Δt. The cull times are given by $t_j = t_0 + j\Delta t, j = 1, 2, 3, \ldots$ with $t_0 = 4$. The initial conditions were taken to be

$$M_S(t) = 5000, \quad M_I(t) = 600, \quad B_I(t) = 100$$

for $t \in [-\tau, 0]$. Table 1 gives the meanings and the values used for the various parameters. Note that the parameter b is that which appears in our choice for the birth rate function (4.36) and equals the maximum daily egg production per adult mosquito.

From Figs. 1, 2, 3 and 4 and other simulations we made the following general observations:

- Under the same culling rates (i.e. if $b_j = c_j$) and frequencies, adulticide seems to be more effective than larvicide. However, for the reasons given below, adulticide is more difficult in practice. Larvicide alone is perfectly capable of eradicating the disease. If the culling frequency is such that a typical larval cohort is likely to experience only one cull, then a large fraction

Fig. 1 Parameter values are $b_j = 0.95$, $c_j = 0.4$, $b = 10$, $\Delta t = 7$ and other parameters have the values shown in Table 1
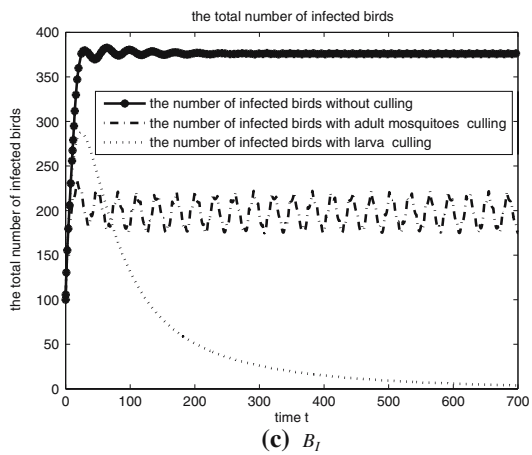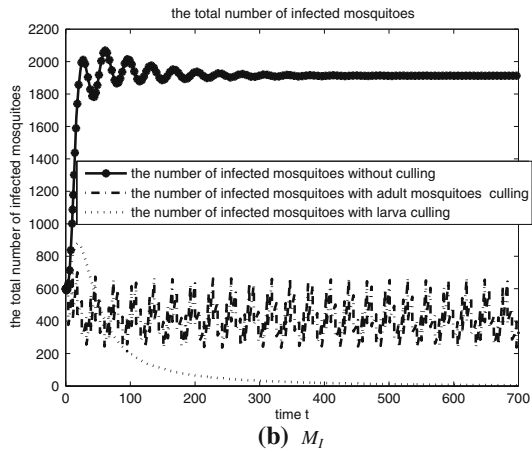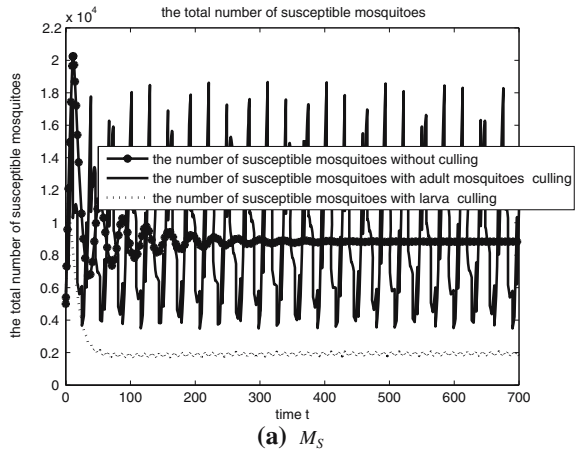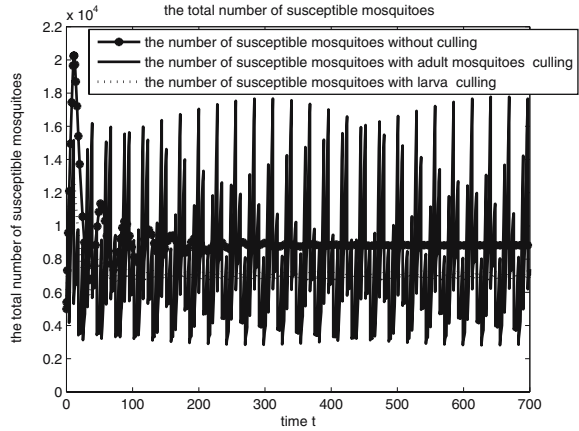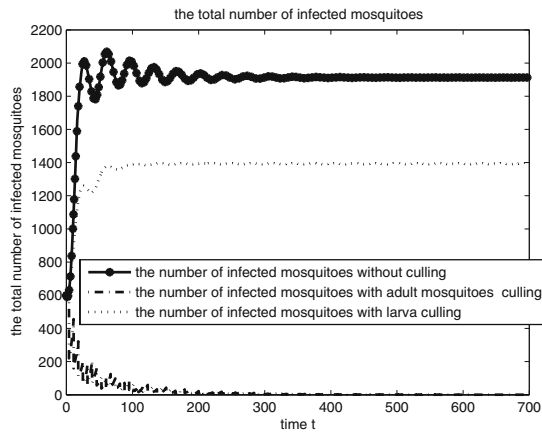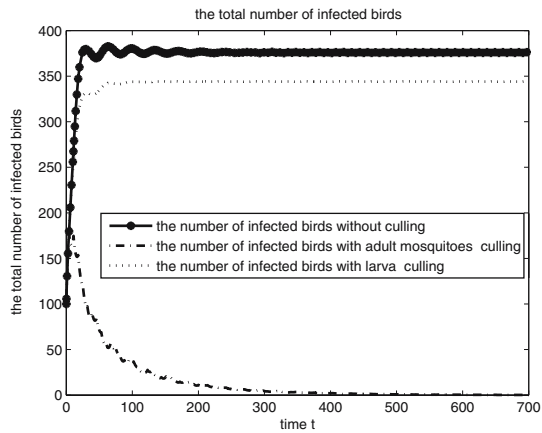

(a) M_S

(b) M_I

(c) B_I

Fig. 2 Parameter values are
$b_j = 0.5$, $c_j = 0.65$, $b = 10$,
$\Delta t = 7$ and other parameters
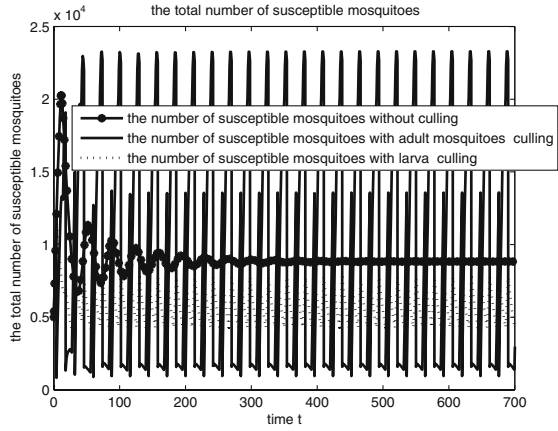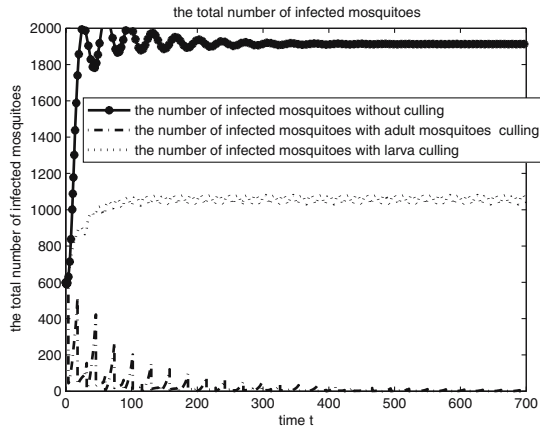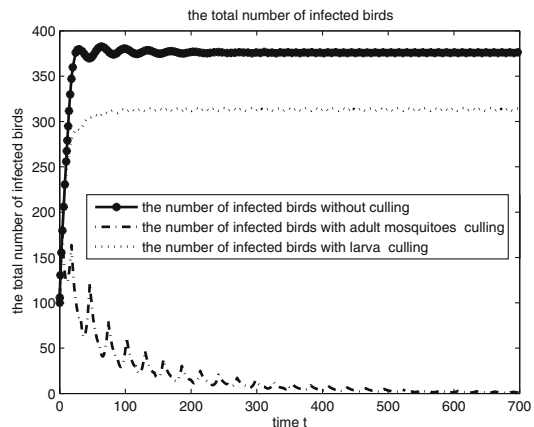have the values shown in
Table 1

(a) M_S

(b) M_I

(c) B_I

Fig. 3 Parameter values are
$b_j = 1, c_j = 0.93, b = 10,$
$\Delta t = 14$ and other parameters
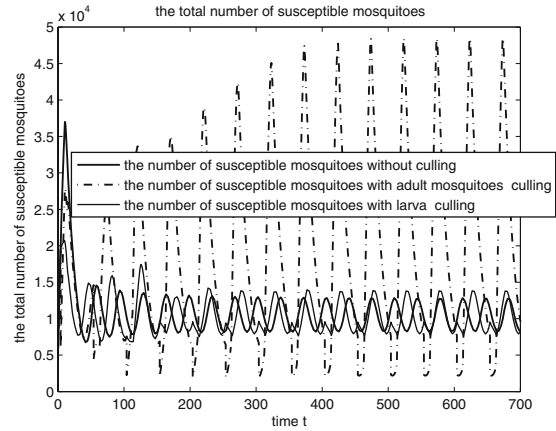have the values shown in
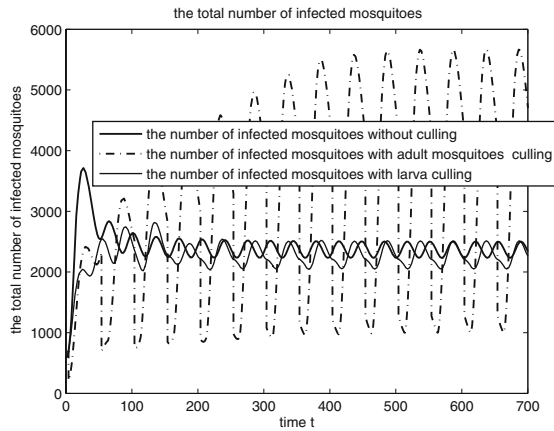Table 1
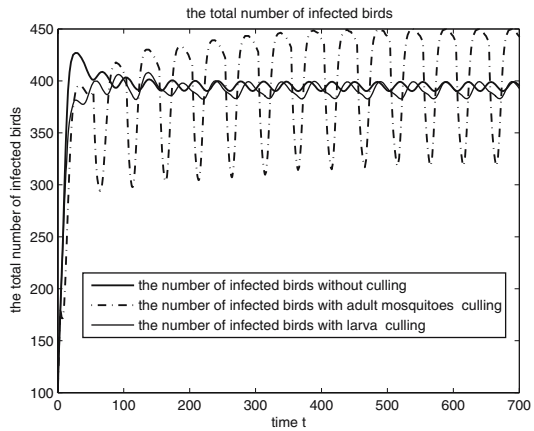

(a) M_S

(b) M_I

(c) B_I

Fig. 4 Parameter values are
$b_j = 0.7$, $c_j = 0.7$, $b = 20$,
$\Delta t = 50$ and other parameters
have the values shown in
Table 1

(a) M_S

(b) M_I

(c) B_I

Table 1 Parameter values used for the simulations

Para.	Meaning	Value
d_L	Per capita death rate of mosquito larva (per day)	0.1
τ	Maturation time of mosquito larva (days)	10
d_M	Per capita natural death rate of mosquito (per day)	0.05
d_B	Disease-induced death rate of infected bird (per day)	0.1
N_B	Total number of birds	500
β	Contact rate between infected mosquito and susceptible birds	$0.0144/N_B$
γ	Contact rate between susceptible mosquito and infected birds	$0.0792/N_B$
b	Maximum per capita daily egg production rate	variable
$1/a$	Size of mosquito population at which egg laying is maximized	2,500
b_j	Fraction of larva removed at the cull at time t_j	Variable
c_j	Fraction of adult mosquito removed at the cull at time t_j	Variable
$1/\Delta t$	Culling frequency	Variable

The data was obtained from [12,6,1]. Those that vary from simulation to simulation are shown in the figure captions

of the larvae have to be killed at each cull. The fraction that have to be destroyed drops quickly as the culling frequency increases.

- If we increase the culling frequency (i.e. decrease Δt), the effect of both larvicide and adulticide increases. If the culling frequency is high enough the disease dies out.
- In the cases of both larvicide and adulticide, the disease dies out for sufficiently large proportions b_j and c_j respectively provided, in the case of larvicide, that the intervals between culls are such that a larval cohort can never escape a cull.
- Very infrequent culling could be counterproductive, as illustrated by Fig. 4 in particular.

The purpose of Figs. 3 and 4 is to illustrate what happens if the interval between successive culls is larger than the maturation delay $\tau = 10$, a situation that is not really covered by the analytical results. If this happens, certain larva cohorts may completely escape a cull. Figure 3 shows that, as a consequence of this, the disease can persist even when larva culling is maximized ($b_j = 1$). The disease can still be eradicated via adult culling but only with a very high proportion $c_j = 0.93$ removed each time. The number of susceptible mosquitoes oscillates wildly. Figure 4 illustrates that if the interval between culls is very high indeed compared to the maturation delay (we have used $\Delta t = 50$ days with $\tau = 10$ days), then the culling is not having any useful effect at all. Indeed, with culling of adults at 50 day intervals, the number of infected mosquitoes appears to oscillate with an even higher mean than the oscillation with no culling at all. Note that the oscillation in Fig. 4 has entrained to the culling as it has the same frequency. What appears to be happening is that each cull reduces the mosquito numbers to a level that is actually better for them from an egg laying point of view (recall the reasons we gave for the choice (4.36) for the birth function); after the 10 day maturation a period of rapid exponential growth occurs, and

just after the numbers start to drop off the next cull occurs. Infrequent culling is thus less beneficial than nature's own methods of regulating mosquito numbers. Without the interruption of culling, the number of infected mosquitoes follows a typical infection curve: rapid exponential growth followed by slower decay. When culling takes place but is inadequate there will be multiple exponential growths (occurring after each culling) during the entire course of the epidemic, thus increasing the mean. Note also from Fig. 4 that larval culling at 50 day intervals has almost no effect, even when 70% of the larvae are removed each time.

Finally let us remark that condition (3.8), though only a sufficient condition for disease eradication, seems close in at least some parameter regimes to being a necessary condition as well. If we take $b = 10$, $\Delta t = 7$ and other parameter values given in Table 1, then condition (3.8) predicts disease eradication if $b_j > 0.9676$ for each j. Condition (3.8) is a sufficient condition. Trial and error numerical simulation indicates that a necessary and sufficient condition for eradication is approximately $b_j > 0.949$ so that the critical b_j is close to the analytical estimate of 0.9676. Figure 1 gives the results when $b_j = 0.95$, showing that the disease slowly disappears in this case. This further emphasizes our point that if the disease is to be eradicated via larval culling only, then very large fractions of larvae have to be destroyed at each cull if we cull at a frequency of once every 7 days ($\Delta t = 7$). We chose this frequency to ensure that every larval cohort (we have taken the larval stage as lasting 10 days) is subject to at least one cull with some cohorts experiencing two (the function $S(t)$ defined by (2.17) takes care of this automatically). However, one could of course increase the culling frequency. The function $S(t)$, and therefore the number S^∞ in (3.8), goes down quickly as the culling becomes more frequent, leading to vastly less stringent conditions on the b_j.

In fact, effective mosquito control programs usually emphasize larval control. One knows where to look for mosquito breeding activity (a pool cover, ornamental pool, bird bath, gutter or even an old tire is all they need). Larvicides can provide up to a month of control (adulticides only a few hours) and larvicides can be applied in such a way that there is less human exposure. In WNv endemic areas of the US the use of mosquito adulticides is in fact usually a measure of last resort because of health risks associated from exposure to the insecticide, which is released into the atmosphere in the form of very fine droplets. People need to be advised in advance and to be given precautions such as remaining indoors during spraying and to take other precautions. To justify the use of adulticides public health officials have to have reached the view that the risks from WNv are higher than those associated with exposure to the insecticide, and they need to inform the public and advise on precautions. For these reasons it could be difficult in practice to do it as frequently as in our simulations.

References

1. Bowman, C., Gumel, A.B., van den Driessche, P., Wu, J., Zhu, H.: A mathematical model for assessing control strategies against west nile virus. Bull. Math. Biol., **67**, 1107–1133 (2005)
2. Centers for Disease Control and Prevention. Outbreak of West Nile-like viral encephalitis-New York, 1999. MMWR Morb. Mortal. Wkly. Rep. **48**, 845–849 (1999)
3. Hayes, C.G.: West Nile virus: Uganda, 1937, to New York City, 1999. Ann. N. Y. Acad. Sci. **951**, 25–37 (2001)
4. Hubálek, Z., Halouzka, J.: West Nile fever: a reemerging mosquito-borne viral disease in Europe. Emerg. Infect. Dis. **5**, 643–650 (1999)
5. Kuang, Y.: Delay differential equations with applications in population dynamics. In: Mathematics in Science and Engineering, vol 191. Academic, Boston (1993)
6. Lord, C.C., Day, J.F.: Simulation studies of St. Louis encephalitis and West Nile virues: the impact of bird mortality. Vector Borne Zoonotic Dis. **1**(4), 317–329 (2001)
7. Nash, D., Mostashari, F., Fine, A., et al.: The outbreak of West Nile virus infection in the New York City area in 1999. N. Eng. J. Med. **344**, 1807–1814 (2001)
8. Petersen, L.R., Anthony, A.M.: West Nile virus: a primer for the clinician. Ann. Intern. Med. **137**, 173–179 (2002)
9. Simons, R.R.L., Gourley, S.A.: Extinction criteria in stage-structured population models with impulsive culling. SIAM. J. Appl. Math. **66**, 1853–1870 (2006)
10. Smith, H.L.: Monotone dynamical systems. An introduction to the theory of competitive and cooperative systems. American Mathematical Society, Providence (1995)
11. Smithburn, K.C., Hughes, T.P., Burke, A.W., Paul, J.H.: A neurotropic virus isolated from the blood of a native of Uganda. Am. J. Trop. Med. **20**, 471–492 (1940)
12. Wonham, M.J., de-Camino-Beck, T., Lewis, M.: An epidemiological model for West Nile virus: invasion analysis and control applications. Proc. R. Soc. Lond. Ser. B **271**, 501–507 (2004)