Imperial College London short course on *Epidemiology & Control of Infectious Diseases*
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Vector-borne microparasitic infections: building a simple model of malaria transmission

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Introduction

Vector-borne microparasitic infections, such as *Malaria*, can be characterised by high transmission intensity, and due to the linear dependency between the basic reproductive ratio and the vector to host ratio (V/H), by large values of (entomologically estimated) R_0. In this practical we will begin by gaining some understanding of the components which contribute to R_0 and how interventions such as vector control, bed-nets, and treatment (chemotherapy) influence transmission. Later in the practical you will construct a model of malaria transmission to look at the effects of latency in vectors, and seasonal variation of vector population numbers.

The primary aims of the practical will be to:

1. Familiarise yourselves with the components of the basic reproduction number for vector-borne microparasitic infections (reinforcing concepts already learned in the lecture).
2. Gain further familiarity with model construction (using Berkeley Madonna).
3. Investigate the effects of introducing the extrinsic incubation period.
4. Introduce seasonality (optional).

Part 1. The basic reproductive number R_0

In the lecture we explored a simple model for malaria transmission by mosquitoes from human host to vector, and from vector to human host. This indirect transmission means that the basic reproductive number consists of $R_{0\text{vector-host}} \times R_{0\text{host-vector}}$. We shall consider each of these individually. Please pay attention to the units and write them down as you write your answers.

Consider a population of 1000 vectors (V) and 100 human hosts (H).

What is the value of the vector to host ratio?
_____

Suppose that each vector feeds once every 3 days and that all blood-meals are taken from humans.

What is the value of the biting rate per mosquito on humans, a?
_____

Assume that if a vector bites an infected human the vector becomes instantaneously infected / infectious with probability 5%

What is the value of parameter b_v ?
_____

If vectors live for L_v = 10 days on average,

What is the value of the per capita vector mortality rate, μ_v?
_____

If a human receives an infectious bite, assume that the human becomes infected with probability 20%

What is the value of parameter b_h ?
_____

If a human remains infectious for an average of D_h = 50 days,

What is the value of the per capita recovery *rate*, *r* ?
_____

Remember that L_v is the mean duration of vector life (or vector life-expectancy) and that D_h is the mean duration of infection/infectiousness in the human host. The reciprocal of these durations are the daily mortality rate of vectors and the daily recovery rate of humans, respectively. Table 14.4 of Anderson & May (1991) gives values for the life expectancy of various vector species. We concentrate here on *Anopheles gambiae* and *An. funestus* as the main malaria vectors in Sub-Saharan Africa (Table 1).

Table 1. The average life expectancy (in the field) of malaria vectors in Africa

Vector	Expected life span (days)	Reference
Anopheles funestus	5.6	Krafsur & Garrett-Jones 1977
Anopheles funestus	5.9	Gillies & Wilkes 1963
Anopheles funestus	10.2	Garrett-Jones & Grab 1964
Anopheles gambiae	11.3	Gillies & Wilkes 1965
Anopheles gambiae	15.4	Garrett-Jones & Shidrawi 1969
Anopheles gambiae	8.0	Garrett-Jones & Grab 1964

Commence by creating, with the information given above, your own table of parameter values and respective units.

Table 2. Parameter values and units used in this practical

Symbol	**Value**	**Definition**	**Units**

- What are we assuming about the mortality rate of vectors with respect to time or insect's age?

- Draw a small plot to represent this in two ways: a) the vector mortality rate vs. time (age); b) the survivorship function of vectors vs. time (age)

Vector mortality rate vs. time (age)	Survivorship function vs. time (age)

We begin by assuming that a single infected/infective vector is present ($Y_v = 1$) and proceed to calculate, on average, how many new human infections this vector will give rise to. In all that follows make sure you are aware of the units (dimensions) of each parameter, coefficient, and variable. Remember that proportions are dimensionless, rates are per unit time. You are working in days. Write down the dimensions accompanying each element of the proposed operations. See if and when they cancel out. Ask yourselves if the result obtained is expressed in the correct units.

- What is the initial proportion of infected/infective vectors in the vector population (y_v)?

1) How many bites will this mosquito take on humans during its lifetime? (daily biting rate per vector on humans × vector lifetime in days)

2) If these bites are *homogeneously* distributed among all human hosts, what is the probability that any single host is bitten by the infective vector during its lifetime? (total no. bites on humans/ number of hosts)

3) On average, how many hosts will this vector infect during its lifetime? (probability that a host is bitten by the infective vector × probability that host becomes infected/ infectious following an infective bite × number of hosts)

$\boldsymbol{R_{0\ \text{vector-host}}}$ =

Now compare this result from the one obtained by the expression $R_{0\text{vector-host}} = a\ b_h/\mu_v$ that we presented in the lecture. Do you follow the logic?

Now assume that all vectors are susceptible and that a single infected human is present in the population ($Y_h = 1$), and estimate how many vectors that human will infect.

- What is the initial proportion of infected/infective humans in the human population (y_h)?

1) What is the total number of feeds taken by the 1000 vectors per day, if these bites are *homogeneously* distributed among *all* human hosts? (daily biting rate per vector on humans × number of vectors / number of hosts)

2) On average, how many vectors will become infected/infective during the human host's infectious period? (number of bites per host per day × probability of vector becoming infected following an infectious bite × duration of infectiousness)

$\boldsymbol{R_{0\ \text{host-vector}}}$ =

Now compare the result you have obtained following this train of thought with the expression we presented last term, $R_{0\ \text{host-vector}} = (V/H)\ a\ b_v/r$

What assumptions have we made to get this answer?

- About anthropophagy?

- About latency (incubation periods)?

- About host or vector survival?

- About heterogeneity in the vector or human population?

The basic reproductive number is the product $R_0 = R_{0\ \text{vector-host}} \times R_{0\ \text{host-vector}}$. What do you notice about this number? About its dimensions? Is it greater or less than 1?

$R_0 =$

Again, compare with the expression $R_0 = (V/H)\ a^2\ b_h\ b_v\ /\ (r\ \mu_v)$

The endemic (equilibrium) prevalences in humans y^*_h and vectors y^*_v predicted by the model are determined by the equations,

$$y_h^* = \frac{(R_0 - 1)}{(R_0 + ab_v L_v)} \qquad \text{and} \qquad y_v^* = \frac{(R_0 - 1)\left(\frac{ab_v L_v}{1 + ab_v L_v}\right)}{R_0}$$

Calculate these values and express them as percentages

- Prevalence of infection in humans _____ %
- Prevalence of infection in vectors _____ %

What do you notice about their relative magnitudes? Why might this be the case?

-
-
-

As an exercise, try deriving the above expressions from the model equations,

$$\frac{dy_h}{dt} = \left(\frac{V}{H}\right) a\, y_v (1 - y_h) b_h - r\, y_h \qquad \text{and} \qquad \frac{dy_v}{dt} = a(1 - y_v)\, y_h\, b_v - \mu_v\, y_v$$

Remember that at equilibrium, dy_h/dt and dy_v/dt are equal to zero.

In your course notes, and for *directly* transmitted microparasitic infections in a constant population size, the endemic prevalence of infection in the host population, y^*, is given by the expression

$y^* = 1 - \frac{1}{R_0}$. (Remember that this approximation comes from $R_0 = 1/x^*$.)

What value of prevalence (in the human population) you get if you apply this expression to the problem in hand?

Is this a good approximation for vector-borne infections? Under which circumstances?

The following table (from Anderson & May, 1991) gives the prevalence of infection in vector population samples:

Table 3. The prevalence of infection in vector population samples

Vector	Parasite	Study area	Prevalence (%)	Reference
An. gambiae	*P. falciparum*	Ethiopia	1.87	Krafsur & Garrett-Jones 1977
An. funestus	*P. falciparum*	Ethiopia	1.23	Krafsur & Garrett-Jones 1977

The influence of population sizes

What happens when the population of humans doubles to 200 and the number of vectors remains 1000 (all other parameters remain unchanged)?

1) If a single infectious vector is present, on average, how many human hosts will the vector infect? ($a\ b_h\ L_v$)

human hosts infected

2) For a single infected host we calculated the rate of being *bitten* by assuming that all bites are evenly distributed. What is the rate of being bitten now that the population of humans has doubled? (V/H) a

Each host is *bitten* times per day

3) On average how many vectors will be infected during the human host's duration of infectiousness? ($bitten\ b_v\ D_h$)

vectors infected

4) What is the new basic reproductive number?
R_0 =

Repeat this calculation when the number of vectors doubles to 2000 and the number of human hosts remains at 100.

R_0 =

Notice that changing the vector to host ratio changes the rate at which human hosts are bitten, but not the rate at which vectors bite (1 blood meal every 3 days)

Complete the following table:

Table 4. The influence of population sizes

H	V	$R_{0\text{vector-host}}$	$R_{0\text{host-vector}}$	R_0
100	1000			
200	1000			
100	2000			

As previously said, the basic reproductive number R_0 is given by the equation

$R_0 = (V/H)\, a^2\, b_h\, b_v\, L_v\, D_h$ if latency in the vector is ignored.

What control strategies does this relationship suggest might be most effective in controlling vector-borne infections?

To which of these parameters does R_0 respond linearly?, and non-linearly?

Consider a 50% reduction in vector numbers, in biting rate, and in duration of infectiousness:

Table 5. Sensitivity of the basic reproductive number to changes in parameter values (Part I)

50% reduction in	Parameter value	R_0	Possible control measure that effects this reduction
Vector numbers (V)	i.e. 500		
Biting rate per vector on humans (a)			
Duration of infectiousness ($1/r$)			

There are various approaches to malaria vaccines. A former approach was based on the circumsporozoite (CS) epitope, hoping to prevent invasion of hepatocytes by the sporozoites. Anti-disease vaccines would be targeted against asexual, erythrocytic stages. A transmission-blocking vaccine (TBV) would be addressed against the stages within the mosquito. Which parameters of the model will be influenced by these approaches and how?

Table 6. Malaria vaccines and the components of R_0 that they target

Type of vaccine	Parameter(s) that this type of vaccine would influence	Effect on the basic reproduction number
Vaccines preventing infection of hepatocytes by sporozoites		
Vaccines preventing infection of erythrocytes by merozoites		
Vaccines targeting stages within the mosquitoes		

Part II. Building a model of malaria transmission

Now that you understand the basic reproduction number and its influence on transmission, we can solve the model numerically using Berkeley-Madonna. The full model for malaria transmission has four compartments, susceptible hosts (X_h), infected hosts (Y_h), susceptible vectors (X_v) and infected vectors (Y_v). For the purposes of this practical we shall ignore the per capita rate of human mortality in comparison with the per capita rate of recovery because the human life-span is measured in years in contrast to days for the duration of infection ($\mu_h << \nu$). To maintain population size constant, the per capita birth rate is equal to the mortality rate. We will ignore the complications of the vector life-cycle (holometabolous with eggs, larvae, pupae and imagoes) and assume that the rate of recruitment of susceptible (nulliparous) flies equals $\mu_v V$.

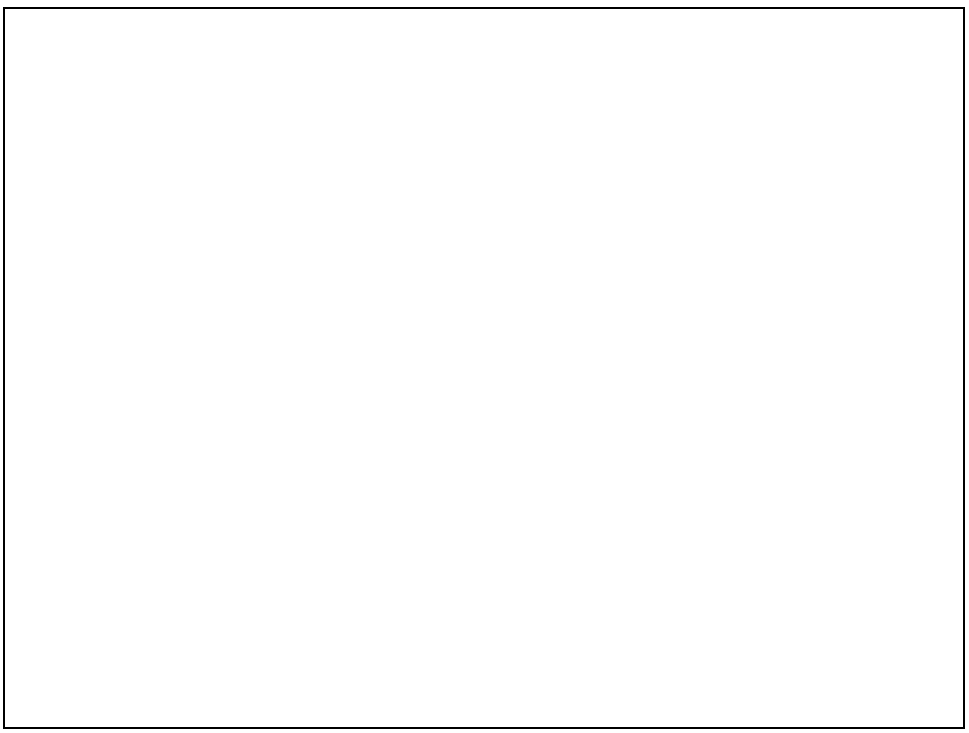
$$dX_h/dt = -(V/H)\, a\, b_h\, (Y_v/V)\, X_h + rY_h$$
(eqn 1)

$$dY_h/dt = (V/H)\, a\, b_h\, (Y_v/V)\, X_h - rY_h \quad \text{(eqn 2)}$$

$$dX_v/dt = \mu_v V - a\, b_v\, (Y_h/H)\, X_v - \mu_v X_v \quad \text{(eqn 3)}$$

$$dY_v/dt = a\, b_v\, (Y_h/H)\, X_v - \mu_v Y_v$$
(eqn 4)

Draw a flow diagram to represent the above equations



Begin by opening Berkeley Madonna. Choose **New** from the **File** menu. Madonna creates a new model (Untitled) and opens its equation window. You will need to start by choosing a method of numerical integration (choose Runge Kutta 4). You should also think about the time-scales we are interested in. All units have been expressed in terms of days. A typical time-step will be 1 day and a year 365 days. To gain sufficient accuracy with the model simulations set STOPTIME to run for 1 year (stop value of 365) with 365 output steps.

METHOD Euler (Change this to RK4)

STARTTIME = 0
STOPTIME=10 (Since we are working in days, change to 365)
DT = 0.02 (This is the default integration time-step)
DTOUT = 1 (the outputs will be in days)

Now give the initial values of your state variables. We will commence with 1 infective host and 99 susceptible hosts. For the mosquito population, we will start with 1000 susceptible mosquitoes and none infected.
E.g.

init (Xh) = 99

Proceed by writing your equations (1) to (4) as given above (for Madonna Syntax go to **Equation Help** in the **Help** menu).
E.g.

d/dt(Xh) = -(V/H)*a*bh*(Yv/V)*Xh + r*Yh

Since we must keep track of the total population size, add the variables H and V. Insert the equations **Xh+Yh** (for H) and **Xv+Yv** (for V). (eqns 5, 6)

You could add a variable for the basic reproduction number R_0, with equation
(V/H)* (a ^ 2)*bv*bh/(muv*r)
(eqn 7)

or the vectorial capacity, *C*,
(V/H)* (a ^ 2)*bv*bh/(muv) (eqn 8)

and the Entomological Inoculation Rate (EIR) expressed per year
(V/H)* a *(Yv/(Xv+Yv)) * 365
(eqn 9)

Now add the parameters from the following list as discussed above

a (in day^{-1})	bh	r (in day^{-1})	bv	muv (in day^{-1})
0.33 [1/(3d)]	0.2	0.02 [1/(50d)]	0.05	0.1 [1/(10d)]

The model is now ready to **Run**.
Graphs will be prepared with the first eight variables, which you can toggle to see represented. You can add pages and have each page representing a variable or a couple of variables. You can also

choose which variables to plot: In the Window containing the graph, double click on the background and a Choose Variables Box dialogue will appear; add or remove variables and click on OK. The new variable tabs will appear in the bottom. Click on the tab. Click on **Run** to obtain the plot.

It is a good idea to check that the model is behaving in the way it should. Prepare a graph of the number of vectors, V, and of hosts, H against time and check that they remain constant and at the levels you set out at the beginning. Also inspect the graph for the basic reproduction number. Is it the same as you calculated in the first part of this practical?

To plot prevalences define two new variables hostprev (equation: **100*Yh/H**) and vectorprev (equation: **100*Yv/(Xv+Yv)**).

What do you predict will happen? Will the epidemic be severe? On a new graph plot the prevalences of host and vector infections. You can edit axes, series, graph names (Double click on the axes to edit them). What do you notice? Why is this the case?

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Save your model under a name (e.g. Vectors 1.mmd)

Observed endemic vector prevalences for a number of vector-borne infections are listed in Table 14.5 of Anderson & May (1991) and are in general much lower than the numbers predicted here (see Table 3 above). What has been left out of the model to give this discrepancy?

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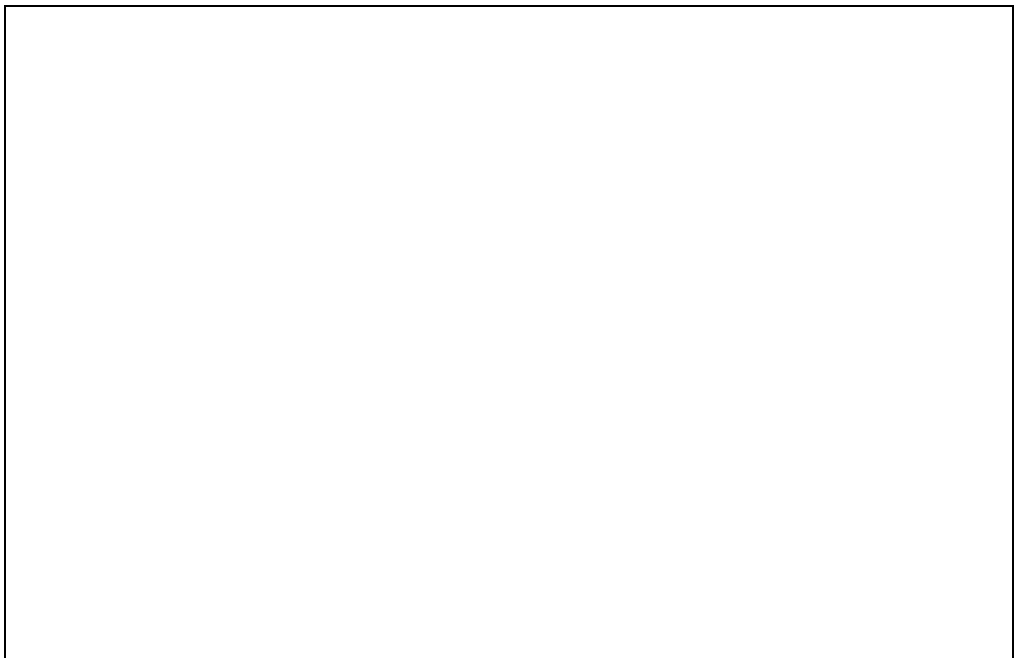
Can you think of how to modify the equations for the vector compartments to correct this? Write down a new model flow diagram, which includes a compartment, Iv, for vector incubation.



Suppose vectors incubate for a period of 9-12 days (see Table 27.1 of Kettle (1995) for latent periods of the four *Plasmodium* species which infect humans). In your **Equations Window** add a new parameter **gamma** and set its value to 0.0833 day^{-1}[1/(12 d)]. You will need to add a new variable to your model with Iv for "Incubating" or latent vectors and add its initial value, **init (Iv)**. Since we started the previous run with no infected mosquitoes, set the latent vectors to zero initially. Also you will have to change your equation for Yv to Iv (since infections now lead to an incubating phase rather than to infection). The loss terms for this equation will have to be modified to include loss of incubating mosquitoes that become infective (**-gamma*Iv**), and mortality of incubating mosquitoes (**-muv*Iv**). Now add an equation from the incubating stage Iv to the infective stage Yv. The new equation is **gamma*Iv** for the gain term, but don't forget that infective mosquitoes also die with net mortality **muv*Yv**. Lastly, to keep track of the number of vectors, change the definition of the variable V so that V = **Xv+Yv+Iv**, and the definition of vectorprev = **100***Yv/(Xv+Yv+Iv)**.

Run the model. What are the new endemic prevalences?

- In humans _____%
- In vectors _____%

Run a "sensitivity analysis" for various values of the incubation parameter **gamma**. From the **Parameters** menu choose **Parameter plot**. Choose **gamma** as the **Parameter**. In **no. of runs** choose 10. Choose **Geometric** for **Series type**. Try from **Initial Value** 0.05 day^{-1} (20 day incubation), to **Final Value** 50 day^{-1} (incubation of 0.02 days or nearly no incubation). You should **Add** vectorprev and hostprev as Variables for the **Y axis** and tick **Final** for the output. The results are plotted against **gamma**. Double click on the **gamma** axis to change this (**x**) axis to Log scale. You should see that incubation period has a marked effect on vector prevalence. Why is this so?

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Notice that the human host prevalence can be high but the vector prevalence can be very low. Section 14.4.1 of Anderson & May (1991) covers this subject in much greater detail.

You may also want to try a **Parameter plot** changing the values of the biting rate, ***a***, say from 0.01 (vectors are nearly zoophagic) to 0.33 (all blood-meals are taken on humans and vectors bite every 3 days, i.e. only once per gonotrophic cycle). If blood-meals were interrupted and vectors bite more than once per gonotrophic cycle, you may want to increase ***a*** up to 1 (vectors bite every day).

Different mathematical representations of latency in the vectors and their biological interpretations

When we incorporate latency by including an additional compartment, we are making the assumption that the rate of progression between the 'incubating' compartment and the 'infectious' compartment is

constant. Therefore there will be an exponential distribution of latent periods; not all vector will become infective at once (but most of them will do almost immediately).

An alternative representation, which mirrors a different biological process, is to assume that the latent period is fixed, and that once the incubation period has elapsed all vectors become infectious. In this case, the differential equations are modified to include a delay (delay-type of differential equation), and if the survival of the vector is of the essence (which is, given the fact that latent periods are long in comparison to the vector's life expectancy), then the proportion of mosquitoes surviving the extrinsic incubation period is also included,

$$dY_v(t)/dt = a\ b_v\ [Y_h(t-\tau)/H]\ X_v(t-\tau)\ \exp(-\mu_v\ \tau) - \mu_v Y_v\ (t)$$

and the value of τ would be 1/gamma, or equal to n as in the lecture (the number of days necessary for an infected mosquito to become infective).

The Berkeley Madonna equations are:

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d/dt(Xv)=muV*V-a*bV*(Yh/H)*Xv-muV*Xv
d/dt(Iv)=a*bV*(Yh/H)*Xv-(a*bV*(delay(Yh/H,tau))*delay(Xv,tau)*exp(-muV*tau))-muV*Iv
d/dt(Yv)=a*bV*(delay(Yh/H,tau))*delay(Xv,tau)*exp(-muV*tau)-muV*Yv
```

and you must add parameter tau to your list

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tau=12 (this is equivalent to n)
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Write the expression for the proportion of vectors becoming infectious when there is a constant rate of progression, gamma (γ), between the latent and the infectious compartment, and the mosquitoes die at a constant rate μ_v

Write the expression for the proportion of mosquitoes becoming infective when vectors become infectious after a fixed period τ and die at a constant rate μ_v

See Holmes, Bartley & Garnett (1998) for a discussion of these two alternative representations in the context of dengue transmission.

The basic reproductive ratio with latency

We end up this part of the practical by remembering the expression of R_0 with latency in the vectors given in the lecture notes:

$$R_0 = (V/H)\, a^2\, b_h\, b_v\, D_h\, L_v\, p^n \text{ , or}$$

$$R_0 = (V/H)\, a^2\, b_h\, b_v\, D_h\, L_v \exp(-\mu_V\, n)$$

where p is the probability of mosquito daily survival, n = 1/gamma, and $\mu_V = -\ln(p)$. In our case p = 0.90 (= $e^{-0.1}$), implying that 90% of vectors survive from one day to the next.

Modify the expression for R_0 in your model accordingly.

Now you can see that R_0 is linearly related to vector density; it will change mildly non-linearly with changes in a (which is squared because the vector needs to bite at least twice to pick up and transmit the infection), but it will respond strongly non-linearly with changes in p (which is to the power of n, the average extrinsic incubation period). Compare reducing by 50% the value of p, with the changes in R_0 exerted by those explored in Table 5 above. (Remember the relationship that exists between p, μ_V and L_v.)

Table 5. Sensitivity of the basic reproductive number to changes in parameter values (Part II)

50% reduction	Parameter value	R_0
In vector numbers (V)	i.e. 500	
In biting rate per vector on humans (a)		
In duration of infectiousness ($1/r$)		
In the probability of daily survival (p)		

What is the role of adulticides (as opposed to larvicides) in malaria control programmes?

Reading List

Chapter 14: Indirectly transmitted microparasites. In: Anderson, R.M. & May, R.M. (1991) *Infectious Diseases of Humans. Dynamics and Control.* Oxford: Oxford Science Publications.

Chapter 5: The population dynamics of malaria (J.L. Aron & R.M. May). In: Anderson RM, ed. (1982). *Population dynamics of Infectious Diseases. Theory and Applications*. London: Chapman and Hall.

Bailey, N.T.J. (1982). *The Biomathematics of Malaria*. London: Charles Griffin & Co.

Dye, C. (1986). Vectorial capacity: must we measure all its components? *Parasitology Today* 2(8): 203-209.

Dye, C. (1990). Epidemiological significance of vector-parasite interactions. *Parasitology* 101: 409-415.

Dye, C. (1992). The analysis of parasite transmission by bloodsucking insects. *Annual Review of Entomology* 37: 1-19.

Kettle, D.S. (1995). *Medical and Veterinary Entomology*. 2nd edition. CABI Publishing.

Koella, J.C. & Antia, R. (2003). Epidemiological models for the spread of anti-malarial resistance. *Malaria Journal* 2(3): 1-11.

Gilles, H.M. (1993). *Bruce-Chwatt's Essential Malariology*. Third Edition. London: Arnold

Holmes, E.C., Bartley, L.M. & Garnett, G.P. (1998). The emergence of dengue: past, present, and future. Chapter 10, In: *Emerging Infections*. London: Academic Press, pp. 301-325.

Pull, J.H. & Grab, B. (1974). A simple epidemiological model for evaluating the malaria inoculation rate and the risk of infection in infants. *Bulletin of the World Health Organization* 51: 507-516.

Rogers, D.J. (1988). The dynamics of vector-transmitted diseases in human communities. *Philosophical Transactions of the Royal Society of London* (series B) 321: 513-539.

An example of a paper incorporating latency in the vector as we have here:
Ghani A et al (2009). Loss of Population Levels of Immunity to Malaria as a Result of Exposure-Reducing Interventions: Consequences for Interpretation of Disease Trends. *PLoS One*. 4(2): e4383

And for those of you who speak Spanish, the following may be a useful reference:
Basáñez M-G & Rodríguez D (2004). Dinámica de transmisión y modelos matemáticos en enfermedades transmitidas por vectores (Transmission dynamics and mathematical models of vector-borne diseases). *Entomotropica* 19: 113-134.

The following section of the practical is entirely *optional*, and you may wish to complete it at your leisure.

At this point you may want to save your model with a different name (e.g Vectors latency.mmd) and introduce the modifications that follow. This way, you will have a model without seasonality (the previous exercise) in one file, and a model with seasonality (next exercise) in a different file, and be able to compare both.

The effect of variable mosquito density

Macdonald (1957) suggested that areas of "stable" high transmission malaria should be less sensitive to fluctuations in mosquito density than areas of low transmission. The basic model you have constructed can be used to test this very easily. Suppose that the vector population fluctuates seasonally with rainfall (affecting availability of breeding sites and therefore recruitment into the vector population) but has a constant background component. In the **Window** menu, reselect **Equations**, and change the equation for the variable V to read

1000*(0.55+0.45*Sin(2*PI*TIME/365))

where PI is 3.1416. This is a sinusoidal function with period 365 days and goes from a minimum background of V about 100 vectors to a maximum of 1000 during the course of a year with a mean of about 500. Now rerun the model for 10 years (STOPTIME = 3650). You should see the seasonal fluctuations clearly. For more clarity as to the scale of the X Axis, double click on it and change it from Auto to Minimum 0, Maximum 3650, Div 10. This should allow you to see clearly the number of years in the X Axis.

What happens to R_0?

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What do you think this means in terms of a critical vector density?

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Draw a **Phase Plane Plot** of hostprev against vectorprev. In the **Help** menu, go to **How do I**

Make a Phase Plane Plot

- Run the model
- Double click anywhere in the x-y plane of the graph (or select *Choose Variables* from the *Graph* menu)
- Remove all variables from the Y axis with the exception of hostprev.
- Replace TIME on the x axis with vectorprev by selecting vectorprev in the drop down *X Axis* menu.
- Click *OK*. You may have to double-click in the X Axis and return to Auto.

Can you see the cycles now?

In order to get a mean prevalence which is closer to your previous values, the mean no. of vectors would have to be 1000. If you want to confirm this, go back to the Equations window and change V to read **1000*(1+0.9*Sin(2*PI*TIME/365)).** Re-run the model, prepare graphs of V vs. time, of R_0 vs. time, and of the prevalence of infection in humans and mosquitoes vs. time. Take a look at the

average values and also at how the peaks and troughs of the different variables relate to each other. You may wish to change the Y Axis to Log (Tick Log and Auto).
Explain the following:

- R_0 mirrors Vector density

- Peak infection prevalence in vectors takes place at lowest vector density values

- How infection prevalence in hosts and vectors track each other?

You should now have a feeling for the dynamic properties of vector-borne infections.