Statics and Dynamics of Malaria Transmission in Plasmodium Falciparum Carriers

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Abstract:

The present paper explores a simple dynamic model from which we review the classic formulae in malaria epidemiology that relate entomological parameters to malaria transmission. In addition, we document the dynamics of malaria, illustrating the impact of control strategies and how the bites per mosquito have a larger effect on transmission intensity than the mosquito mortality, the ratio of mosquitoes to humans, or the transmission efficiency.

The model has been built following the System Dynamics methodology, explicitly representing the variables, the feedbacks and the nonlinearities, i.e. the structure that governs the dynamics of the disease. In this sense, the paper offers a new way to obtain the most representative malaria indicators derived from stock-and-flow diagrams that encompass the causal relationships that exist between the attributes of such a system.

Based on the obtained formulae from the human and mosquito sectors, we are able to eliminate three degrees of freedom, allowing us to calculate the temporal steady state relationship between Plasmodium falciparum prevalence in humans and mosquitoes.

The model is generic in nature and may be parameterized to portray a wide variety of locations, different malaria parasites, vector species, and to cater for seasonality.

Given that the model includes the principle mechanisms of malaria transmission, it acts as a foundation for simulations that represent the dynamics between humans and mosquitoes. Such model has been developed based on a number of simplifying assumptions. To the extent possible, the validity of the model under these assumptions has been analyzed by way of mathematic equations.

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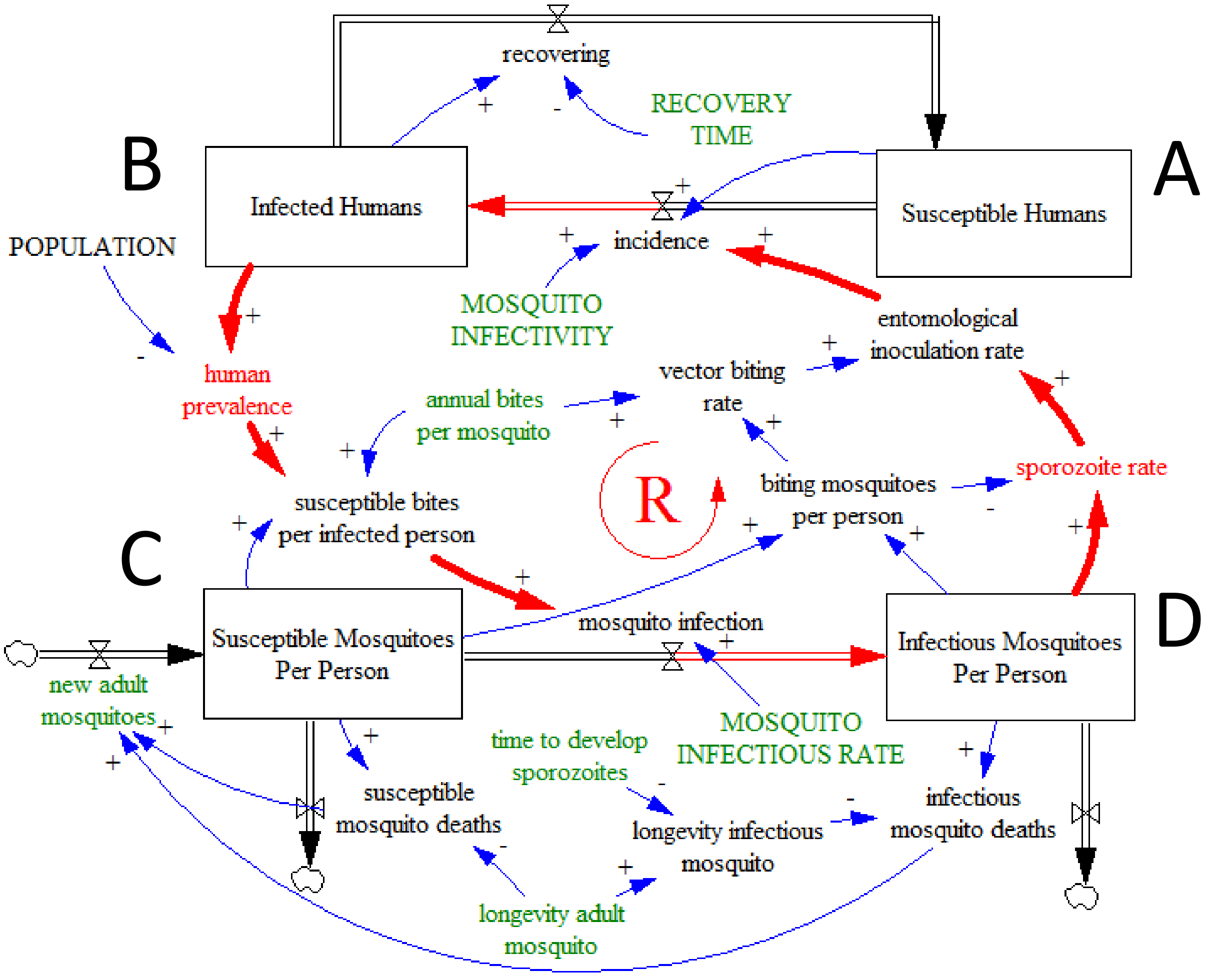
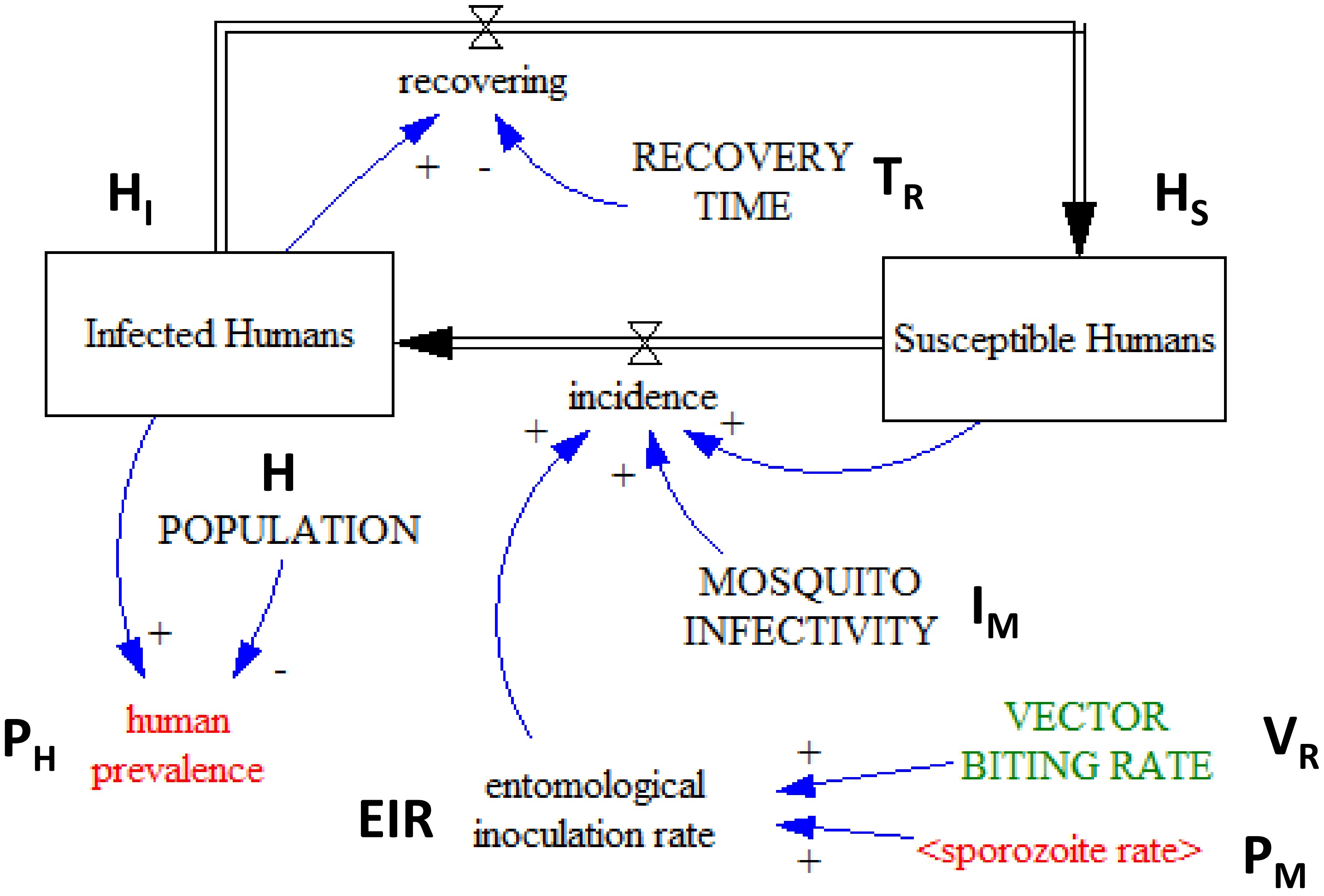
1. Review formulae in malaria epidemiology

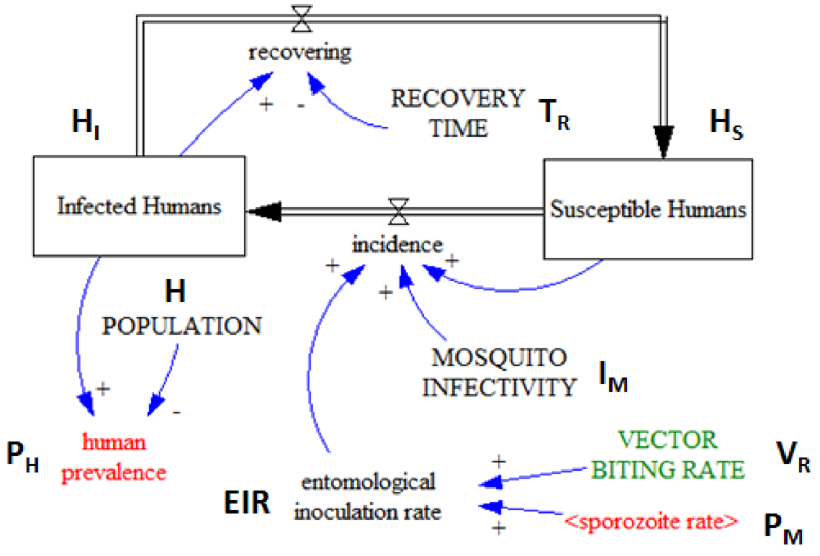
Human Sector

Mosquito Sector



Human sector





$$\boxed{EIR = V_R \cdot P_M}$$

Eq. 1

$$\text{Recovering} = \frac{H_I}{T_R} = \frac{H \cdot P_H}{T_R}$$

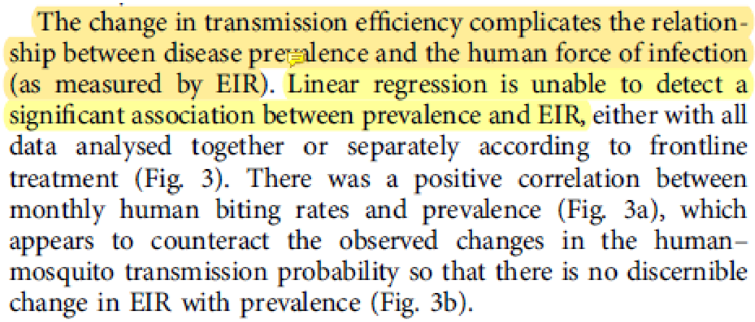
$$\text{Incidence} = H_S \cdot EIR \cdot I_M = H \cdot (1 - P_H) \cdot EIR \cdot I_M$$

$$\text{Recovering} = \text{Incidence} \rightarrow \frac{H \cdot P_H}{T_R} = H \cdot (1 - P_H) \cdot EIR \cdot I_M \Rightarrow \frac{P_H}{T_R} = (1 - P_H) \cdot EIR \cdot I_M \Rightarrow$$

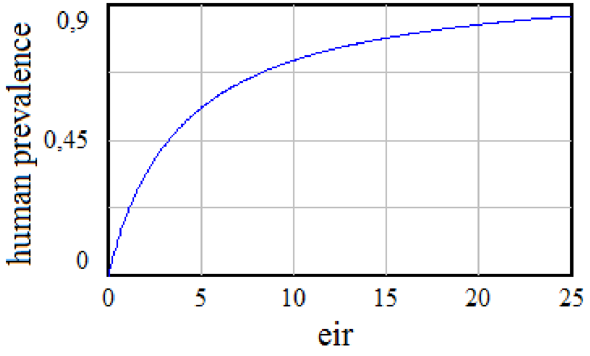
$$\Rightarrow P_H = (1 - P_H) \cdot EIR \cdot I_M \cdot T_R \Rightarrow P_H + P_H \cdot EIR \cdot I_M \cdot T_R = EIR \cdot I_M \cdot T_R \Rightarrow \left[\boxed{P_H = \frac{EIR \cdot I_M \cdot T_R}{1 + EIR \cdot I_M \cdot T_R}} \right]$$

Eq. 2

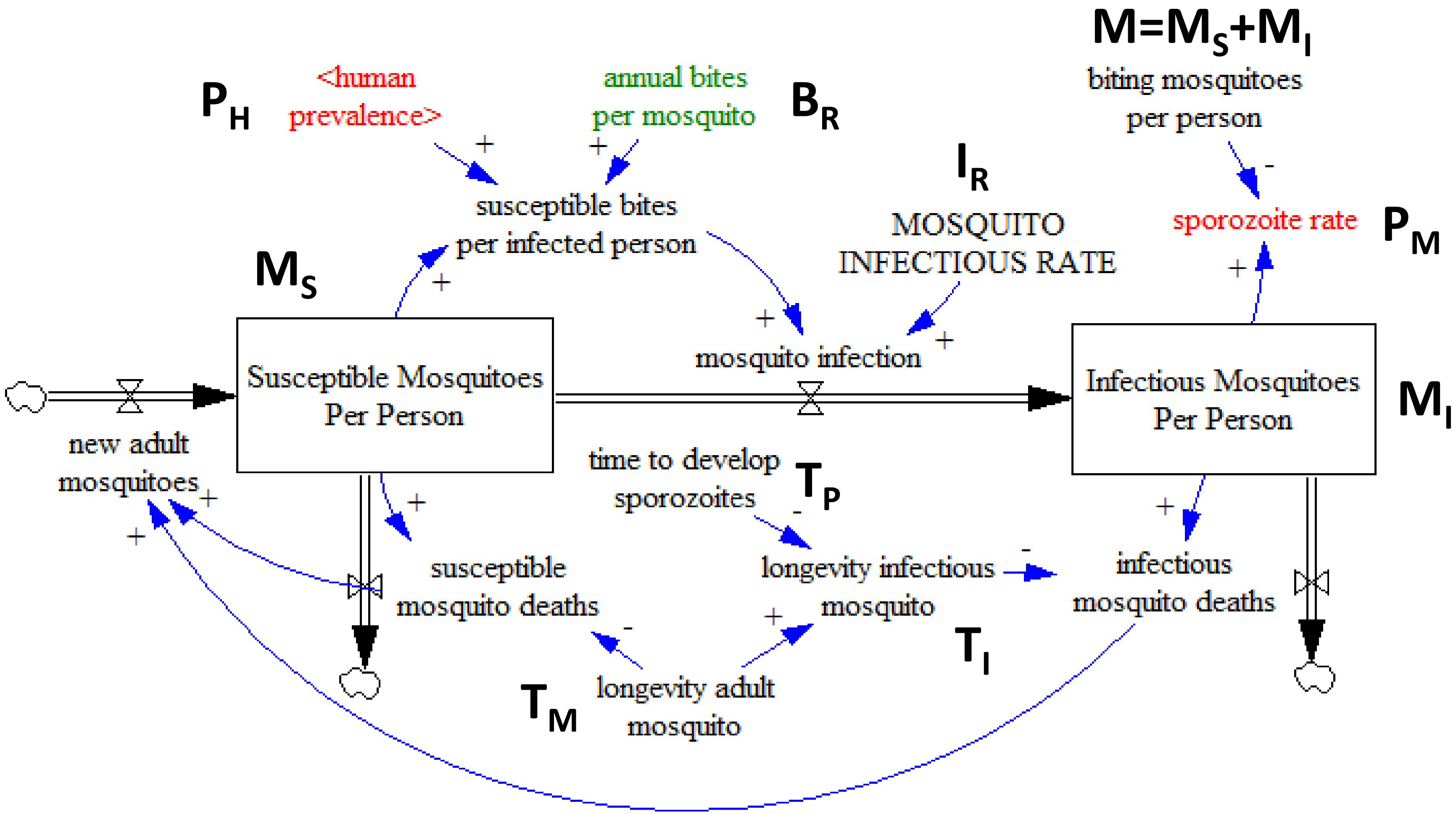
Thomas S. Churcher. Human-to-mosquito transmission efficiency increases as malaria is controlled



The change in transmission efficiency complicates the relationship between disease prevalence and the human force of infection (as measured by EIR). Linear regression is unable to detect a significant association between prevalence and EIR, either with all data analysed together or separately according to frontline treatment (Fig. 3). There was a positive correlation between monthly human biting rates and prevalence (Fig. 3a), which appears to counteract the observed changes in the human–mosquito transmission probability so that there is no discernible change in EIR with prevalence (Fig. 3b).



Mosquito sector

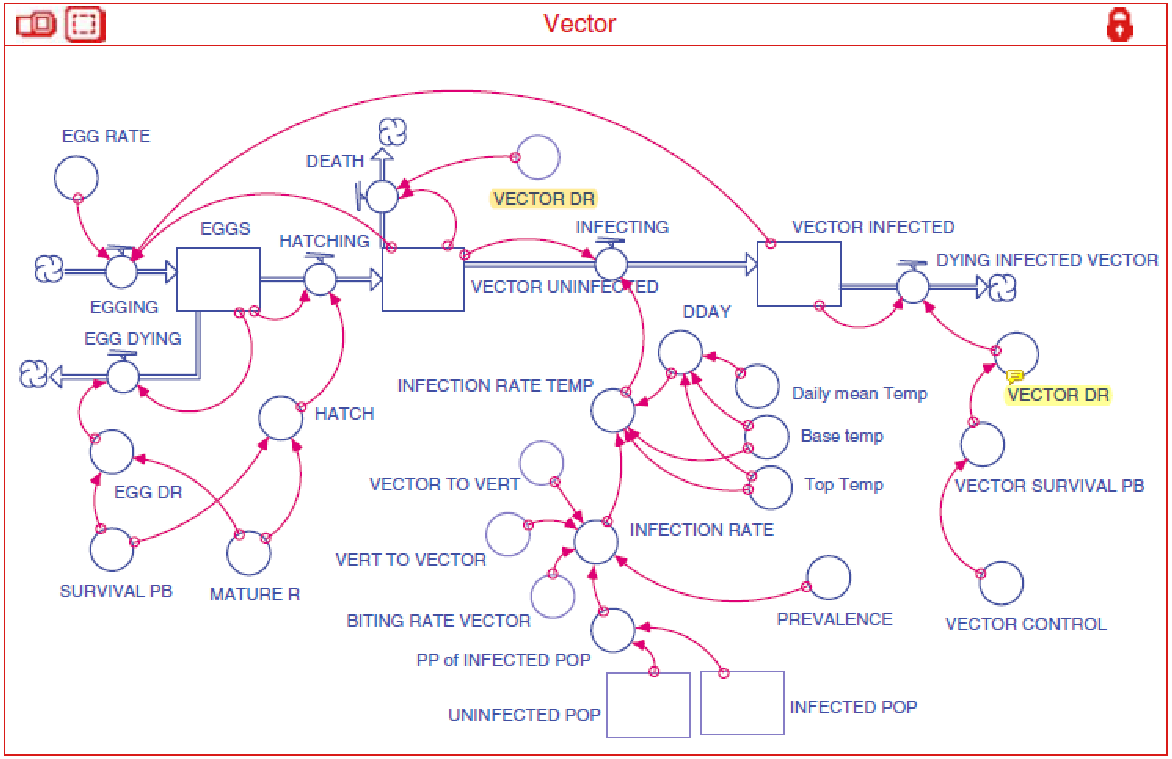


Mosquito sector

Other models use the same mortality for both uninfected and infected mosquitoes:

1. **Dynamic Modeling of Diseases and Pests.** Bruce Hannon and Matthias Ruth

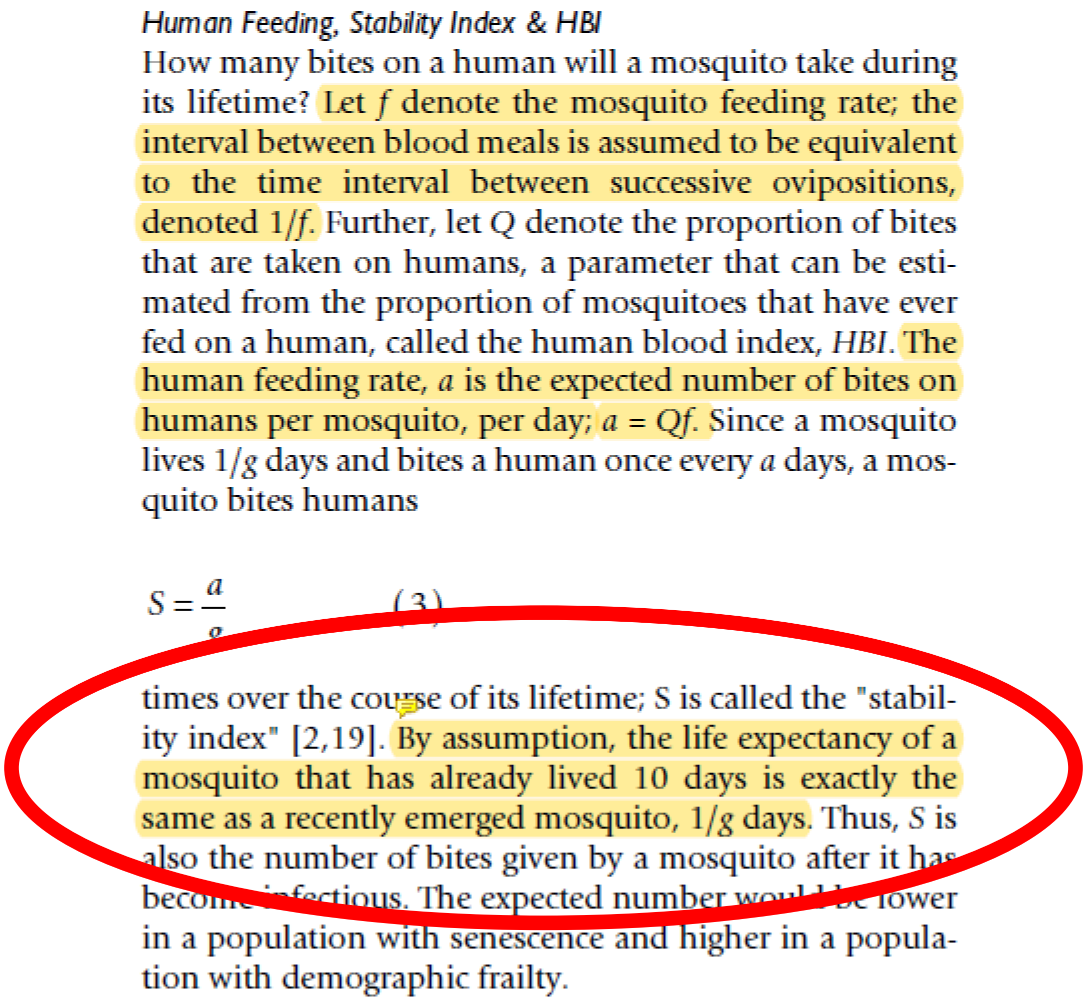
4.1 Malaria 67



Mosquito sector

2. Statics and dynamics of malaria infection in Anopheles mosquitoes

David L Smith and F Ellis McKenzie



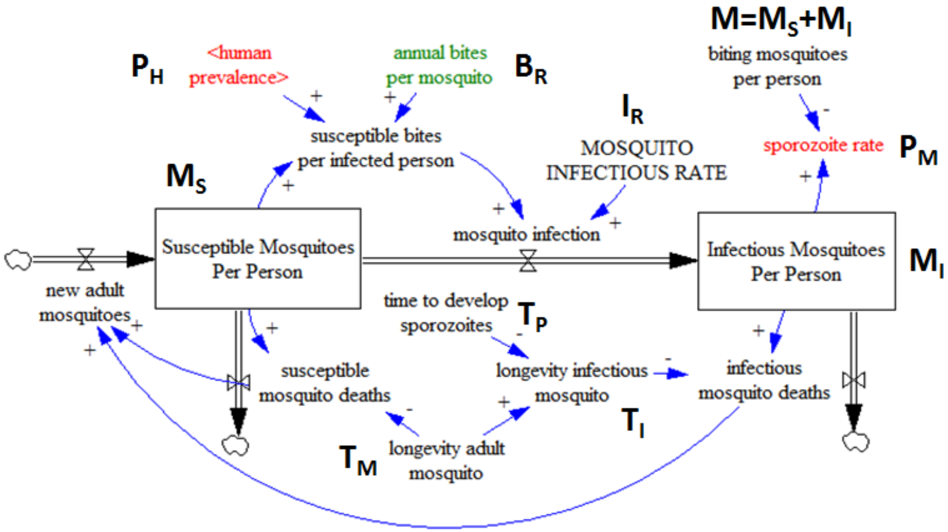
Human Feeding, Stability Index & HBI

How many bites on a human will a mosquito take during its lifetime? Let f denote the mosquito feeding rate; the interval between blood meals is assumed to be equivalent to the time interval between successive ovipositions, denoted $1/f$. Further, let Q denote the proportion of bites that are taken on humans, a parameter that can be estimated from the proportion of mosquitoes that have ever fed on a human, called the human blood index, *HBI*. The human feeding rate, a is the expected number of bites on humans per mosquito, per day; $a = Qf$. Since a mosquito lives $1/g$ days and bites a human once every a days, a mosquito bites humans

$$S = \frac{a}{g} \qquad (3)$$

times over the course of its lifetime; S is called the "stability index" [2,19]. By assumption, the life expectancy of a mosquito that has already lived 10 days is exactly the same as a recently emerged mosquito, $1/g$ days. Thus, S is also the number of bites given by a mosquito after it has become infectious. The expected number would be lower in a population with senescence and higher in a population with demographic frailty.

2. Number of mosquitoes per person (M)



Eq. 3

$$\boxed{V_R = B_R \cdot M}$$

$$T_I = \frac{T_M - T_P}{2}$$

$$\text{Infectious Mosquito Deaths} = \frac{M_I}{T_I} = \frac{M \cdot P_M}{T_I}$$

$$\text{Susceptible Bites per Infected Person} = \mathrm{S_I} = \mathrm{M_S} \cdot B_R \cdot P_H = M \cdot (1 - P_M) \cdot \frac{V_R}{M} \cdot P_H = (1 - P_M) \cdot V_R \cdot P_H$$

$$\text{Mosquito Infection} = I_R \cdot S_I = I_R \cdot (1 - P_M) \cdot V_R \cdot P_H$$

$$\text{Infectious Mosquito Deaths} = \text{Mosquito Infection} \Rightarrow$$

Eq. 4

$$\Rightarrow \frac{M \cdot P_M}{T_I} = I_R \cdot (1 - P_M) \cdot V_R \cdot P_H \Rightarrow \boxed{\left[M = \frac{T_I \cdot I_R \cdot V_R \cdot P_H \cdot (1 - P_M)}{P_M} \right]}$$

Human sector

$$\left.\begin{array}{ll} \text{Eq. 1} & P_H = \dfrac{EIR\cdot I_M\cdot T_R}{1+EIR\cdot I_M\cdot T_R} \\ \text{Eq. 2} & EIR = P_M\cdot V_R \end{array}\right\} \Rightarrow \left[P_H = \dfrac{P_M\cdot V_R\cdot I_M\cdot T_R}{1+P_M\cdot V_R\cdot I_M\cdot T_R}\right] \quad \text{Eq. 5}$$

Mosquito sector

$$\left.\begin{array}{ll} \text{Eq. 3} & V_R = B_R\cdot M \\ \text{Eq. 4} & M = \dfrac{T_I\cdot I_R\cdot V_R\cdot P_H\cdot(1-P_M)}{P_M} \end{array}\right\} \Rightarrow M\cdot P_M = T_I\cdot I_R\cdot B_R\cdot M\cdot P_H\cdot(1-P_M) \Rightarrow$$

$$\Rightarrow P_M + T_I\cdot I_R\cdot B_R\cdot P_H\cdot P_M = T_I\cdot I_R\cdot B_R\cdot P_H \Rightarrow \left[P_M = \dfrac{T_I\cdot I_R\cdot B_R\cdot P_H}{1+T_I\cdot I_R\cdot B_R\cdot P_H}\right] \quad \text{Eq. 6}$$

3. Relationship between prevalence in mosquitoes and humans (P_M/P_H)

$$\left.\begin{array}{l} \dfrac{P_M}{P_H} = \dfrac{T_I \cdot I_R \cdot B_R \cdot \left(\dfrac{1 + V_R \cdot I_M \cdot T_R}{V_R \cdot I_M \cdot T_R} \right)}{1 + T_I \cdot I_R \cdot B_R} \\ V_R \cdot I_M \cdot T_R >> 1 \end{array}\right\} \Rightarrow \left[\frac{P_M}{P_H} \approx \frac{T_I \cdot I_R \cdot B_R}{1 + T_I \cdot I_R \cdot B_R} \right]$$

Eq. 7

$$1 + T_I \cdot I_R \cdot B_R \approx 1 \quad \text{then,} \quad \boxed{\left[\frac{P_M}{P_H} \approx T_I \cdot I_R \cdot B_R \right] \; \mathit{where}\; T_I = \frac{T_M - T_P}{2}}$$

4. Larger effect of the variable bites per mosquito (B_R)

$$\left.\begin{aligned}
&\text{Eq. 3} \qquad & V_R &= B_R \cdot M \\
&\text{Eq. 6} \qquad & P_M &= \frac{T_I \cdot I_R \cdot B_R \cdot P_H}{1 + T_I \cdot I_R \cdot B_R \cdot P_H} \\
&\text{Eq. 1} \qquad & EIR &= V_R \cdot P_M
\end{aligned}\right\} \Rightarrow EIR = \frac{B_R^2 \cdot M \cdot T_I \cdot I_R \cdot P_H}{1 + T_I \cdot I_R \cdot B_R \cdot P_H}$$

$$\text{Eq. 8} \qquad EIR \approx B_R^{\enclose{circle}{2}} \cdot M \cdot T_I \cdot I_R \cdot P_H$$

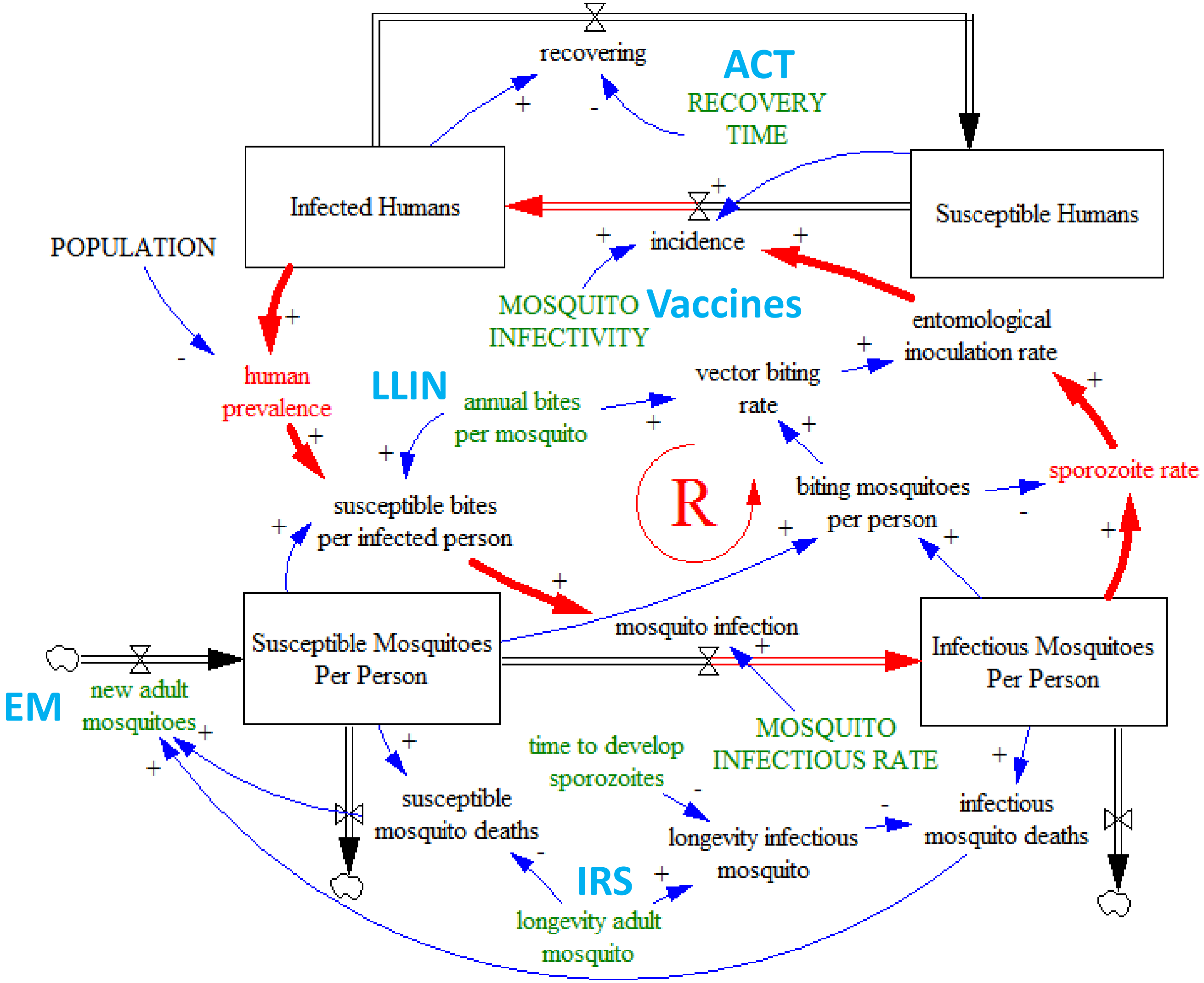
5. Impact of malaria control strategies.

Eq. 5
$$P_H = \frac{P_M \cdot V_R \cdot I_M \cdot T_R}{1 + P_M \cdot V_R \cdot I_M \cdot T_R}$$

$P_M \cdot V_R \cdot I_M \cdot T_R = 0$ Malaria elimination: Which element can turn into zero?

- P_M intimately related with P_H by means of B_R: $P_M/P_H \approx T_I \cdot I_R \cdot B_R$
- V_R can be reduced through the implementation of IVM interventions: $V_R = M \cdot B_R$
- I_M is smaller when individuals are protected with sporozoite-based vaccines.
- T_R can be reduced targeting infectious population with gametocidal drugs.

5. Impact of malaria control strategies.



recovering

ACT

RECOVERY TIME

Infected Humans

Susceptible Humans

POPULATION

incidence

MOSQUITO INFECTIVITY

Vaccines

entomological inoculation rate

human prevalence

LLIN

annual bites per mosquito

vector biting rate

R

biting mosquitoes per person

sporozoite rate

susceptible bites per infected person

mosquito infection

Susceptible Mosquitoes Per Person

Infectious Mosquitoes Per Person

EM

new adult mosquitoes

MOSQUITO INFECTIOUS RATE

time to develop sporozoites

susceptible mosquito deaths

longevity infectious mosquito

infectious mosquito deaths

IRS

longevity adult mosquito

Conclusions:

We have fitted a simple stock and flow model which allows us to understand the most important mechanisms of malaria transmission in P. falciparum carriers. Although the starting model is very simple, the results obtained after increasing the model complexity are very similar.

The mathematical relationships established in the model can help us to obtain or validate the value of the main malaria transmission indicators by eliminating three degrees of freedom. In this sense, one of the most relevant results from this study is the calculated ratio or relationship between mosquito and human prevalence (P_M/P_H), which is approximately equal to a constant that depends on the entomological and environmental conditions of the area, multiplied by the average bites on humans per mosquito B_R.

Regarding B_R, it can be also calculated using other indicators obtained empirically and is particularly relevant for malaria transmission as it would enable high levels of human prevalence even in environments with low mosquito densities.

Although the relationships in the model are obtained from the perspective of a static analysis, the inclusion of data would allow the model to simulate over time and to manifest the behavior of the variables driven by the different feedback loops of the system, thus permitting also dynamic analyses.

As a result, the models can be used as decision-support tools to improve the design of strategies against malaria in different locations.