Analysis of the Spread of Malaria Disease

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SMILE 2011
Malaria

- Mosquito-borne
- Prevalent in tropical and sub-tropical regions
- 225 million cases annually
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- Differential equations
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  - Differential equations equal zero
  - The infected population is zero
- **Disease endemic equilibrium point**
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  - The infected population is greater than zero
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The number of individuals that become infected from introducing one infected into a totally susceptible population.

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then the disease persists

If the number is less than one...

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S'_h = \lambda_h N_h - \frac{\alpha S_h I_m}{N_h} - \mu_h S_h + \alpha_h I_h
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From Figure 1, we derive the following system of differential equations:

\[
\begin{align*}
S_h' &= \lambda_h N_h - \frac{\alpha S_h I_m}{N_h} - \mu_h S_h + \alpha_h I_h \\
I_h' &= \frac{\alpha S_h I_m}{N_h} - \alpha_h I_h - \mu_h I_h \\
S_m' &= \lambda_m N_m - \frac{\gamma S_m I_h}{N_h} - \mu_m S_m \\
I_m' &= \frac{\gamma S_m I_h}{N_h} - \mu_m I_m
\end{align*}
\]
Change of Variables

\[
\begin{align*}
    s_h &= \frac{S_h}{N_h}, \quad s_m = \frac{S_m}{N_m}, \quad i_h = \frac{I_h}{N_h}, \quad \text{and} \quad i_m = \frac{I_m}{N_m} \\
    s'_h &= \lambda_h (1 - s_h) + \alpha_h i_h - \alpha_1 s_h i_m \\
    i'_h &= \alpha_1 s_h i_m - \lambda_h i_h - \alpha_h i_h \\
    s'_m &= \lambda_m (1 - s_m) - \gamma s_m i_h \\
    i'_m &= \gamma s_m i_h - \lambda_m i_m
\end{align*}
\]
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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By differentiating...
- $s'_h = -i'_h$ and $s'_m = -i'_m$. 
After substituting $1 - i_h$ for $s_h$, and $1 - i_m$ for $s_m$, the system becomes

\[
\begin{align*}
    i'_h &= \alpha_1 (1 - i_h) i_m - \lambda_h i_h - \alpha_h i_h \\
    i'_m &= \gamma (1 - i_m) i_h - \lambda_m i_m,
\end{align*}
\]

which is the system that we will analyze.
To find our equilibrium points we will set our systems equal to zero and solve for $i_h$ and $i_m$.

\[
0 = \alpha_1(1 - i_h)i_m - \lambda_h i_h - \alpha_h i_h \\
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The **disease free equilibrium point**, the point at which no humans or mosquitos are infected, is $(i_h, i_m) = (0, 0)$. 
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**Equilibrium Points**
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Equilibrium Points
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.
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From this we can obtain a value of \(i_h\) in terms of \(i_m\).

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

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

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Calculating $R_0$

\[
(i^*_h, i^*_m) = \left( \frac{\alpha_1 \gamma - \lambda_m \alpha_h - \lambda_m \lambda_h}{\alpha_1 \gamma + \alpha_h \gamma + \lambda_h \gamma}, \frac{\alpha_1 \gamma - \alpha_h \lambda_m - \lambda_h \lambda_m}{\alpha_1 \lambda_m + \alpha_1 \gamma} \right)
\]

\[i^*_h, i^*_m > 0\]

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 $R_0$ is the basic reproduction number.
Calculating $R_0$

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

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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

\[ \begin{align*}
    x' &= ax + by \\
    y' &= cx + dy
\end{align*} \]

This can be expressed as

\[ x' = Ax, \]

where

\[ A = \begin{bmatrix} a & b \\ c & d \end{bmatrix} \]

and

\[ x = \begin{bmatrix} x \\ y \end{bmatrix}. \]
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\[ x = \begin{bmatrix} x \\ y \end{bmatrix}. \]
A nonzero vector \( v \) is an \textbf{eigenvector} of \( A \) and the constant \( \lambda \) is called an \textbf{eigenvalue} of \( A \) if
\[
A v = \lambda v
\]
for the system \( x' = Ax \).

**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.
A nonzero vector $v$ is an **eigenvector** of $A$ and the constant $\lambda$ is called an **eigenvalue** of $A$ if

$$Av = \lambda v$$

for the system $x' = Ax$.

**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.
A nonzero vector $v$ is an **eigenvector** of $A$ and the constant $\lambda$ is called an **eigenvalue** of $A$ if

$$Av = \lambda v$$

for the system $x' = Ax$.

**Theorem**

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

Then when $\lambda_1, \lambda_2 < 0$ the solution will stabilize.
To find the eigenvalues of $A$ solve the characteristic equation of $A$ for $\lambda$:

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

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

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

Note that $\text{tr}$ is the trace of the matrix, which is defined as the sum of the entries along main diagonal. Then

$$\lambda^2 - \text{tr}(A)\lambda + \det(A) = 0,$$
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$$\lambda^2 - \text{tr}(A)\lambda + \det(A) = 0,$$
Using the quadratic formula, the roots of our characteristic equation are given by

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

and

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

From this, we can see that

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

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From this, we can see that

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and

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When

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

**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{align*}
\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{align*}

Our final Jacobian matrix is

\[ J(i_h, i_m) = \begin{bmatrix} -\lambda_h - \alpha_1 i_m - \alpha_h & \alpha_1 (1 - i_h) \\ \gamma (1 - i_m) & -\lambda_m - \gamma i_h \end{bmatrix} \]
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\[ J(i_h, i_m) = \begin{bmatrix} -\lambda_h - \alpha_1 i_m - \alpha_h & \alpha_1 (1 - i_h) \\ \gamma (1 - i_m) & -\lambda_m - \gamma i_h \end{bmatrix}. \]
Local Asymptotic Stability

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

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

\[
\det(J(0, 0)) = \lambda_m(\lambda_h + \alpha_h) - \alpha_1 \gamma
\]

\[
\text{tr}(J(0, 0)) = -(\lambda_m + \lambda_h + \alpha_h)
\]
Local Asymptotic Stability

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\begin{align*}
\det(J(0, 0)) &= \lambda_m(\lambda_h + \alpha_h) - \alpha_1 \gamma \\
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\end{align*}
\]

\[
\text{tr}(J(0, 0)) < 0
\]

Recall

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

\[R_0 < 1 \iff \lambda_m(\lambda_h + \alpha_h) > \alpha_1 \gamma\]

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

\[R_0 > 1 \iff \lambda_m(\lambda_h + \alpha_h) < \alpha_1 \gamma\]

Then (0,0) is unstable when \( R_0 > 1 \).
Local Asymptotic Stability

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\begin{align*}
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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}
-\gamma(\alpha_1 + \lambda_h + \alpha_h) & \alpha_1(\alpha_h \gamma + \gamma \lambda_h + \alpha_h \lambda_m + \lambda_m \lambda_h) \\
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det(J(i^*_h, i^*_m)) = \gamma \alpha_1 - \lambda_m(\alpha_h + \lambda_h)
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tr(J(i^*_h, i^*_m)) = -\left(\frac{\gamma(\alpha_1 + \lambda_h + \alpha_h)}{\lambda_m + \gamma} + \frac{\alpha_1(\lambda_m + \gamma)}{\alpha_1 + \alpha_h + \lambda_h}\right)
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R_0 > 1 \implies \lambda_m (\lambda_h + \alpha_h) < \alpha_1 \gamma
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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.
Global Asymptotic 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 $L : U \rightarrow \mathbb{R}$ 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. $\frac{dL}{dt} < 0$ 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

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

**Theorem**

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

**Proof:**

First, let

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

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

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.

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

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

$$\frac{dL}{dt} = \gamma [ (\alpha_1 - i_h) - (\lambda_h + \alpha_h)i_h ] - (\lambda_h + \alpha_h)(-\lambda_m i_m + \gamma i_h (1 - i_m))$$

$$= -[\lambda_m (\lambda_h + \alpha_h) - \alpha_1 \gamma] i_m - \alpha_1 \gamma i_h i_m - \gamma (\lambda_h + \alpha_h) i_h i_m.$$ 

Since $R_0 < 1$ implies that $\lambda_m (\alpha_h + \lambda_h) > \alpha_1 \gamma$, it is evident that that

$$\frac{dL}{dt} < 0$$

in $\Omega \setminus (0,0)$, so we may conclude that $(0,0)$ is globally asymptotically stable when $R_0 < 1$. 
Global Asymptotic Stability

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

\[
\frac{dL}{dt} = \gamma \left[ (\alpha_1 - i_h) - (\lambda_h + \alpha_h)i_h \right] - (\lambda_h + \alpha_h)(-\lambda_m i_m + \gamma i_h(1 - i_m))
\]

\[
= -[\lambda_m(\lambda_h + \alpha_h) - \alpha_1 \gamma]i_m - \alpha_1 \gamma i_h i_m - \gamma(\lambda_h + \alpha_h)i_h i_m.
\]

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

Parameter Values

\[ R_0 = 0.6667 \]

<table>
<thead>
<tr>
<th>Parameter Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \lambda_h )</td>
</tr>
<tr>
<td>( \lambda_m )</td>
</tr>
<tr>
<td>( \alpha_1 )</td>
</tr>
<tr>
<td>( \gamma )</td>
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<tr>
<td>( \alpha_h )</td>
</tr>
</tbody>
</table>
Practical Application of Theoretical Findings

Parameter Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
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<tr>
<td>$\lambda_m$</td>
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<tr>
<td>$\alpha_h$</td>
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</tr>
</tbody>
</table>

$R_0 = 1.8286$
Thank you!