Modelling Mosquito-Bourne Control: Insecticide-Treated Nets and Immunity

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Overview

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Problem Statement

How do widespread ITN interventions impact long-term mosquito-borne disease transmission dynamics and immunity development, and what role can complementary interventions, such as vaccines, play in mitigating the trade-offs between reduced exposure and immunity buildup?

Introduction

- In tropical parts of the world, malaria is a life-threatening disease that remains one of the most widespread human diseases.
- In 2018, there were 228 million cases and 405,000 deaths, while in 2022, the cases rose to 249 million with 608,000 deaths due to malaria-related causes.
- It is a parasite-caused disease by multiple species of the *Plasmodium* genus type.
- Humans contract malaria when a female Anopheles mosquito bites them while they are consuming the blood required for egg formation. [8]

Mosquito Life Cycle

- Adult male mosquitoes feed on flower nectar and plant juices; they live for about 1 to 2 weeks.
- Adult female mosquitoes feed on blood to develop eggs; they can live for a few weeks to 2 months.

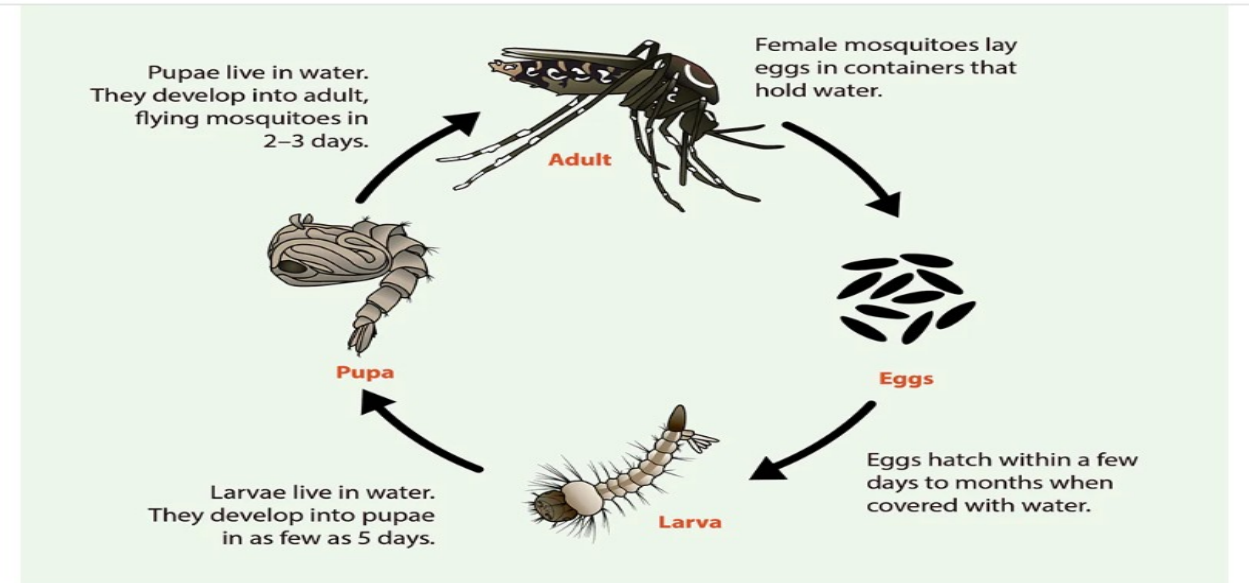


Figure: Life cycle of a mosquito

- Numerous mathematical models have been developed to understand the transmission dynamics of malaria and its control measures. [4, 6, 2]
- Insecticide-treated nets (ITNs) are highly used in reducing human-mosquito interactions. However, the effectiveness of these nets has been inconsistent, as many people either neglect to repair holes, do not use them regularly, or use them for activities such as fishing.

Figure: Mosquito net

Transfer Diagram

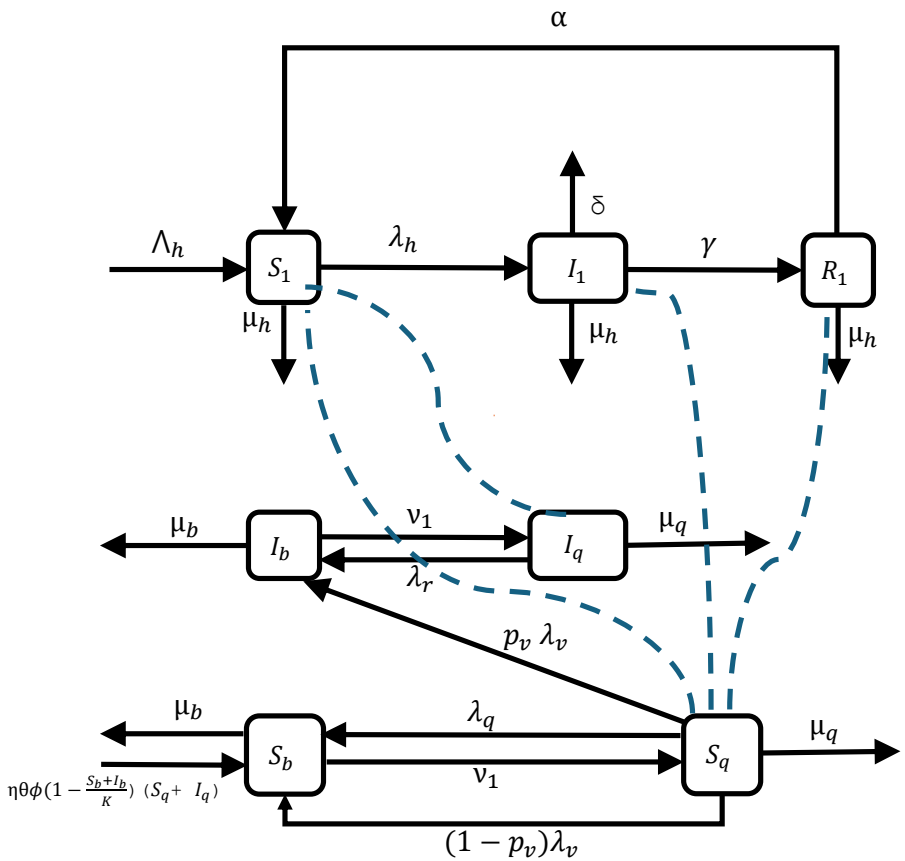


Figure: Flow diagram of the simple model

Model variables

Variables	**Definition**
S	Susceptible individuals
I	Infected individuals
R	Recovered individuals
S_b	Susceptible mosquitoes in breeding sites
I_b	Infected mosquitoes in breeding sites
S_q	Susceptible questing mosquitoes
I_q	Infected questing mosquitoes

Table: Model variables

Model Equations

The system of equations for the model is [4, 5],

$$
\begin{cases}
\dot{S} = \Lambda - \dfrac{p\beta(b)SI_q}{N_h} - \mu_h S + \alpha R, \\
\dot{I} = \dfrac{p\beta(b)SI_q}{N_h} - (\mu_h + \gamma + \delta)I, \\
\dot{R} = \gamma I - (\mu_h + \alpha)R, \\
\dot{S}_b = \eta\theta\phi(S_q + I_q)\left(1 - \dfrac{S_q + I_q}{K}\right) - (\mu_b + \nu_1)S_b \\
\qquad + \dfrac{\beta(b)S_q(\hat{a}_1 S + \hat{b}_1 R)}{N_h} + \dfrac{(1 - p_v)\beta(b)IS_q}{N_h}, \\
\dot{I}_b = \dfrac{p_v\beta(b)IS_q}{N_h} - (\mu_b + \nu_2)I_b + \dfrac{\beta(b)I_q(S + aI_1 + b_1 R)}{N_h}, \\
\dot{S}_q = \nu_1 S_b - \mu_q(b)S_q - \dfrac{\beta(b)S_q(\hat{a}_1 S + I + \hat{b}_1 R)}{N_h}, \\
\dot{I}_q = \nu_2 I_b - \mu_q(b)I_q - \dfrac{\beta(b)I_q(S + a_1 I + b_1 R)}{N_h}, \\
\dot{I}_m = \dfrac{\frac{\sigma\beta(b)pI_v}{N_h}S_h}{c + \frac{\beta(b)pI_v}{N_h}S_h} - \left(\omega + \dfrac{\delta I_h}{N_h} + \mu_h\right)I_m,
\end{cases}
\tag{1}
$$

with $\beta(b) = \beta_M - b(\beta_M - \beta_m)$ and $\mu = \mu_0 + \mu_1 b$.

This system of equations is subject to initial conditions:

$$S(0) = S^0 \geq 0, \quad I(0) = I^0 \geq 0, \quad R(0) = R^0 \geq 0,$$
$$S_b(0) = S_b^0 \geq 0, \quad I_b(0) = I_b^0 \geq 0, \quad S_q(0) = S_q^0 \geq 0, \quad I_q(0) = I_q^0 \geq 0.$$

Model parameters

Parameter	Epidemiological interpretation
Λ_1	Recruitment constant in S.
b	Efficacy of bed nets used.
β	Interactions function between susceptible in S and infected mosquitoes.
β_M	Maximum interaction rate between susceptible in S and infected mosquitoes.
β_m	Minimum interaction rate between susceptible in S and infected mosquitoes.
$a_1(\hat{a}_1)$	Modification interaction parameter between mosquitoes in $I_q(S_q)$ and humans in $I(S)$ as compared to β.
$b_1(\hat{b}_1)$	Modification interaction parameter between mosquitoes in $I_q(S_q)$ and humans in R as compared to β.
ν_1	Mosquitoes questing rate in $S_b(I_b)$.
$\mu(\mu_b)$	Natural mortality rate of humans (mosquitoes in breething sites).
μ_q	Natural mortality rate of questing mosquitoes.
θ	Number of eggs laid by a female mosquitoes.
η	Probability of eggs surviving from the egg to the adult stage.
ϕ	Rate at which an egg develops to an adult.

Model parameters

Parameter	Epidemiological interpretation
p_v	Probability for mosquitoes to be infected after biting.
p	Probability for humans to be infected after being bitten.
K	Carrying capacity of breeding sites.
a	Immunity efficacy of individuals .
γ	Recovery rate .
δ	Death due to disease.
α	Immunity wasting rate after recovery in R.

Modeling Mosquito Life Cycle

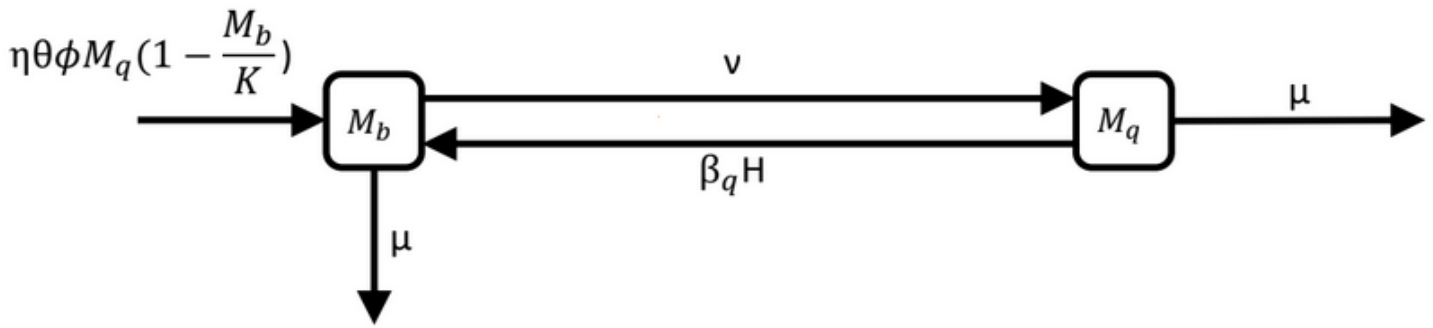


Figure: Mosquito life cycle

Dynamics of mosquitoes

The system of equations for the dynamics of mosquitoes is [4],

$$\begin{cases} \dot{M}_b = \eta\theta\phi M_q \left(1 - \frac{M_b}{K}\right) - (\mu + \nu)M_b + \beta_q M_q H, \\ \dot{M}_q = \nu M_b - \mu M_q - \beta_q M_q H. \end{cases} \tag{2}$$

Variable	Definition
M_b	Mosquitoes in breeding sites
M_q	Mosquitoes which are questing
H	Human population (blood supply)

Table: Model variables for mosquito life cycle [1]

Well-posedness of the model

Theorem

The model is a dynamical system on the biologically feasible region Ω defined as:

$$\Omega = \Omega_h \times \Omega_v \subset \mathbb{R}^3_+ \times \mathbb{R}^4_+,$$

where:

$$\Omega_h = \{(S_1, E_1, I_1) \in \mathbb{R}^3_+ \mid N_h \leq \frac{\Lambda_1}{\mu_h}\},$$

$$\Omega_v = \{(S_b, I_b, S_q, I_q) \in \mathbb{R}^4_+ \mid S_q + I_q \leq K,\ N_v \leq \frac{\eta\theta\phi K}{\mu_v}\}$$

Thus, from the theorem, our model admits a unique global solution for non-negative initial conditions.

Disease-Free Equilibrium

To find the Disease-Free Equilibrium (DFE) of the system described, we assume no individuals in the infected classes (I_1, I_b, I_q) and analyze the steady state where all derivatives in Equation (2) are zero. The disease-free equilibrium of the system given by (2) is:

$$E_0 = (S_1^0, I_1^0, R_1^0, S_b^0, S_q^0, I_b^0, I_q^0)$$

where

$$S_1^0 = \frac{\Lambda_1}{\mu_h}, \qquad I_q^0 = 0$$

$$I_1^0 = 0, \qquad I_b^0 = 0$$

$$R_1^0 = 0,$$

$$S_b^0 = \frac{(\eta\theta\phi + \beta(b)\hat{a_1})\, S_q^0}{(\mu_b + \nu_1) + \frac{\eta\theta\phi S_q^0}{K}},$$

$$S_q^0 = \frac{K\,(\mu_b + \nu_1)}{\eta\theta\phi}\left(\frac{\nu_1\,(\eta\theta\phi + \beta(b)\hat{a_1})}{(\mu_q(b) + \beta(b)\hat{a_1})\,(\mu_b + \nu_1)} - 1\right).$$

The Basic Reproduction Number $\mathcal{R}_0$

Definition: Basic Reproduction Number [7]

The basic reproduction number, $\mathcal{R}_0$, is the average number of cases generated by one infected introduced into a completely susceptible population during all its infectious period.

Let $\boldsymbol{x}$ denote the infected compartments, that is,

$$\boldsymbol{x} = (I_1, I_b, I_q).$$

The infected compartments of the dynamical system can be written of the form,

$$\frac{d\boldsymbol{x}}{dt} = \mathcal{F} - \mathcal{V}, \tag{3}$$

where:

- $\mathcal{F}$ is the rate at which the infected compartments population sizes increase due to secondary infections.
- $\mathcal{V}$ the rate of disease transfer out of the disease compartments.

Linearising the system about the disease-free equilibrium, $(S_1^0, R_1^0, S_b^0, S_q^0)$ gives the linear system (of the infected compartments),

$$\frac{d\boldsymbol{x}}{dt} = (F - V)\boldsymbol{x}, \tag{4}$$

where,

$$F = \begin{pmatrix} 0 & 0 & p\beta(b) \\ \frac{p_v\beta(b)S_q^0}{N_1^0} & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \mu_h + \gamma + \delta & 0 & 0 \\ 0 & \mu_b(b) + \nu_2 & -\beta(b) \\ 0 & -\nu_2 & \mu_b(b) + \beta(b) \end{pmatrix} \tag{5}$$

The next generation matrix, K, is calculated as follows,

$$K = FV^{-1}.$$

Theorem [7]:

The basic reproduction number, $\mathcal{R}_0$, with appropriate coefficients is,

$$\mathcal{R}_0 = \rho(K) = \sqrt{\frac{p_v\ [\beta(b)]^2\ S_q^0\ p\ \nu_2}{N_1^0(\mu+\gamma+\delta)A_1}}, \tag{6}$$

where $\rho(K)$ is the spectral radius of the next generation matrix, K.

More specifically [3],

$$\mathcal{R}_0 = \sqrt{\mathcal{R}_{0h}\mathcal{R}_{0v}}, \tag{7}$$

where,

- $\mathcal{R}_{0h}$ is the expected number of humans infected by 1 infected mosquito.
- $\mathcal{R}_{0v}$ is the expected number of mosquitoes infected by 1 infected human.

$$\mathcal{R}_{0v} = \frac{p_v\beta(b)}{\mu+\gamma+\delta} \quad \text{and} \quad \mathcal{R}_{0h} = \frac{\beta(b)\ S_q^0\ p\ \nu_2}{N_1^0 A_1}.$$

Local Stability

Theorem

The disease free-equilibrium is locally asymptotically stable when the basic reproduction number $R_0 < 1$, and unstable for $R_0 > 1$ (Van den Driessche, P. and Watmough, J., 2002) provided that

$$\frac{\nu_1 \left(\eta\theta\phi + \beta(b)\hat{a_1}\right)}{\left(\mu_q(b) + \beta(b)\hat{a_1}\right)\left(\mu_b + \nu_1\right)} > 1$$

Conclusions based on R_0 Stability of DFE:

- $R_0 < 1$: The DFE is locally asymptotically stable, meaning that the infection will die out without further interventions.
- $R_0 > 1$: The DFE is unstable meaning that the disease may persist.

Numerical Simulations

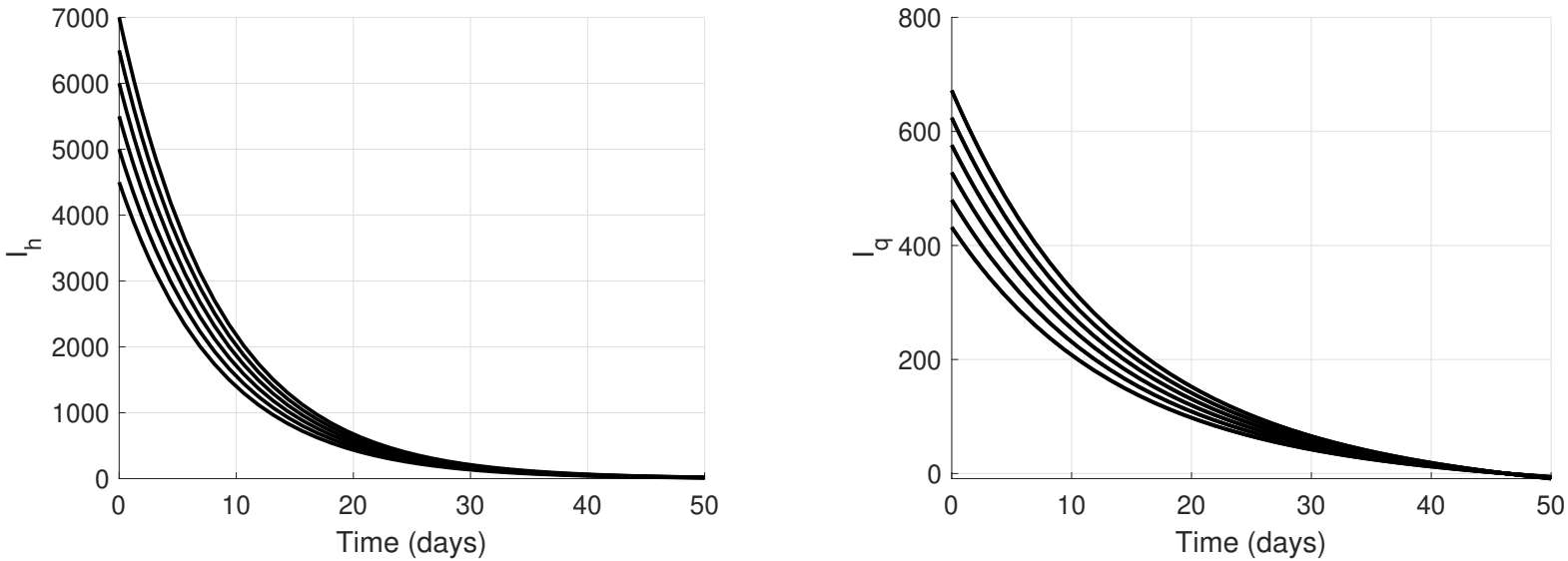
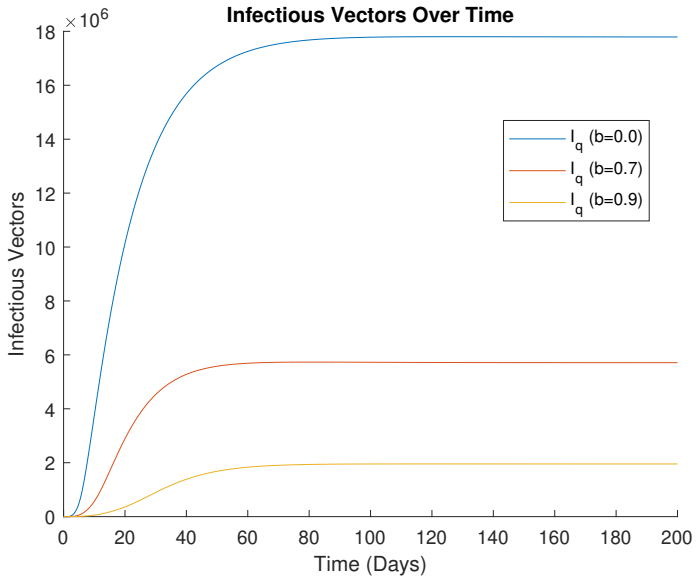
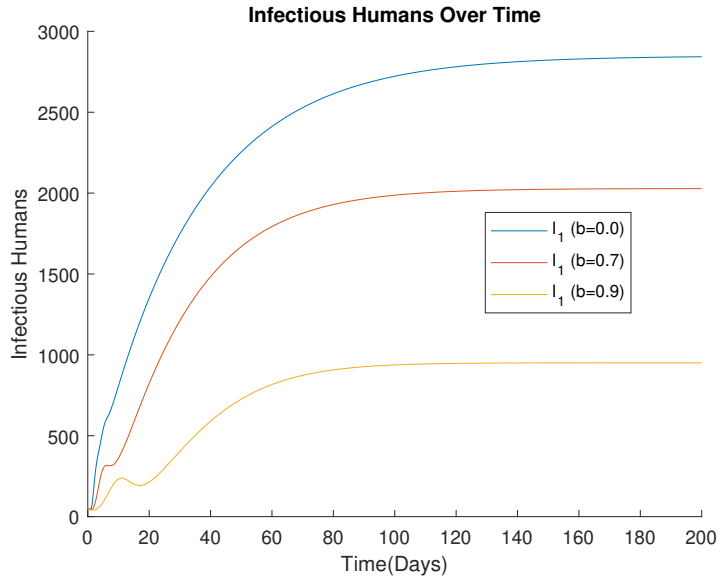


Figure: $\mathcal{R}_0 < 1$

Numerical Simulations



((a)) Infectious vectors



((b)) Infectious human

Figure: Efficacy of bed nets

Numerical Simulations

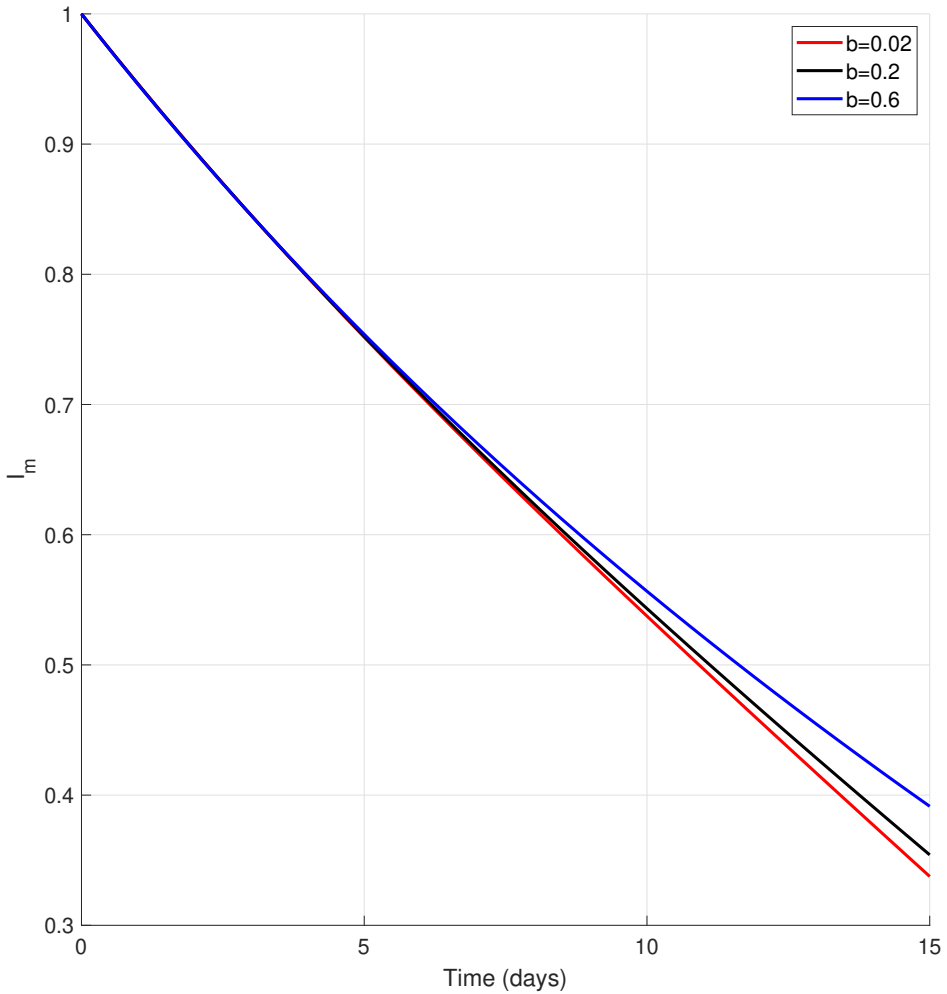


Figure: Immunity waning

Conclusion and future work

- The greatest reductions in I_h and I_v are observed when bed nets are more used. Meanwhile, immunity decreases as bed net use increases.
- Fit the model to the real cases in one country.
- Develop an in-depth mathematical analysis of the work.
- Incorporate the influence of immunity waning on the dynamics of malaria.

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