An Epidemiological Model of HIV

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Outline

- Introduction to mathematical epidemiology
- The HIV model
- Finding the DFE and DEE points
- The threshold parameter
- Proving local stability
- Proving global stability
- Simulations
- Additional considerations
- Future work
- Acknowledgements

Introduction

Mathematical Epidemiology

Utilizing mathematical models to determine the existence of a disease, such as HIV, in a population and the likelihood that the disease will become an endemic or go extinct.

What do we hope to gain?

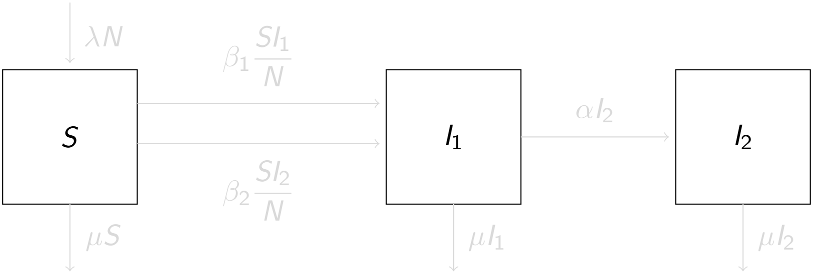
- Determine the conditions under which the HIV disease persists and dies out
- Examine the stability of these conditions

HIV/AIDS

Background on the disease

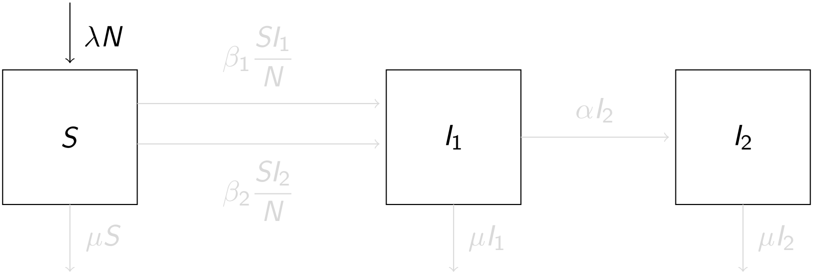
- 1981
- More than 25 million deaths
- Estimated 33.3 million people living with HIV and AIDS
- HIV progresses to AIDS - Acquired Immune Deficiency Syndrome
- Weakened immune system

The Model



- λ - birth rate
- μ - natural death rate
- β_1 - rate of infection from susceptibles to I_1
- β_2 - rate of infection from susceptibles to I_2
- α - rate of progression from HIV to AIDS

The Model



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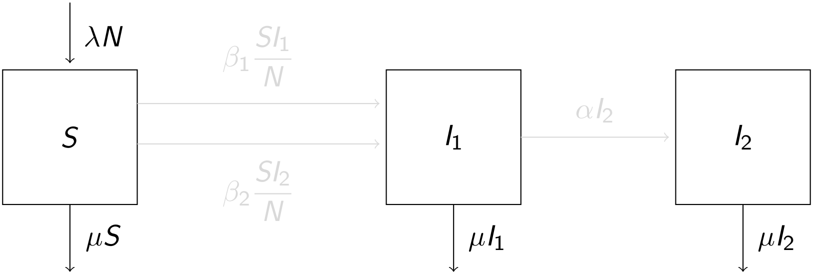

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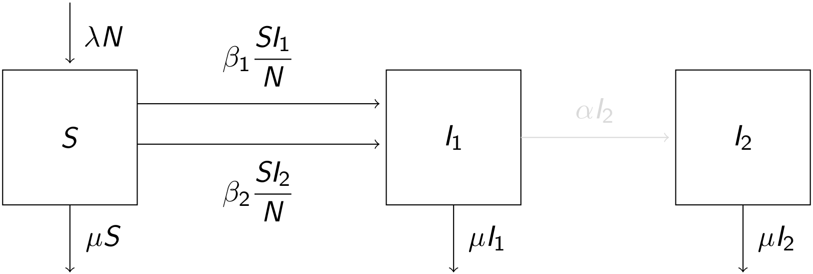

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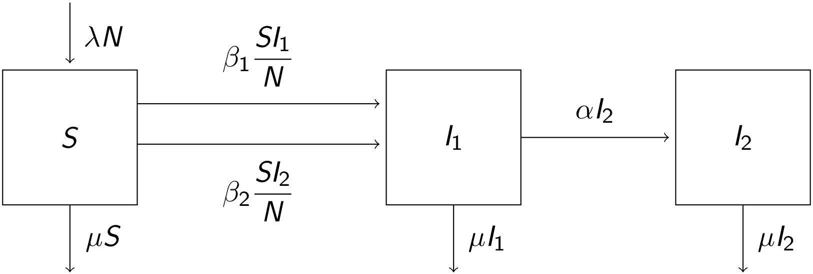

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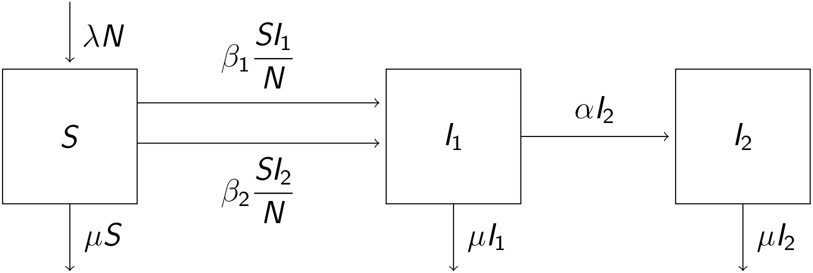
Equations from the model



$$
\begin{aligned}
\frac{dS}{dt} &= \lambda N - \mu S - \beta_1 \frac{SI_1}{N} - \beta_2 \frac{SI_2}{N} \\
\frac{dI_1}{dt} &= \beta_1 \frac{SI_1}{N} + \beta_2 \frac{SI_2}{N} - \alpha I_1 - \mu I_1 \\
\frac{dI_2}{dt} &= \alpha I_1 - \mu I_2
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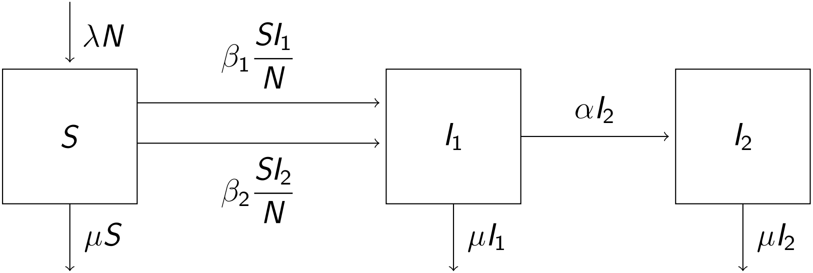
Equations from the model



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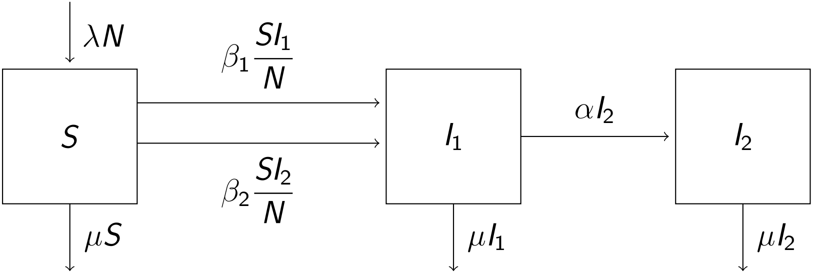

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\end{aligned}
$$

Equations from the model

A non constant population requires a change of variables.

$$s = \frac{S}{N} \quad i_1 = \frac{I_1}{N} \quad i_2 = \frac{I_2}{N}$$

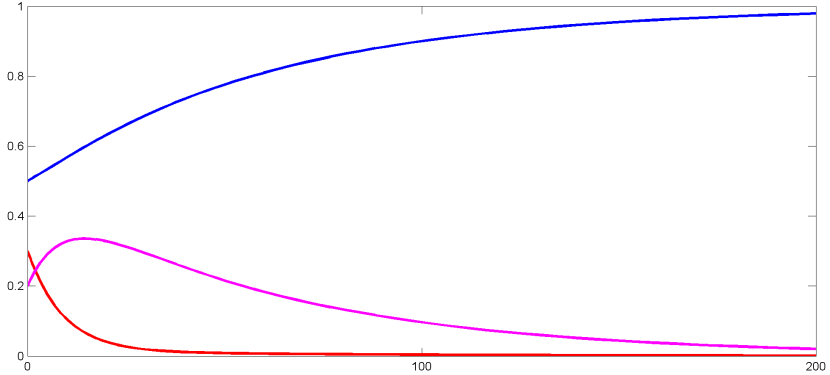
We now have three new differential equations to work with:

$$\begin{aligned}
\frac{ds}{dt} &= \frac{1}{N}\frac{dS}{dt} - \frac{1}{N}\frac{dN}{dt}s \\
&= \lambda(1-s) - \beta_1 s i_1 - \beta_2 s i_2 \\
\frac{di_1}{dt} &= \beta_1 s i_1 + \beta_2 s i_2 - (\lambda + \alpha) i_1 \\
\frac{di_2}{dt} &= \alpha i_1 - \lambda i_2
\end{aligned}$$

Finding the DFE and DEE points

The Disease Free Equilibrium

The disease free equilibrium point (DFE) is the value to which the three populations converge under the condition that there are no infected individuals within the population. $s = 1$.



The Disease Free Equilibrium Point

With no individuals moving from the susceptible class into the infected classes, $\frac{ds}{dt} = 0$ and $i_1 = i_2 = 0$.

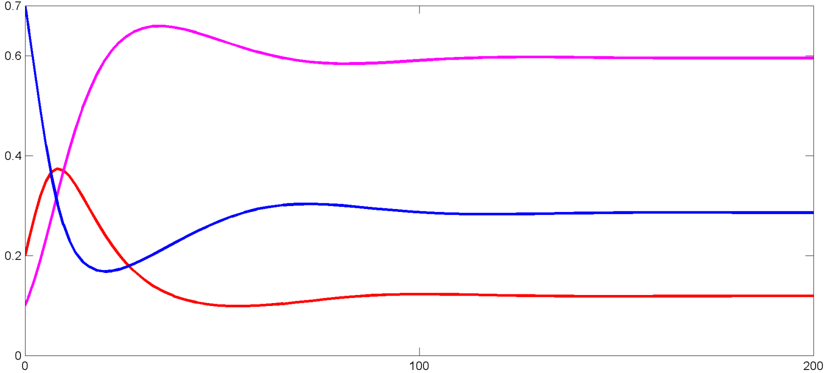
$$\begin{aligned} \frac{ds}{dt} &= \lambda(1-s) - \beta_1 s i_1 - \beta_2 s i_2 \\ &= \lambda(1-s) = 0 \\ s &= 1 \end{aligned}$$

Our DFE point is $(s, i_1, i_2) = (1, 0, 0)$.

Finding the DFE and DEE points

The Disease Endemic Equilibrium

The disease endemic equilibrium point (DEE) is the value to which the three populations converge under the condition that the disease persists.



The Disease Endemic Equilibrium Point

Solve for i_1 and i_2 by setting $\frac{di_1}{dt} = 0$ and $\frac{di_2}{dt} = 0$.

$$\frac{di_1}{dt} = \beta_1 s i_1 + \beta_2 s i_2 - (\lambda + \alpha) i_1 = 0$$

and

$$\frac{di_2}{dt} = \alpha i_1 - \lambda i_2 = 0$$

$$i_1 = \frac{\lambda}{\alpha} i_2 = \frac{-\beta_2 s i_2}{\beta_1 s - (\lambda + \alpha)}$$

The Disease Endemic Equilibrium Point

Therefore,

$$\frac{\lambda}{\alpha}\beta_1 s - (\lambda + \alpha) = -\beta_2$$

$$s^* = \frac{\lambda^2 + \alpha\lambda}{\lambda\beta_1 + \alpha\beta_2}$$

Using

$$\frac{ds}{dt} = \lambda(1 - s) - \beta_1 s i_1 - \beta_2 s i_2$$

$$i_1{}^* = \frac{\lambda}{\lambda + \alpha} - \frac{\lambda^2}{\lambda\beta_1 + \alpha\beta_2} \qquad i_2{}^* = \frac{\alpha}{\lambda + \alpha} - \frac{\lambda\alpha}{\lambda\beta_1 + \alpha\beta_2}$$

The threshold parameter, R_0

What is the threshold parameter?

R_0 is the average number of secondary cases that a single infected individual produces when introduced into a completely susceptible population.

Its implications

When $R_0 < 1$, the disease goes extinct. When $R_0 > 1$, the disease persists.

The threshold parameter, R_0

To find R_0, we must look at the i_1 from the DEE point. The DEE point means that the disease exists and there are members of the population in the i_1 class.

$$i_1 = \frac{\lambda}{\lambda + \alpha} - \frac{\lambda^2}{\lambda\beta_1 + \alpha\beta_2} > 0$$

$$\frac{\lambda}{\lambda + \alpha} > \frac{\lambda^2}{\lambda\beta_1 + \alpha\beta_2}$$

$$R_0 = \frac{\lambda\beta_1 + \alpha\beta_2}{\lambda(\lambda + \alpha)} > 1$$

Local stability of our equilibrium points

The Jacobian matrix

$$f(i_1, i_2) := \frac{di_1}{dt} = \beta_1 s i_1 + \beta_2 s i_2 - (\lambda + \alpha) i_1$$
$$= \beta_1 (1 - i_1 - i_2) i_1 + \beta_2 (1 - i_1 - i_2) i_2 - (\lambda + \alpha) i_1$$

$$g(i_1, i_2) := \frac{di_2}{dt} = \alpha i_1 - \lambda i_2$$

$$J = \begin{bmatrix} \frac{\delta f}{\delta i_1} & \frac{\delta f}{\delta i_2} \\ \frac{\delta g}{\delta i_1} & \frac{\delta g}{\delta i_2} \end{bmatrix} = \begin{bmatrix} \beta_1(1 - i_1 - i_2) - \beta_1 i_1 - (\lambda + \alpha) & \beta_2(1 - i_1 - i_2) - i_1\beta_1 - i_2\beta_2 \\ \alpha & -\lambda \end{bmatrix}$$

Local stability

Using the trace and determinant

- Eigenvalues of the 2x2 matrix are both negative.
- $Tr(J) < 0$ and $Det(J) > 0$
- A sink is produced - implies locally asymptotically stable point.

Local stability - the DFE point

$$J(0,0) = \begin{bmatrix} \frac{\delta f}{\delta i_1}(0,0) & \frac{\delta f}{\delta i_2}(0,0) \\ \frac{\delta g}{\delta i_1}(0,0) & \frac{\delta g}{\delta i_2}(0,0) \end{bmatrix} = \begin{bmatrix} \beta_1 - \lambda - \alpha & \beta_2 \\ \alpha & -\lambda \end{bmatrix}$$

$$Tr(J) = -\lambda - \alpha + \beta_1 - \lambda$$

$$Det(J) = -\lambda(\beta_1 - \lambda - \alpha) - \alpha\beta_2 = -\lambda\beta_1 - \alpha\beta_2 + \lambda(\lambda + \alpha)$$

Local stability - the DFE point

Because we know that

$$R_0 = \frac{\lambda\beta_1 + \alpha\beta_2}{\lambda(\lambda + \alpha)} < 1$$

for the disease to go extinct. Combining this with the $Tr(J)$ and $Det(J)$,

$$Tr(J) = -\lambda - \alpha + \beta_1 - \lambda < -\beta_1 - \frac{\alpha\beta_2}{\lambda} + \beta_1 - \lambda < 0$$

$$Det(J) = -\lambda\beta_1 - \alpha\beta_2 + \lambda(\lambda + \alpha) > 0$$

Therefore, our DFE point is locally asymptotically stable.

Local stability - the DEE point

The new Jacobian

$$J(i_1{}^*, i_2{}^*) = \begin{bmatrix} \beta_1(1 - i_1{}^* - i_2{}^*) - \beta_1 i_1{}^* & \beta_2(1 - i_1{}^* - i_2{}^*) \\ -(\lambda + \alpha) & -i_1{}^*\beta_1 - i_2{}^*\beta_2 \\ & \\ \alpha & -\lambda \end{bmatrix}$$

Recall

$i_1{}^* = \dfrac{\lambda}{\lambda + \alpha} - \dfrac{\lambda^2}{\lambda\beta_1 + \alpha\beta_2}$ and $i_2{}^* = \dfrac{\alpha}{\lambda + \alpha} - \dfrac{\alpha\lambda}{\lambda\beta_1 + \alpha\beta_2}$

$$R_0 = \frac{\lambda\beta_1 + \alpha\beta_2}{\lambda(\lambda + \alpha)} > 1$$

Local stability - the DEE point

$$R_0 = \frac{\lambda\beta_1 + \alpha\beta_2}{\lambda(\lambda+\alpha)} > 1$$

The trace

$$\begin{aligned}
T &= \beta_1\lambda\left(\frac{\lambda+\alpha}{\lambda\beta_1+\alpha\beta_2}\right) - (\lambda+\alpha) - \beta_1\lambda\left(\frac{1}{\lambda+\alpha} - \frac{\lambda}{\lambda\beta_1+\alpha\beta_2} - \lambda\right) \\
&= (\lambda+\alpha)^2\left[\frac{\beta_1\lambda}{(\lambda\beta_1+\alpha\beta_2)(\lambda+\alpha)} - \frac{(\lambda\beta_1+\alpha\beta_2)}{(\lambda\beta_1+\alpha\beta_2)(\lambda+\alpha)}\right] \\
&- \beta_1\lambda\left[\frac{(\lambda\beta_1+\alpha\beta_2) - \lambda(\lambda+\alpha)}{(\lambda\beta_1+\alpha\beta_2)(\lambda+\alpha)}\right] - \lambda < 0
\end{aligned}$$

Local stability - the DEE point

The determinant

$$\begin{aligned} D &= \lambda\beta_1\left(\frac{\lambda}{\lambda+\alpha} - \frac{\lambda^2}{\lambda\beta_1+\alpha\beta_2}\right) \\ &- \lambda\left[1 - \left(\frac{\lambda}{\lambda+\alpha} - \frac{\lambda^2}{\lambda\beta_1+\alpha\beta_2}\right) - \left(\frac{\alpha}{\lambda+\alpha}\frac{\alpha\lambda}{\lambda\beta_1+\alpha\beta_2}\right)\right] \\ &= \lambda\left[\frac{\lambda(\lambda+\alpha)}{\lambda\beta_1+\alpha\beta_2}\right] - \alpha\beta_2\left[\frac{-\lambda(\lambda+\alpha)}{\lambda\beta_1+\alpha\beta_2}\right] > 0 \end{aligned}$$

Therefore, our DEE point is locally asymptotically stable.

Global stability

Lyapunov Stability

Theorem

Let x^* be an equilibrium point for $X' = f(x)$ and let $L : U \to \mathbb{R}$ be a differentiable function defined on an open set U containing x^*. Suppose further that:

(i) $L(x^*) = 0$ *and* $L(x) > 0$ *if* $x \neq x^*$;

(ii) $\dfrac{dL}{dt} < 0$ *in* $U \backslash x^*$

Then x^* is globally asymptotically stable.

Global stability - the DFE point

(i) $L(x^*) = 0$ and $L(x) > 0$ if $x \neq x^*$;

(ii) $\frac{dL}{dt} < 0$ in $U \backslash x^*$

Stability of the DFE point

$$L(i_1, i_2) = i_1 + \frac{\beta_2}{\lambda} i_2$$

$$\frac{dL}{dt} = \frac{di_1}{dt} + \frac{\beta_2}{\lambda}\frac{di_2}{dt}$$

So for the DFE point, $(0, 0)$:

$$L(0, 0) = 0$$

Global stability - the DFE point

Because $R_0 < 1$, we know:

$$\frac{dL}{dt} = i_1(\beta_1(1 - i_1 - i_2) - (\lambda + \alpha)) + \beta_2(1 - i_1 - i_2)i_2 + \frac{\beta_2 \alpha i_1}{\lambda} - \beta_2 i_2$$

$$< i_1(\beta_1 - (\lambda + \alpha)) + \beta_2(1 - i_1 - i_2)i_2 + \frac{\beta_2 \alpha i_1}{\lambda} - \beta_2 i_2$$

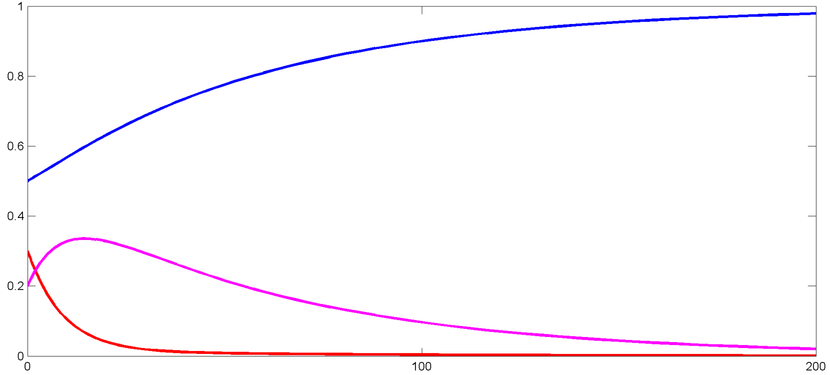
$$= \frac{i_1}{\lambda}(\beta_1 \lambda + \alpha \beta_2 - (\lambda + \alpha)\lambda) + \beta_2(1 - i_1 - i_2)i_2 + \frac{\beta_2 \alpha i_1}{\lambda} - \beta_2 i_2 - \frac{\beta_2 \alpha i_1}{\lambda}$$

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

We can conclude that our DFE point is globally stable.

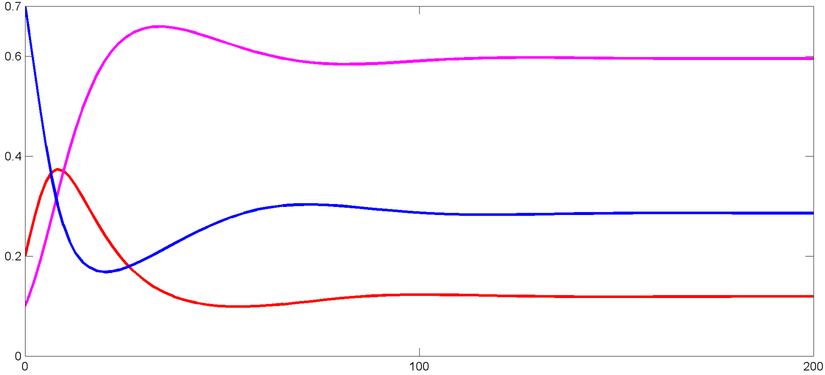
Simulations using MatLab

Disease Free



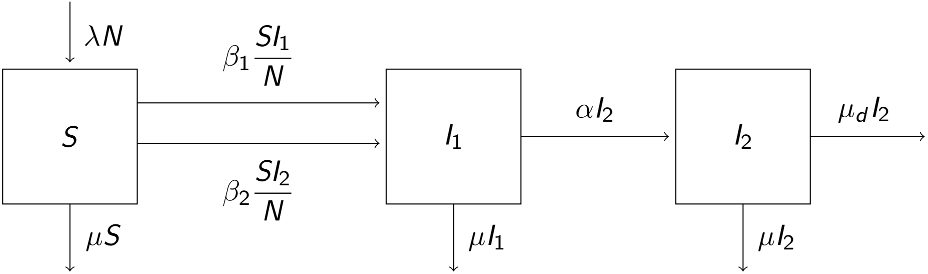
Simulations using MatLab

Disease Endemic



Additional Considerations

The revised model



- μ_d is the death rate of people who have AIDS.

Future work

- Prove the global asymptotic stability for the endemic point.
- Consider the additional intermediate stage of the disease.
- Expand the model for multiple populations.

Acknowledgments

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The End - Questions?