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Population and Individual Based Ross-Macdonald Models: Which one should we use?

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Abstract

Ross-Macdonald models are the most used framework to model vector-borne disease dynamics. Here we present different formulations of the Ross-Macdonald model using systems of ordinary differential equations as well as individual based models. We compare the solutions using different distributions for the infectious and latency periods using statistics, like the epidemic peak, or epidemic final size, to characterize the epidermic curves. The basic reproduction number (R_0) for each formulation is computed and compared with empirical estimations obtained with the individual based models. The importance of considering the latency period distribution, as well as the use of realistic distributions for the infectious periods is demonstrated and discussed.

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1 Introduction

Ross model was published in 1911 [11] and remains as the basis of countless models for vector-borne diseases. Ross considered a simple model for malaria, with births and deaths but with constant populations and infectious periods exponentially distributed. Humans and mosquitoes may have in

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only two classes, Affected and Unaffected, (what here we will denoted by H_i, H_s, V_i, V_s). Then, Ross model in continuous time reads

$$\frac{dH_i}{dt} = \beta_h m \frac{V_i}{V}(H - H_i) - r_h H_i$$
$$\frac{dV_i}{dt} = \beta_v \frac{H_i}{H}(V - Vi) - \mu_v V_i$$

where m is the number of mosquitoes per human (V/H), r_h is the recovery rate for humans, μ_v is the mortality rate for mosquitoes, and is β_j the transmission parameters. This last may be decomposed as $\beta_j = bfp_j$ with b the mosquitoes biting rate, f the proportion of bites in humans, and p_j the probability of transmission per bite.

An equivalent formulation, more frequently used, and preferable is

$$\frac{dH_i}{dt} = \beta_h V_i \frac{H_s}{H} - r_h H_i$$
$$\frac{dV_i}{dt} = \beta_v V_s \frac{H_i}{H} - \mu_v V_i$$

After some contributions by Macdonald, models with these rates of infection were broadly called Ross-Macdonald models. Ross and Macdonald analysis of the models were carried out at epidemiological equilibrium.

For the Ross model, the basic reproduction number (R_0), defined as the number of secondary host cases produced by a typical infected host in a completely susceptible population is

$$R_0 = \frac{\beta_h \beta_v}{r_h \mu_v} \frac{V}{H}$$

This celebrated result from Ross [11] shows that the basic reproduction number is proportional to the number of vectors per host (V/H).

Since then models were developed for vector-borne diseases following this basic model including superinfection, spatiality, time-varying populations and more (see for example [15, 4, 3, 9, 13, 16]).

2 General assumptions and parameters

In all the models considered in this work it is assumed that populations are homogeneously mixed. Vector's bites are divided evenly among hosts, that is, every time a vector bites, chooses a host at random.

Demography. Immigration and emigration are not considered. Births are assumed to take place at a rate Λ. Deaths may be described by the mortality or by the survival function. Mortality (μ) is the number of deaths per individual and per unit of time. In general it is an age-dependent rate. The survival function, $\bar{F}(a)$, is the proportion of individuals still alive at age a, and it is related with the mortality by $\bar{F}(a) = 1 - e^{\int_0^a \mu(a')da'}$.

Epidemiology. Populations are divided in some of the following epidemiological classes: Susceptible, Latent, Infectious, Recovered. Latent (or Exposed) individuals are infected but not infectious (and therefore are unable to transmit the disease). Recovered individuals are immune, and therefore do not participate of the transmission process. Duration of the latent period may be described for a survival function of the age of infection: $\bar{F}_e(s)$ gives the proportion of latent individuals who remain latent at age of infection s (age of infection is the time elapsed since first infection). Analogously,

$\bar{F}_i(s)$ is the proportion of infectious individuals who remain infectious after a time s after the end of latency. Alternatively we can use the, age-of-infection dependent, progression rates (from latency to infectiousness) or recovery rates (from infectiousness to recovery).

All the periods considered (life span, latency period, infectious period) are random variables what may be characterized by a probability distribution. The simple, and commonly used, case of exponentially distributed periods correspond to constant, age independent, rates. For example using a constant mortality rate μ imply the assumption of an exponentially distributed life span. In this work we will consider only two cases: exponentially distributed period or fixed periods (for which the survival function is a step function). In both cases the distributions are fully defined by the its mean T. For an exponentially distributed period the probability density function is $f(t) = \frac{1}{T}e^{-t/T}$, and the associated rate is $\mu = 1/T$. For fixed periods we have $f(t) = \delta(t - T)$ but associated rates are not defined in this case.

Parameters defining the different periods distributions are:

T_h: Host life expectancy (mean lifespan)

T_v=T_{vi}: Vector life expectancy, mean infectious period for vectors

T_{he}: Mean latency period for exposed hosts

T_{hi}: Mean infectious period for hosts

T_{ve}: Mean latency period for vectors

In all cases we considered that vectors are infectious for life.

Entomological parameters. Biting rate on hosts (number of bites per vector, per unit of time, on hosts) is denoted by b. Probabilities of transmission per bite are p_h and p_v (from vectors to hosts and from hosts to vectors respectively). Finally we define $\beta_h = p_h b$, and $\beta_v = p_v b$.

Basic reproduction numbers. For a general Ross-Macdonald model the basic reproduction number may be obtained by simple bookkeeping (Diekman and Heesterbeek 2000). One infectious host will produce an average of $\beta_v V \frac{1}{H}$ infected vectors per unit of time. If the mean infectious period for hosts is T_{hi}, then the total number of infected vectors is $\beta_v V \frac{1}{H} T_{hi}$. Only a fraction f_v will survive the latency period, and therefore, the total number of infectious vectors produced by the initial infectious host is $\beta_v V \frac{1}{H} T_{hi} f_v$. Each infectious vector would produce $\beta_h T_{vi}$ host infections (T_{vi} is the mean infectious period for vectors) and only a fraction f_h will survive the host latency period. Finally the basic reproduction number is given by

$$R_0 = \beta_h \beta_v T_{hi} T_{vi} f_h f_v \frac{V}{H} \tag{1}$$

3 Deterministic Ross-Macdonald models

In a Ross-Macdonald model there are host and vector populations (of size H and V respectively) homogenously mixed. Each population is subdivided in epidemiological classes. For example, susceptible and infectious host and vector populations (H_s, H_i, V_s V_i). Vectors bite at the rate b (daily number of bites per vector, for example). If p_h is the probability of infection transmission to hosts per bite, p_v the probability of vector infection per bite on infectious hosts, then the rate of infection of susceptible hosts is given by $p_h b V_i \frac{H_s}{H}$ while the rate of infection of susceptible vectors by $p_v b V_s \frac{H_i}{H}$. These functional forms for the infection rates are characteristic of all the Ross-Macdonald type models. In the following we will present, discuss and compare the more common deterministic models (without age structure).

3.1 Basic Model

One of the most simple and general model is a SIR model for hosts and a SI model for vectors. Mortalities are denoted by μ while recovery rates by r. Λ's are the recruitment rates. We will assume that all the periods are exponentially distributed and therefore we obtain the following *Basic model*:

$$\frac{dH_s}{dt} = \Lambda_h - \beta_h V_i \frac{H_s}{H} - \mu_h H_s \tag{2}$$

$$\frac{dH_i}{dt} = \beta_h V_i \frac{H_s}{H} - (r_h + \mu_h) H_i \tag{3}$$

$$\frac{dH_r}{dt} = r_h H_i - \mu_h H_r \tag{4}$$

$$\frac{dV_s}{dt} = \Lambda_v - \beta_v V_s \frac{H_i}{H} - \mu_v V_s \tag{5}$$

$$\frac{dV_i}{dt} = \beta_v V_s \frac{H_i}{H} - \mu_v V_i \tag{6}$$

where $\mu_h = 1/T_h$ and $\mu_v = 1/T_v$. Mean infectious period for host includes recovery and mortality, and therefore in this case is given by $T_{hi} = 1/(r_h + \mu_h)$, from where recovery rate r_h can be estimated. Vectors are assumed to be infectious for life and then $\mu_v = 1/T_{vi} = 1/T_v$.

Because in this model there are not latency periods, $f_h = f_v = 1$. The basic reproduction number (1) for this model becomes

$$R_0^{(1)} = \frac{\beta_h \beta_v}{(r_h + \mu_h)\mu_v} \frac{V}{H} \tag{7}$$

The assumption of constant mortality for vectors is plausible as for insects we expect an approximately constant daily probability of death. For hosts like birds, constant mortality are also usually observed. However hosts like humans present a survival of type I: low mortality for ages below the mean followed by a steep decrease in survival. In this case an age structured model for the host population should be used. However in those cases we have that $\mu_h \ll \mu_v$ and therefore we may disregard birth and deaths in the host population when studying the short-term dynamics like in a single outbreak, the case we are studying in this work.

Infectious period is also assumed exponentially distributed, a not realistic assumption. Host may loose immunity becoming susceptible again, a case we do not consider in this work.

3.2 Basic Model with exposed classes

For both, hosts and vectors, there are latent periods and therefore a more realistic model is a $SEIR$ for hosts and a SEI for vectors (as in most cases vectors are infectious for life). The basic model with latent classes (SEIR-SEI model) is:

$$\frac{dH_s}{dt} = \Lambda_h - \beta_h V_i \frac{H_s}{H} - \mu_h H_s \tag{8}$$
$$\frac{dH_e}{dt} = \beta_h V_i \frac{H_s}{H} - (k_h + \mu_h) H_e \tag{9}$$
$$\frac{dH_i}{dt} = k_h H_e - (r_h + \mu_h) H_i \tag{10}$$
$$\frac{dH_r}{dt} = r_h H_i - \mu_h H_r \tag{11}$$

$$\frac{dV_s}{dt} = \Lambda_v - \beta_v V_s \frac{H_i}{H} - \mu_v V_s \tag{12}$$
$$\frac{dV_e}{dt} = \beta_v V_s \frac{H_i}{H} - (k_v + \mu_v) V_e \tag{13}$$
$$\frac{dV_i}{dt} = k_v V_e - \mu_v V_i \tag{14}$$

Here, k_h and k_v are the progression rates from latency to infectiousness, and in this context are given by $k_j = 1/T_{je}$ with T_{je} the mean latency period ($j = h$ for hosts, and $j = v$ for vectors).

In this case the basic reproduction number is

$$R_0^{(2)} = \frac{\beta_h \beta_v}{(r_h + \mu_h)\mu_v} \left(\frac{k_v}{k_v + \mu_v}\right) \left(\frac{k_h}{k_h + \mu_h}\right) \frac{V}{H} \tag{15}$$

where $f_j = k_j/(k_j + \mu_j)$ are the fractions of exposed individuals who survives the latency period.

The assumptions in this model are the same discussed above but here it also assumed that latent periods are exponentially distributed a not realistic assumption neither. Once again $k_h \gg \mu_h$ and then $\frac{k_h}{k_h + \mu_h} \approx 1$.

3.3 Models with arbitrary distributions for the waiting periods

The assumption of exponentially distributed periods is appealing because the corresponding ODE models have constant parameters. However latency or infectious periods are, in general, random variables with non-exponential distributions.

In our case, where we are considering that vectors remains infectious for life, the infectious period is the vector lifespan. In this case a constant mortality is a realistic choice and therefore the infectious period is exponentially distributed. However this is not the case of vector's latent period or latent and infectious host's periods.

As an example we will consider the simple case of a $SIR - SI$ model. For vectors we have the equations 5-6. For the host population we will consider that the infectious period (T_{hi}) is a random variable with probability distribution function $f(s)$. As usual, the cumulative distribution is denoted by $F(s)$. The complementary cumulative distribution, $\bar{F}(s) = 1 - F(s)$, is known as the survival function and gives the probability that an individual infected in $t = 0$ remains infected at time s. Because only the fraction $\bar{F}(t - s)$ of the infections produced at time s survives until time t we obtain the integral Volterra equations

$$H_s(t) = H_s(0) - \int_0^t \frac{\beta_h}{H} V_i(s) H_s(s) ds$$
$$H_i(t) = H_i(0)\bar{F}(t) + \int_0^t \frac{\beta_h}{H} V_i(s) H_s(s) \bar{F}(t - s) ds$$
$$H_r(t) = H - H_s(t) - H_i(t)$$

Differentiation of Volterra equation gives the following system of integro-differential equations,

$$\begin{aligned}\frac{dH_s}{dt} &= -\beta_h V_i \frac{H_s}{H} \\ \frac{dH_i}{dt} &= H_i(0)\frac{d\bar{F}}{dt} + \beta_h V_i \frac{H_s}{H}\bar{F}(0) + \int_0^t \frac{\beta_h}{H} V_i(s) H_s(s) \frac{d\bar{F}}{dt}(t-s)ds \\ &= -H_i(0)f(t) + \beta_h V_i \frac{H_s}{H} - \int_0^t \frac{\beta_h}{H} V_i(s) H_s(s) f(t-s)ds\end{aligned}$$

Realistic distributions for infectious or latent periods are bell shaped and therefore survival function is of type I. Then, a simple but realistic distribution is obtained for the limiting case of fixed infectious period T_{hi}. In this case the survival function is a step function, the probability density distribution is $\delta(t - T_{hi})$, and therefore we obtain the delayed equation

$$\frac{dH_i}{dt} = -H_i(0)\delta(t - T_{hi}) + \beta_h V_i \frac{H_s}{H} - \beta_h V_i(t - T_{hi})\frac{H_s(t - T_{hi})}{H} \tag{16}$$

3.3.1 Delayed Model

As mentioned before, vectors are usually infectious for life and mortality is approximately constant (age-independent). Therefore the assumption of an exponentially distributed period of life is a realistic choice. Latency periods, in hosts and vectors, are not exponentially distributed neither the host infectious period. In this case, the choice of fixed periods introduce more realism into the models while retaining simple numerical integration.

Disregarding births and deaths in the host population, a general and realistic model with latent and infectious classes is the *Delayed Model*

$$\frac{dH_s}{dt} = -\beta_h V_i \frac{H_s}{H} \tag{17}$$

$$\frac{dH_e}{dt} = \beta_h V_i \frac{H_s}{H} - \beta_h V_i(t - T_{he})\frac{H_s(t - T_{he})}{H} \tag{18}$$

$$\frac{dH_i}{dt} = -H_i(0)\delta(t - T) + \beta_h V_i(t - T_{he})\frac{H_s(t - T_{he})}{H} - \beta_h V_i(t - T_{he} - T_{hi})\frac{H_s(t - T_{he} - T_{hi})}{H} \tag{19}$$

$$\frac{dH_r}{dt} = \beta_h V_i(t - T_{he} - T_{hi})\frac{H_s(t - T_{he} - T_{hi})}{H} \tag{20}$$

$$\frac{dV_s}{dt} = \Lambda_v - \beta_v V_s \frac{H_i}{H} - \mu_v V_s \tag{21}$$

$$\frac{dV_e}{dt} = \beta_v V_s \frac{H_i}{H} - e^{-\mu_v T_{ve}}\beta_v V_s(t - T_{ve})\frac{H_i(t - T_{ve})}{H} - \mu_v V_e \tag{22}$$

$$\frac{dV_i}{dt} = e^{-\mu_v T_{ve}}\beta_v V_s(t - T_{ve})\frac{H_i(t - T_{ve})}{H} - \mu_v V_i \tag{23}$$

where T_{ve}, T_{he}, and T_{hi} are the (fixed) latency and infectious periods of vectors and hosts. As discussed above, vector's infectious period is assumed exponentially distributed as we considered a constant vector mortality rate. Host mortality is disregarded and then all latent host become infectious (and then $f_h = 1$). However only a fraction $f_v = e^{-\mu_v T_{ve}}$ of infected vectors survive the latency period becoming infectious.

Therefore, for this model the basic reproduction number is

$$R_0^{(3)} = \beta_h \beta_v T_{hi} \frac{1}{\mu_v} e^{-\mu_v T_{ve}} \frac{V}{H} \tag{24}$$

From the expressions for the R_0 values, Eqs. 7, 15 and 24 disregarding host mortality, we can observe that

$$R_0^{(2)} = R_0^{(1)} \left(\frac{k_v}{k_v + \mu_v} \right)$$

Since $\frac{k_v}{k_v+\mu_v} < 1$, then $R_0^{(1)} > R_0^{(2)}$. Furthermore, it can be demonstrated that $\frac{k_v}{k_v+\mu_v} \geq e^{-\mu_v T_{ve}}$. Then, the basic reproduction numbers for the different models satisfy

$$R_0^{(1)} > R_0^{(2)} > R_0^{(3)}.$$

Therefore we expect larger and faster epidemics for the simple $SIR - SI$ model (Eqs. 2 - 6). It is possible to implicitly include the effect of latency in the vector population modifying the equation 6 as

$$\frac{dV_i}{dt} = e^{-\mu_v T_{ve}} \beta_v V_s \frac{H_i}{H} - \mu_v V_i \tag{25}$$

The basic reproduction number for the modified model is $R_0^{(3)}$.

4 Individual based models

Individual based models (IBM) are a computational tool which allows to simulate populations dynamics considering the features of each individual in the population and the interaction between them [7]. Although these models require a greater computational processing capacity, it does not represent a strong limitation thanks to the progress of computer technology. Individual based models are considered the most realistic models where the mobility of each individual may be easily incorporated [5, 10].

An IBM was developed to simulate the infection transmission dynamics of a vector-borne disease. The model considers a SEIR for the host population and a SEI for the vector population. For each host and vector, the followings attributes were considered: the epidemiological status (State) and the time at which the epidemiological status changes (T_change). In this work, two different cases were considered: the case in which T_change is exponentially distributed (such as in the SEIR-SEI model) and the case in which (some of) these times have fixed values (such as in the delayed model).

As before, we disregarded host births and deaths, whereas for the vector population we considered constant motality ($\mu_v = 1/T_v$) and a constant birth rate Λ_v. Thus, the probability of a vector dying in a time interval of duration Δt is equal to $1 - e^{-\mu_v \Delta_t}$. The demographic processes in the vector population was simulated as follow. At each time step Δt, and for each individual in the vector population, a uniform distributed pseudo-random number was generated. If this number was less than $1 - e^{-\mu_v \cdot \Delta_t}$, the vector was removed from the vector population. We modeled the number of newborns vectors in a time step by a Poisson random variable with parameter $V_0 \mu_v \Delta t$.

The simulation procedure used is described in the following pseudo-code:

1. Set the host ($H(0)$) and vector ($V(0)$) population sizes.
2. Set the time step Δt, the simulation duration t_{sim} and the present time t equal to 0.
3. Set the values of parameters μ_v, p_v, p_h, k_v, k_h, γ_h, b.
4. Set the initial conditions $H_s(0)$, $H_e(0)$, $H_i(0)$, $H_r(0)$, $V_s(0)$, $V_e(0)$, $V_i(0)$.

5. While $t \leq t_{sim}$ and $0 \leq H_e(t) + H_i(t) + V_e(t) + V_i(t)$ /* this last sentence interrupts the program when infections cannot takes place anymore */

   (a) A random number of susceptible vector are added to the population according to a Poisson distribution with parameter $V_0\mu_v\Delta t$

   (b) For each vector in the population

      i. A uniform random number is generated.

      ii. If the number is less than or equal to $b\Delta t$, the vector bites.

         The host bitten is chosen at random.

         If host.State == INFECTED and vector.State == SUSCEPTIBLE

            A uniform random number is generated.

            If the number is less than or equal to p_v, the mosquito becomes exposed

               vector.State = EXPOSED, $V_s(t) - -$, $V_e(t) + +$

               /* the operator "++" increases in 1 the value of the preceding variable and the operator "- -" decreases in 1 the value of the preceding variable */

               Set a exposed time vector.T_change.

         If host.State == SUSCEPTIBLE and vector.State == INFECTED

            A uniform random number is generated.

            If the number is less than or equal to p_h, the host becomes exposed

               host.State = EXPOSED, $H_s(t) - -$, $H_e(t) + +$

               Set a exposed time host.T_change.

      iii. A uniform random number is generated.

      iv. If the number is less than or equal to $1 - e^{-\mu_v \Delta_t}$

         The vector dies and it is removed from vector population.

      v. Else

         If vector.State == EXPOSED and vector.T_change == t

            vector.State = INFECTED, $V_e(t) - -$, $V_i(t) + +$

   (c) For each host

      i. If host.State == EXPOSED and host.T_change == t

         host.State = INFECTED, $H_e(t) - -$, $H_i(t) + +$

         Set a infectious time host.T_change

      ii. If host.State == INFECTED and host.T_change == t

         host.State = RECOVERED, $H_i(t) - -$, $H_r(t) + +$

5 Some numerical results

In all the cases, a initial population of vectors and hosts of 10000 individuals were considered. The simulations start with one host infected, and all the other individuals susceptible. We used the day as the unit of time.

5.1 Epidemic curves

In figure 1 we compare numerical solutions of the models for low and high values of the basic reproduction number ($b = 0.3$ and $b = 0.5$, respectively) considering the parameter values in the table 1.

Parameter	Value
p_v	0.75
p_h	0.75
T_{he}	6 [days]
T_{hi}	5 [days]
T_{ve}	7 [days]
T_v	10 [days]

Table 1: Parameter values used in the simulations. In all cases we set host mortality equal to zero (μ_h=0) while $\mu_v = 1/T_v$ =0.1 days^{-1}.

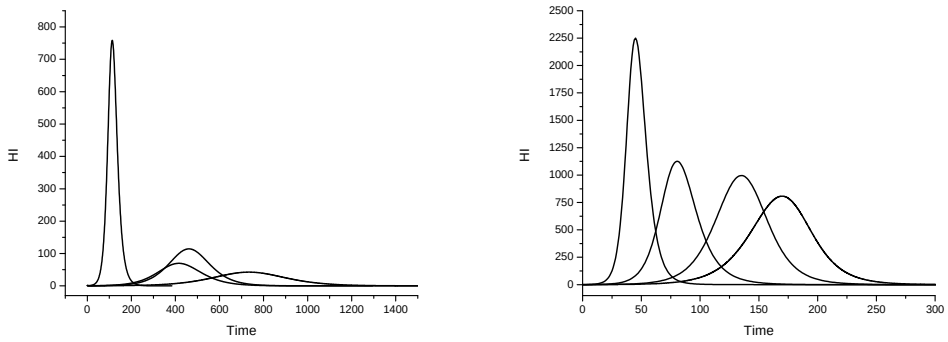

Figure 1: Solutions of the deterministic models (Host infectious population). Left panel: low R_0 ($b = 0.3$), right panel, high R_0 ($b = 0.5$). From left to right: basic model (Eqs. 2 - 6), basic model modified (Eq. 25), SEIR-SEI model (Eqs. 8 - 14), delayed model (Eqs. 17 - 23). Time units in days.

In table 2 we show the corresponding R_0 and some statistics of the epidemic curves (number of infected host at the epidemic peak, time in which it is reached and the final epidemic size as proportion of the total host population size) for each of the simulations presented in figure 1 corresponding to the different deterministic models.

Similar results obtained with the individual based model are presented in table 3, where we considered only the case of exponentially distributed periods (corresponding to the SEIR-SEI model 8 - 14, and fixed periods (corresponding to the Delayed model 17 - 23).

As we can see, the basic model produces faster epidemics with a higher epidemic final size (in both cases). In the cases with low R_0, the differences in the epidemic final size between the basic model and the other model is really notorious, being more than double in some cases.

The basic model modified and the delayed model present the same R_0 value and a similar epidemic final size in both cases. However, the first one produces higher peaks in shorter times, resulting in a epidemic that spreads through the population faster and runs out earlier. It is important to note that taken into account the latency period in hosts and vectors produces lower epidemics, in comparison with the basic model.

To compare the solution of the deterministic SEIR-SEI (Eqs. 8 - 14) and delayed models (Eqs. 17 - 23) with the IBM results, we realized simulations following the procedure explained above considering the same parameter values (table 1), population sizes and initial conditions used with the deterministic models.

Considering periods exponentially distributed, it can be observed that, if $b = 0.3$ (Fig. 2 - left panel) the IBM simulations (in red) produce epidemic curves with different peaks values. In some

Model	R_0	Epidemic Peak	Time	Epidemic Final Size
Basic model	2.53	759	113	0.86
Basic model modified	1.26	69.7	415	0.365
SEIR-SEI model	1.49	114.3	461.25	0.559
Delayed model	1.26	42.5	733.4	0.37

Model	R_0	Epidemic Peak	Time	Epidemic Final Size
Basic model	7.03	2250	45	0.99
Basic model modified	3.50	1126	80	0.925
SEIR-SEI model	4.14	809	140	0.965
Delayed model	3.50	682	175	0.94

Table 2: Basic reproduction number, peak of the epidemic, duration from source case introduction to peak and epidemic final size for the solutions of the different Ross-Macdonald models considered in in figure 1 left panel (top) and right panel (bottom).

Type of model	b	Epidemic Peak Mean (SE)	Time Mean (SE)	Epidemic Final Size Mean (SE)	Number of Simulations
Exponential	0.3	144.64 (1.66)	363 (5.53)	0.56 (0.0023)	200
periods	0.5	842.88 (2.17)	131.94 (1.08)	0.96 (0.00019)	200
Fixed	0.3	69.48 (1.22)	517.91 (10.48)	0.36 (0.0043)	200
periods	0.5	714.5 (1.86)	166.30 (1.38)	0.94 (0.00028)	200

Table 3: Peak of the epidemic, duration from source case introduction to peak and epidemic final size for the solutions of the different IBM Ross-Macdonald models.

cases higher than the deterministic result (in black), and in other cases lower. It is due to the fluctuations (produced for the aleatory nature of the simulations), are large considering the values of the epidemic curve. This situation is not observed in the epidemic curves resulting taking b = 0.5 (Fig. 2 - right panel). In this case, the epidemic curves produced by the IBM simulations (in red) are similar in amplitude and height to the resulting considering the deterministic Ross-Macdonald model. The observed differences in these situations can be explained taken into account the R_0 value. In the cases in which R_0 is not large, the stochastic fluctuations play an important role in the epidemic dynamics producing very different epidemic curves. As R_0 increase, the stochasticity produce a shift of the epidemic curve (to the left or to the right of the deterministic result), but it does not greatly affect the height of the peak and the amplitude of the epidemic curve.

When we consider fixed periods (Fig. 3) we observe similar results. As the R_0 value is smaller than the value corresponding to periods exponentially distributed (considering $b = 0.3$), the stochastic fluctuations are greater (Fig. 3 - left panel) and the differences between the IBM epidemic curves and the deterministic are more significant. On the other hand, considering $b = 0.5$, it can be observed that the epidemic curves are similar, as observed before.

5.2 Computing R_0 from the Individual Based Model

To compute R_0 in the case of the individual based model, we have to follow the infectious generation of hosts and vectors. So, the procedure realized is as follow. The first infected host is the only host of first infected generation. The vectors infected by a host of first generation, are vectors of first infected generation. When a vector of first infected generation, infects a susceptible hosts, these host are second infected generation. In general, when a host of infected generation m infects a vector, the infected generation of the vector is m. Then, when a vector of infected generation m infects a

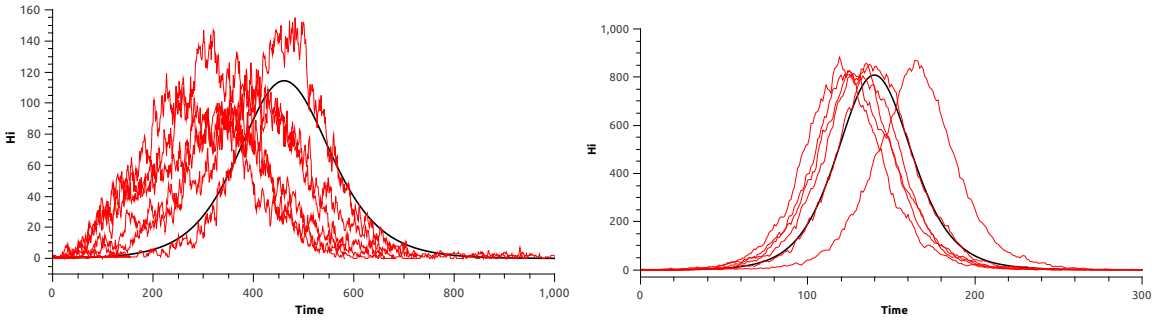

Figure 2: Disease dynamics considering periods exponentially distributed and the parameters in table 1. In black the deterministic result, and in red the IBM simulation. Left panel: low R_0 (b = 0.3); right panel, high R_0 (b = 0.5).

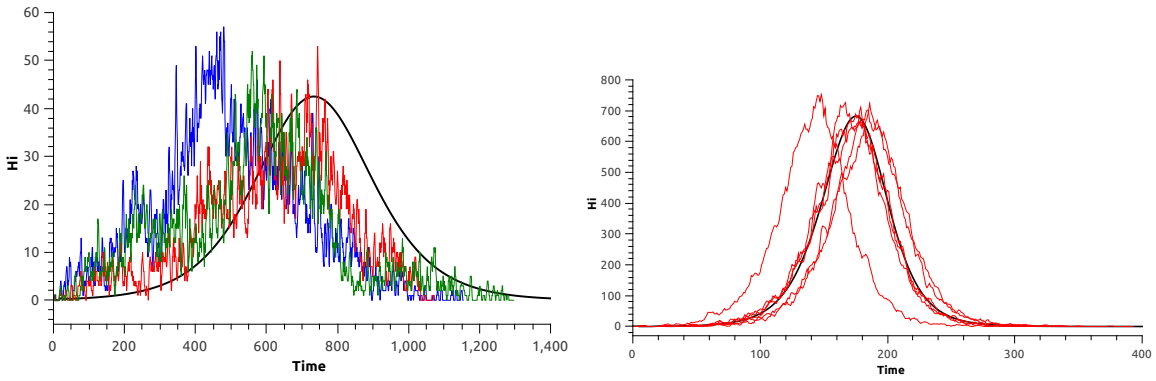

Figure 3: Disease dynamics considering fixed periods and the parameters in table 1. In black the deterministic result, and in red the IBM simulation. Left panel: low R_0 (b = 0.3); right panel, high R_0 (b = 0.5).

host, then infected generation of the host is $m + 1$.

Let H_m be the number of infected-host generation m. Then, R_0 can be estimated as $R_0 \approx H_3/H_2$ [2]. Due to the stochasticity of the IBM simulations, it is important to realize a considerable number of simulations and then calculate the mean of the R_0 value estimated for each simulation. An R_0 estimation for the simulations analyzed en the previous section is presented in the table 4.

Type of model	b	Deterministic R_0	Estimation $R_0 \approx H_3/H_2$	SE	Number of simulations
Exponential	0.3	1.25	1.28	0.13	200
periods	0.5	3.49	3.60	0.26	200
Fixed	0.3	1.49	1.45	0.12	200
periods	0.5	4.14	4.03	0.22	200

Table 4: Estimation of R_0 from the IBM model.

As we can see in Eqs. 15 and 24, given the parameters of the host and vector populations, R_0 is a linear function of the relation V/H. So, varying the relation V/H, we can obtain different values

of R_0.

Considering the parameters in the table 1 and a biting rate equal to 0.3 ($b = 0.3$), we estimated the value of R_0 from the individual based model for different values of V/H. The results considering exponentially distributed periods and fixed period are shown in the Fig. 4, respectively. In all the cases, a initial population of 10000 hosts was considered, with only one infected host. Each estimation of the basic reproduction number was realized with 200 simulations.

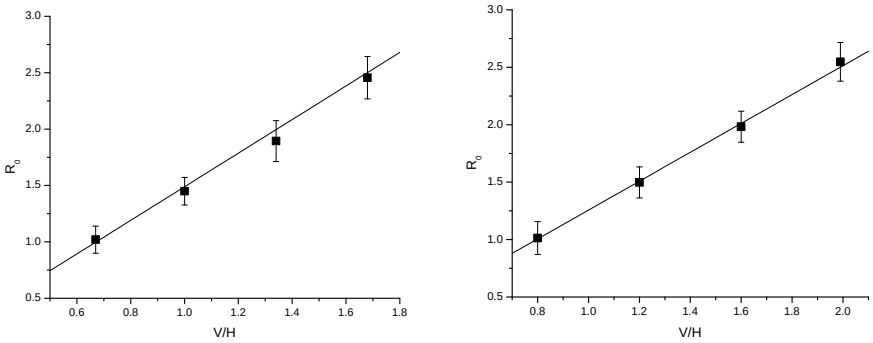

Figure 4: Empirical estimates of the Basic reproduction numbers (squares, bars are standard errors) obtained with the IBM for the cases of exponentially distributed periods (left) and fixed period (right). Continuous line are the corresponding theoretical values given by expressions (15) and (24).

As can be seen in the figure 4 numerical estimations of the basic reproductive number match the theoretical values within the inherent error of the random nature of the IBM results.

6 Discussion and Conclusions

Ross-Macdonald model has been studied and applied to model the dynamic of different infectious diseases such as: malaria, dengue, yellow fever, among others (see for example [14, 12, 9, 1]). It provides a simple framework to model vector-borne diseases.

In this work we present different formulations of the Ross-Macdonald model using ordinary differential equations. In the most general case we included latency periods in both vectors and hosts. We also considered different distributions for latency and infectious periods: exponentially distributed periods and fixed periods. Then, we developed the analogous individual based models and compared the results of the simulations. The more realistic case includes fixed latency periods and infectious periods (except for vector's infectious periods which are already well modeled by an exponential distribution).

A central assumption of the Ross-Macdonald models is homogeneous random mixing: probability of biting in a susceptible host is proportional to the fraction of susceptible host in the entire population. This hypothesis may hold for some local, relatively small, populations. Larger populations may be modeled using a meta-population approach, for example. If local populations have some degree of synchronization, the total population disease dynamics could be quasi-deterministic (see for example [6]), and perhaps a Ross-Macdonald model may describe the global dynamics of the system. In this work we considered populations of 10^4 individuals, a large enough population for which it is not obvious that the assumption of homogeneous mixing holds. For low values of the basic reproduction number, solutions of the deterministic models and realizations of the individual based model are statistical similar (see fig. 3 and tables 2 and 3), but each realization may be significantly different from the deterministic solution.

As we show in this work, disregarding latency periods has a dramatic effect in the dynamics. This is quite apparent for low basic reproduction numbers (see Fig. 1). As in most vector-borne diseases vector's latency periods and life expectancy are of the same order of magnitude, disregarding latency overestimate the basic reproduction number, and therefore we observed faster epidemics with significantly higher peaks. A substantial improvement is achieved with the simple modification (25) which produces the same values of R_0 as the delayed model but still the epidemic curves are significantly different.

Not only the inclusion of latency periods is important but also its distributions. Using exponentially distributed periods leads to slightly smaller basic reproduction numbers and still a noticeable differences in the epidemic curves.

Deterministic models, like the SEIR-SEI model 8-14, are simple ordinary differential equations systems with constant parameters, more amenable for analysis. Numerical integration is straightforward using Runge-Kutta of fourth order, for example. The more realistic choice of fixed periods is modeled by delayed differential equations. Analysis is more complex for these type of models but numerical integration is easily implemented too.

For the individual based model there are not differences, neither in the difficulty of the coding or in the computational cost for both cases, and therefore non-exponentially distributed periods (like fixed periods) is the recommended choice.

In our simulations we considered parameter values compatible with some vector-borne diseases in humans like dengue. In all cases the number of vectors per host was set equal to one at demographic equilibrium. For low values of the basic reproduction number epidemics obtained with the (most realistic) fixed period models have a duration of more than two years (see Fig. 3, left panel), which is never observed in real epidemics. This results highlights the importance of including seasonality when modeling some vector-borne diseases. Vector populations usually have seasonal fluctuations, driven by rainfall, for example, which shape the duration of the epidemics.

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