Analysis of the Spread of Malaria Disease

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Introduction

- Malaria
    - Mosquito-borne
    - Prevalent in tropical and sub-tropical regions
    - 225 million cases annually

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- Tools to analyze these equations

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    - Differential equations equal zero
    - The infected population is zero
- Disease endemic equilibrium point
    - Differential equations equal zero
    - The infected population is greater than zero

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  - Solutions near the equilibrium point tend to stay near the equilibrium point with time.
- Global stability
  - Solutions at any point on the graph will tend toward the equilibrium point with time.

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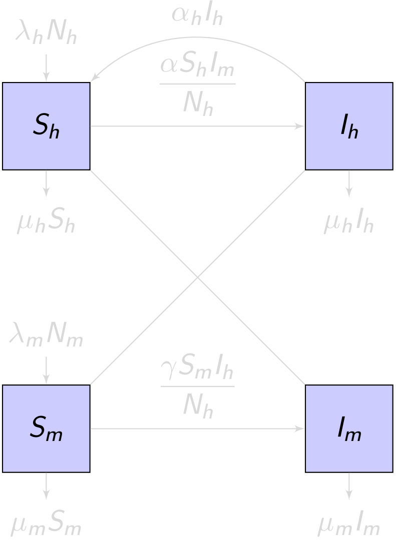

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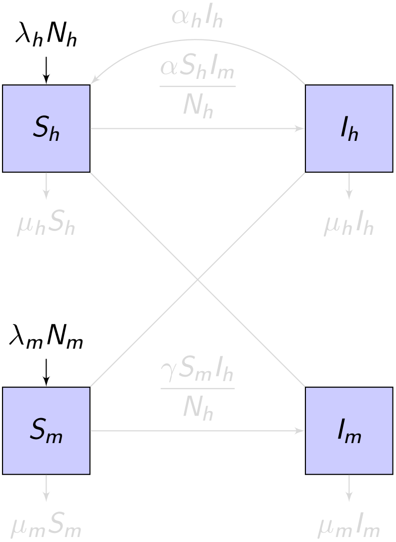
Table 1. Parameters for the malaria model.

λ_h	Birthrate of humans
λ_m	Birthrate of mosquitos
μ_h	Natural death rate of humans
μ_m	Natural death rate of mosquitos
α	Human infection rate
γ	Mosquito infection rate
α_h	Human recovery rate

Mathematical Model of Malaria



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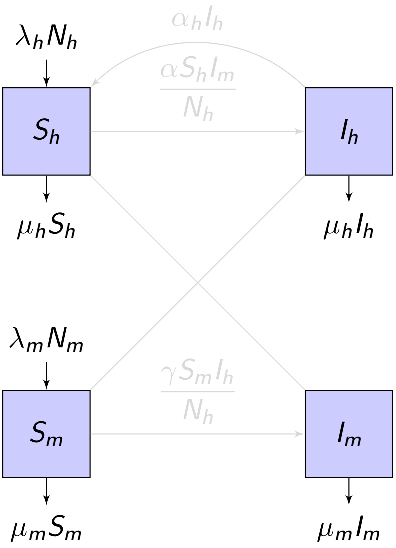

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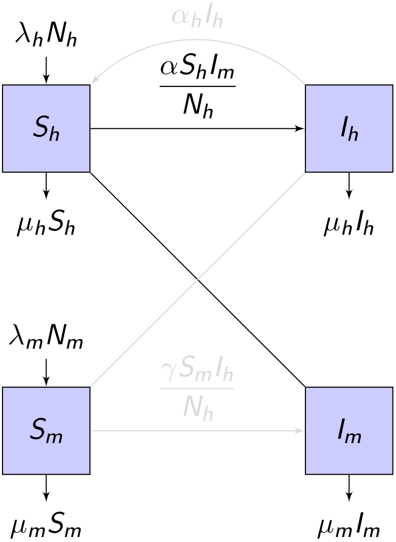

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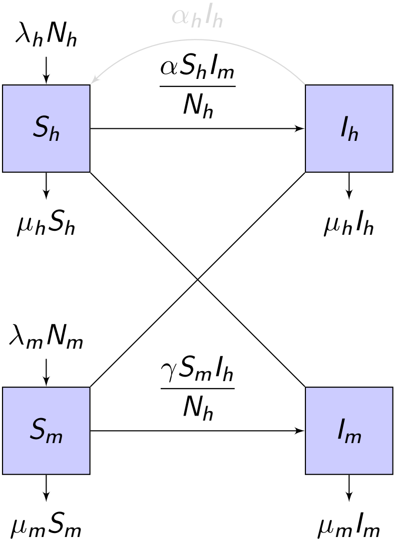

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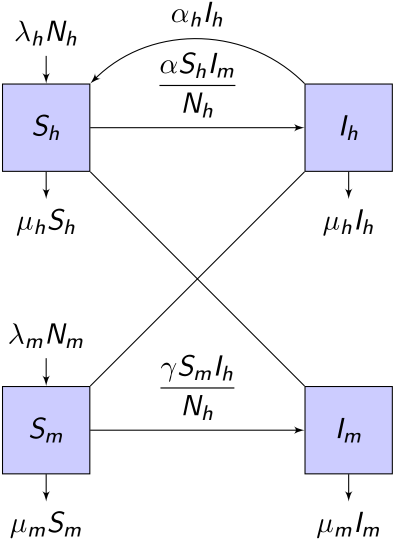

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System of Equations

From Figure 1, we derive the following system of differential equations:

$$
\begin{aligned}
S_h' &= \lambda_h N_h - \frac{\alpha S_h I_m}{N_h} - \mu_h S_h + \alpha_h I_h \\
I_h' &= \frac{\alpha S_h I_m}{N_h} - \alpha_h I_h - \mu_h I_h \\
S_m' &= \lambda_m N_m - \frac{\gamma S_m I_h}{N_h} - \mu_m S_m \\
I_m' &= \frac{\gamma S_m I_h}{N_h} - \mu_m I_m
\end{aligned}
$$

Change of Variables

$$s_h = \frac{S_h}{N_h}, \;\; s_m = \frac{S_m}{N_m}, \;\; i_h = \frac{I_h}{N_h}, \;\; \text{and} \quad i_m = \frac{I_m}{N_m}$$

$$\begin{aligned}
s_h' &= \lambda_h(1 - s_h) + \alpha_h i_h - \alpha_1 s_h i_m \\
i_h' &= \alpha_1 s_h i_m - \lambda_h i_h - \alpha_h i_h \\
s_m' &= \lambda_m(1 - s_m) - \gamma s_m i_h \\
i_m' &= \gamma s_m i_h - \lambda_m i_m
\end{aligned}$$

Change of Variables

- Since $S_h + I_h = N_h$ and $S_m + I_m = N_m$,
  - $s_h + i_h = 1$ and $s_m + i_m = 1$.
  - Thus, $s_h = 1 - i_h$ and $s_m = 1 - i_m$.
- By differentiating...
  - $s_h' = -i_h'$ and $s_m' = -i_m'$.

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Change of Variables

After substituting $1 - i_h$ for s_h, and $1 - i_m$ for s_m, the system becomes

$$\begin{aligned} i_h' &= \alpha_1(1 - i_h)i_m - \lambda_h i_h - \alpha_h i_h \\ i_m' &= \gamma(1 - i_m)i_h - \lambda_m i_m, \end{aligned}$$

which is the system that we will analyze.

Equilibrium Points

To find our equilibrium points we will set our systems equal to zero and solve for i_h and i_m.

$$\begin{aligned} 0 &= \alpha_1(1 - i_h)i_m - \lambda_h i_h - \alpha_h i_h \\ 0 &= \gamma(1 - i_m)i_h - \lambda_m i_m, \end{aligned}$$

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Disease Endemic Equilibrium Point

The **disease endemic equilibrium point**, denoted (i_h^*, i_m^*), is the equilibrium point at which the disease persists. Then

$$(i_h, i_m) \neq (0, 0) \, .$$

By setting $i_m' = 0$ we see that

$$0 = \gamma(1 - i_m)i_h - \lambda_m i_m.$$

From this we can obtain a value of i_h in terms of i_m.

$$i_h = \frac{\lambda_m i_m}{\gamma(1 - i_m)}$$

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Substituting this quantity into the equation $i_h' = 0$ gives the following expression for i_m^*:

$$i_m^* = \frac{\alpha_1\gamma - \alpha_h\lambda_m - \lambda_h\lambda_m}{\alpha_1\lambda_m + \alpha_1\gamma}\,.$$

By plugging i_m^* into our previously obtained expression for i_h, we find the corresponding value of i_h^* to be

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Calculating R_0

$$(i_h^*, i_m^*) = \left(\frac{\alpha_1\gamma - \lambda_m\alpha_h - \lambda_m\lambda_h}{\alpha_1\gamma + \alpha_h\gamma + \lambda_h\gamma}, \quad \frac{\alpha_1\gamma - \alpha_h\lambda_m - \lambda_h\lambda_m}{\alpha_1\lambda_m + \alpha_1\gamma} \right)$$

$$i_h^*, i_m^* > 0$$

Then

$$\alpha_1\gamma - \lambda_m\alpha_h - \lambda_m\lambda_h > 0.$$

From this inequality we see that

$$R_0 = \frac{\alpha_1\gamma}{\lambda_m(\alpha_h + \lambda_h)} > 1.$$

We conjecture that $\mathbf{R_0}$ **is the basic reproduction number**.

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Classification of Systems of Differential Equations

Before moving into asymptotic stability, we will need to consider systems of first order linear differential equations of the form

$$\begin{aligned} x' &= ax + by \\ y' &= cx + dy \end{aligned}$$

This can be expressed as

$$\mathbf{x}' = A\mathbf{x},$$

where

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A nonzero vector $\mathbf{v}$ is an **eigenvector** of A and the constant λ is called an **eigenvalue** of A if

$$A\mathbf{v} = \lambda \mathbf{v}$$

for the system $\mathbf{x}' = A\mathbf{x}$.

Theorem

Suppose A has a pair of real eigenvalues $\lambda_1 \neq \lambda_2$ and associated eigenvectors v_1 and v_2 then the general solution of the linear system $x' = Ax$ is given by

$$x(t) = \alpha e^{\lambda_1 t} v_1 + \beta e^{\lambda_2 t} v_2$$

where $\alpha, \beta \in \mathbb{R}$.

Then when $\lambda_1, \lambda_2 < 0$ the solution will stabilize.

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$$\det(A - \lambda I) = 0$$

$$(a - \lambda)(d - \lambda) - bc = 0,$$

$$\lambda^2 - (a + d)\lambda + (ad - bc) = 0.$$

Note that **tr** is the trace of the matrix, which is defined as the sum of the entries along main diagonal. Then

$$\lambda^2 - \mathrm{tr}(A)\lambda + \det(A) = 0,$$

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$$\lambda^2 - (a + d)\lambda + (ad - bc) = 0.$$

Note that **tr** is the trace of the matrix, which is defined as the sum of the entries along main diagonal. Then

$$\lambda^2 - \mathrm{tr}(A)\lambda + \det(A) = 0,$$

Using the quadratic formula, the roots of our characteristic equation are given by

$$\lambda_1 = \frac{\text{tr}(A) + \sqrt{\text{tr}(A)^2 - 4\text{det}(A)}}{2}$$

and

$$\lambda_2 = \frac{\text{tr}(A) - \sqrt{\text{tr}(A)^2 - 4\text{det}(A)}}{2}.$$

From this, we can see that

$$\lambda_1 + \lambda_2 = \text{tr}(A)$$

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Classification of Systems of Differential Equations

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Classification of Systems of Differential Equations

When

$$\text{tr}(A)^2 - 4\text{det}(A) > 0,$$

Stable Case:

$$\text{tr}(A) < 0 \text{ and } \det(A) > 0 \implies \lambda_1, \lambda_2 < 0$$

Unstable Case:

In any other case, the equilibrium point will be unstable.

Local Asymptotic Stability

Theorem

i.) If $R_0 < 1$, then the disease free equilibrium point is locally asymptotically stable.

ii.) If $R_0 > 1$, then the disease free equilibrium point is unstable and the disease endemic equilibrium point is locally asymptotically stable.

Local Asymptotic Stability

We will analyze our system using Jacobian matrices.

$$J(i_h, i_m) = \begin{bmatrix} \frac{\partial i_h'}{\partial i_h} & \frac{\partial i_h'}{\partial i_m} \\ \frac{\partial i_m'}{\partial i_h} & \frac{\partial i_m'}{\partial i_m} \end{bmatrix}$$

$$\begin{aligned} \frac{\partial i_h'}{\partial i_h} &= -\lambda_h - \alpha_1 i_m - \alpha_h \\ \frac{\partial i_h'}{\partial i_m} &= \alpha_1(1 - i_h) \\ \frac{\partial i_m'}{\partial i_h} &= \gamma(1 - i_m) \\ \frac{\partial i_m'}{\partial i_m} &= -\lambda_m - \gamma i_h \end{aligned}$$

Our final Jacobian matrix is

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Local Asymptotic Stability

Evaluating at our disease-free equilibrium point $(0, 0)$, we obtain the Jacobian matrix, trace and determinant:

$$J(0,0) = \begin{bmatrix} -\lambda_h - \alpha_h & \alpha_1 \\ \\ \gamma & -\lambda_m \end{bmatrix}$$

$$\begin{aligned} \det(J(0,0)) &= \lambda_m(\lambda_h + \alpha_h) - \alpha_1\gamma \\ \mathrm{tr}(J(0,0)) &= -(\lambda_m + \lambda_h + \alpha_h) \end{aligned}$$

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$$\mathrm{tr}(J(0,0)) < 0$$

Recall

$$R_0 = \frac{\alpha_1\gamma}{\lambda_m(\alpha_h + \lambda_h)}.$$

$$R_0 < 1 \implies \lambda_m(\lambda_h + \alpha_h) > \alpha_1\gamma$$

Then (0,0) is locally asymptotically stable when $R_0 < 1$.

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Local Asymptotic Stability

We now evaluate the Jacobian at the disease endemic equilibrium point (i_h^*, i_m^*).

$$J(i_h^*, i_m^*) = \begin{bmatrix} \frac{-\gamma(\alpha_1+\lambda_h+\alpha_h)}{\lambda_m+\gamma} & \frac{\alpha_1(\alpha_h\gamma+\gamma\lambda_h+\alpha_h\lambda_m+\lambda_m\lambda_h)}{\gamma(\alpha_1+\alpha_h+\lambda_h)} \\ \frac{\gamma\lambda_m(\alpha_1+\alpha_h+\lambda_h)}{\alpha_1(\lambda_m+\gamma)} & \frac{-\alpha_1(\lambda_m+\gamma)}{\alpha_1+\alpha_h+\lambda_h} \end{bmatrix}$$

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Global Asymptotic Stability

- If all solutions of a system converge to the equilibrium point, then that equilibrium point is considered globally asymptotically stable.
- We will study the global asymptotic stability of our disease free equilibrium point, $(i_h, i_m) = (0, 0)$, using Lyapunov's second method for stability.

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Global Asymptotic Stability

Definition

Lyapunov Stability:
Let x^* be an equilibrium point for $x' = F(x)$, where $F(x)$ is a system of differential equations. Let $L : U \to \mathbb{R}$ be a continuous function defined on an open set U containing x^*. Suppose further that

1. $L(x^*) = 0$ and $L(x) > 0$ if $x \neq x^*$
2. $\dfrac{dL}{dt} < 0$ in $U \setminus x^*$

then x^* is globally asymptotically stable.

Global Asymptotic Stability

Theorem

If $R_0 < 1$, then $(0,0)$ is globally asymptotically stable.

Proof:

First, let

$$\Omega = \{(i_h, i_m) \in \mathbb{R}_+^2 : 0 \leq i_h \leq 1, 0 \leq i_m \leq 1\}$$

be all possible values of i_h and i_m.

Define the *Lyapunov function* $L : \Omega \to \mathbb{R}$ by

$$L(i_h, i_m) = \gamma i_h + (\lambda_h + \alpha_h) i_m$$

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Global Asymptotic Stability

We can see that $L(i_h, i_m) = 0$ at our disease-free equilibrium point $(0, 0)$, and for all $(i_h, i_m) \in \Omega \setminus (0, 0)$, we see that $L(i_h, i_m) > 0$, then condition (1) of Lyapunov stability is satisfied.

Taking the total derivative of $L(i_h, i_m)$, we see

$$\frac{dL}{dt} = \frac{\partial L}{\partial i_h}\frac{di_h}{dt} + \frac{\partial L}{\partial i_m}\frac{di_m}{dt}$$

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Global Asymptotic Stability

Taking the partial derivatives of L and substituting in i'_h and i'_m we find

$$\begin{aligned}\frac{dL}{dt} &= \gamma\left[(\alpha_1 - i_h) - (\lambda_h + \alpha_h)i_h\right] - (\lambda_h + \alpha_h)(-\lambda_m i_m + \gamma i_h(1 - i_m)) \\ &= -[\lambda_m(\lambda_h + \alpha_h) - \alpha_1\gamma]i_m - \alpha_1\gamma i_h i_m - \gamma(\lambda_h + \alpha_h)i_h i_m.\end{aligned}$$

Since $R_0 < 1$ implies that $\lambda_m(\alpha_h + \lambda_h) > \alpha_1\gamma$, it is evident that that $\dfrac{dL}{dt} < 0$ in $\Omega \setminus (0,0)$, so we may conclude that (0, 0) is globally asymptotically stable when $R_0 < 1$.

$\square$

Global Asymptotic Stability

Taking the partial derivatives of L and substituting in i_h' and i_m' we find

$$\begin{aligned}\frac{dL}{dt} &= \gamma\left[(\alpha_1 - i_h) - (\lambda_h + \alpha_h) i_h\right] - (\lambda_h + \alpha_h)(-\lambda_m i_m + \gamma i_h (1 - i_m)) \\ &= -[\lambda_m(\lambda_h + \alpha_h) - \alpha_1\gamma] i_m - \alpha_1 \gamma i_h i_m - \gamma(\lambda_h + \alpha_h) i_h i_m.\end{aligned}$$

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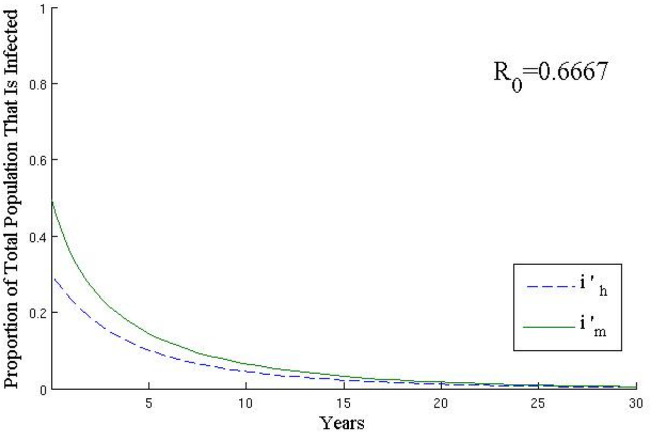
Practical Application of Theoretical Findings



Parameter Values	
λ_h	0.4
λ_m	0.6
α_1	0.4
γ	0.7
α_h	0.3

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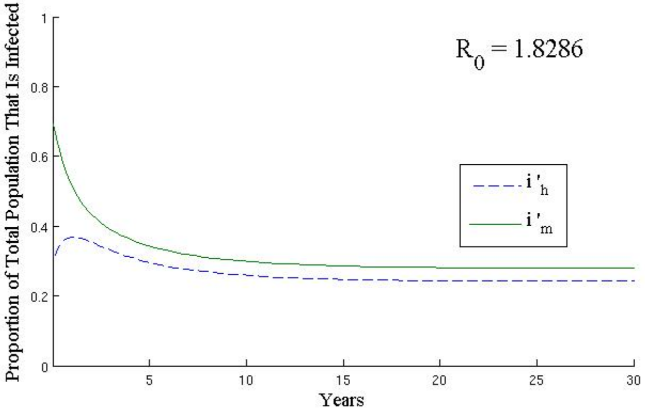

Parameter Values	
λ_h	0.4
λ_m	0.5
α_1	0.8
γ	0.8
α_h	0.3

Image by Teresa Portone