

Analysis of a malaria model with two infectious classes

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Abstract

In this paper we study a deterministic differential equation model for the spread and control of malaria, which involve two infectious classes. We derived the conditions for disease free and endemic equilibria. A comparison of this model and three other models is made and tables of ranges of parameter values are established.

The main results shows that a simplified NDM-system has a unique endemic equilibrium for certain values of the ratio of mosquito to human population, which is always a global attractor. Otherwise, there is no endemic equilibrium and the disease-free equilibrium is a global attractor. When the ratio of mosquito to human population changes the endemic equilibrium changes and forms a curve C_e in the phase space

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parameterized by this ratio. For a certain range of the rate of human population entering the susceptible class (either by birth or migration) the original NDM-system has an equilibrium on the curve C_e . This equilibrium is a saddle with a four dimensional stable and one dimensional unstable manifold. The unstable manifold is well approximated by this curve.

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1 Introduction

Mathematical modeling of malaria has been studied extensively since the days of Ross [2] who was the first to model the dynamics of malaria transmission. Macdonald [3] expounded on Ross work by introducing the theory of superinfection and later, latency into the dynamics of mosquito population. Anderson and May [9] in addition considered latency in human population dynamics models. Inroads into malaria modeling have been made by other authors since then, (see, [6], [7], [4], [11] and [1]).

In this paper we examine the NDM (Nortey-Danso-Marijani) system [13] and compare with other known systems of the same type. In the NDM system two infectious classes are considered:

Case 1: A severe case getting the disease the first time.

Case 2: A re-infectious case having some immunity.

Moreover, we show by numerical experiments, that for realistic time periods of 3-5 years the NDM-system with constant mosquito population (birth rate equals death rate) can be well approximated by a simplified system, (i.e., neglecting changes in total human population size.) We give a summary of realistic ranges of parameters gathering information from different publications. The simplified model can have only one endemic equilibrium, which is always observed to be globally attracting and arising from a disease-free equilibrium through a transcritical bifurcation. Simulation analysis shows that after five years the solution of the original system starts to slowly diverge from the cor-

responding simplified system, but follows approximately, a curve of endemic equilibria for a one-parameter family of simplified systems. The original system either has no endemic equilibria or the endemic equilibria is a saddle, with a one dimensional unstable set, approximately following the equilibria of simplified system. A solution curve approximating the curve of equilibria of the simplified system is always existing and in the absence of the saddle point the host population will either always go to infinity or zero. In the case of existence of saddle point, the host population tends to infinity or zero depending on which side of the stable set we start. In any case the motion on that solution curve is slow and in realistic time (i.e., 3-5 years) we do not move far away from the solution of the simplified system and the change in host population is also small. For large host populations we always get a disease-free situation where the population is slowly growing if birth rate is greater than death rate.

1.1 Background of malaria in Ghana

Malaria is an infectious disease caused by the genus *Plasmodium* - a protozoan parasite transmitted by an infectious female *Anopheles* mosquito. There are four serotypes; *P. falciparum*, *P. vivax*, *P. malarie* and *P. ovale*. Approximately 2.2 billion people are affected by *P. falciparum* in 86 endemic countries, resulting in about 515 million clinical cases worldwide and over 1 million fatalities in Africa every year.

In Ghana, Malaria is hyper endemic in all parts of the country. Ghana's entire population of 24 million is at risk of malaria, although transmission rates are lower in the urban areas.

According to the World Health Organization report on Malaria in Ghana [15], Ghana recorded 3200147 and 3694671 malaria cases in the years 2008 and 2009 respectively. Admissions to hospitals due to malaria also went up from 272802 in 2008 to 277047 in 2009. Death due to malaria from the records of clinics and hospitals stood at 3378 in 2009.

Ghana can be stratified into three malaria epidemiologic zones: the northern savannah; the tropical rainforest; and, the coastal savannah and mangrove swamps. The major vectors are *Anopheles gambiae* and *Anopheles funestus* [17]. Characteristically, these species bite late in the night, are indoor resting, and are commonly found in the rural and peri-urban areas, where socio-economic activities lead to the creation of breeding sites. *Anopheles melas*

is found in the mangrove swamps of the southwest and *Anopheles arabiensis* in the savannah areas of northern Ghana. Northern Ghana experiences pronounced seasonal variations with a prolonged dry season from September to April. The normal duration of the intense malaria transmission season in the northern part of the country is about seven months beginning in April/May and lasting through to September. Malaria is endemic everywhere in Ghana.

There have been significant progress in malaria control in Ghana. This is a result of household ownership of insecticide-treated net (ITN) and indoor residual spraying (IRS), intermittent preventative treatment in pregnant women (IPTP) and also mass spraying just to mention a few.

For pregnant women, the introduction of malaria medication has helped in preventing still born deaths.

1.2 Paper outline

The rest of the paper is organized as follows. In Section 2 we give the necessary notations and preliminaries for building the models. The terms in the models are explained and the meanings of the parameters used are also given. The ranges of the parameter values used are also given in this section.

In Section 3 we give a detailed description of the NDM model and compare with Ross, Chitnis et al and Ngwa et al models. In Section 4 we give detail explanation of the analysis of the NDM-model.

Finally in Section 5 we compare the results obtained using our new method of analyzing the NDM model and compared it to that of the other models.

2 Notations and Preliminaries from Malaria Modeling

2.1 Description of variables and parameters

In epidemic modeling the populations are divided into classes forming the variables in a system of differential equations. The terms in the equations give the transition rates between the population classes. We use the following notations for population classes:

Table 1: Description of variables for the malaria model

Variables	Description
S_H	Susceptible human population
E_H	Latent human population
I_H	Infectious human population
R_H	Recovered with clinical immunity
S_M	Susceptible mosquitoes
E_M	Latent mosquito population
I_M	Infectious mosquitoes
I_{H1}	Infectious human (clinical malaria cases resulting from completely susceptible individuals)
I_{H2}	Re-infectious individuals from clinical immunity
N_H	Total human population
N_M	Total mosquito population
$m = \frac{N_M}{N_H}$	Ratio of mosquito and human population

In addition to the above population class notations, the following parameter notations will also be encountered in the sessions.

Please, note that, the following parameters: σ_h , σ_v , a , β_{hv} , C , β_{vh} , b , $\tilde{\beta}_{vh}$ and \tilde{C}_{hv} are in the incidence terms of Chitnis et al and Ngwa et al models (for full meanings see [6] and [11]).

The NDM-model [13] and the Ross model [2] have no latent classes but Chitnis et al [8] and Ngwa et al [11] models include these classes.

Table 2: Incidence parameters and descriptions

Parameters	Description
β_H	Contact rate between susceptible humans and infectious mosquitoes
β_M	Contact rate between susceptible mosquitoes and infectious humans
c	Constant of proportionality
k	Resistance factor

Table 3: Recovery parameters and descriptions

Parameters	Description
γ	Rate of recovery from infectious class
α	Rate of recovery from re-infectious

Table 4: Loss of immunity parameter and descriptions

Parameters	Description
ω	Rate of loss of clinical immunity

2.2 Terms for transition between population classes

For easy reading we explain the following transitional terms which will be encountered in the paper: incidence, recovery, loss of immunity, birth, death and migration and latency.

2.2.1 Incidence

All epidemic models have an incidence term that measures the rate at which individuals in a population get infectious. For example the incidence

Table 5: Birth and death parameters and descriptions

Parameters	Description
b	Rate of human population entering into susceptible class (i.e., birth and migration)
b_M	Birth rate for the mosquito population entering into susceptible class
μ_H	Natural death rate of human
δ_1	Death rate due to clinical malaria
δ_2	Death rate due to re-infection of malaria
μ_M	Natural death rate of mosquitoes

Table 6: Latency parameters and descriptions

Parameters	Description
ν_H	Latency rate in human
ν_M	Latency rate in mosquitoes

term in the SI model [16] is βIS (i.e., the rate at which individuals move from susceptible to infectious class.)

In general we can have different such incidence terms:

Type 1 is of the form $b(I, S)$. Here S represents a susceptible host or vector population and I an infectious vector or host population correspondingly. The function $b(I, S)$ is increasing in both variables.

Type 2 is of the form $b(R, S)$. Sometimes there is supposed to be possibilities for recovered also to infect. Here R is recovered host and S is the susceptible vector (see [8] and [11]) and the function $b(R, S)$ is increasing in both variables.

Type 3 is of the form $b(I, R)$. Here the recovered individual is not fully immune and therefore capable of being infected. Here I is the infectious vector population, whilst R is the recovered but not fully immune host population and the function $b(I, R)$ is increasing in both variables. In some cases the incidence function is written as a product of two increasing functions g and h in the form $b(I, S) = g(I)h(S)$. The most usual incidence function is the case

when g and h are linear and this is called linear incidence. A general class of non-linear incidence functions in a simple model are studied in [14].

Usual non-linear types of g and h are $h(S) = S^r$ and $g(I) = kI^p$, where p and r are positive numbers. Another type of non-linear incidence function is given by $g(I) = \frac{kI^p}{1+aI^q}$. Many incidence functions are of the special type $b(I, S) = \beta IS$ where β often also depends on host and vector sizes. For example, the mosquito population size usually oscillates between the rainy season and dry season and is bigger during the rainy season and this can then have an effect also on the coefficient β .

In the models we have considered here, the incidence function is written in the form $b(I, S) = \frac{\beta_H}{N_H} IS$ in host equations and $b(I, S) = \frac{\beta_M}{N_H} IS$ in vector population equations.

In Chitnis et al model, β -parameters are dependent on population sizes in a natural way. Where N_H is far larger than N_M , the incidence function in Chitnis et al model coincides with the incidence functions in the other models named above.

More precise: Chitnis et al finds the coefficients for term with $I_M S_H$ and $I_H S_M$ consequently in the form

$$\begin{aligned} B_H &= \frac{\lambda_h}{I_M} = b_h(N_H, N_M) \frac{\beta_{hv}}{N_M} \\ &= \frac{b(N_H, N_M)}{N_H} \frac{\beta_{hv}}{N_M} = \frac{\sigma_h \sigma_v N_M}{\sigma_v N_M + \sigma_h N_M} \frac{\beta_{hv}}{N_M} = \frac{\sigma_v \sigma_h \beta_{hv}}{\sigma_v N_M + \sigma_h N_H} \end{aligned} \quad (1)$$

$$\begin{aligned} B_M &= \frac{\lambda_v}{I_H} = b_v(N_H, N_M) \frac{\beta_{vh}}{N_H} \\ &= \frac{b(N_h, N_H)}{N_M} \frac{\beta_{vh}}{N_H} = \frac{\sigma_h \sigma_v N_H}{\sigma_v N_M + \sigma_h N_H} \frac{\beta_{vh}}{N_H} = \frac{\sigma_v \sigma_h \beta_{vh}}{\sigma_v N_M + \sigma_h N_H} \end{aligned} \quad (2)$$

For N_M small and N_H considerable large, we then get approximately,

$$B_H = \frac{\sigma_v \beta_{hv}}{N_H}, \quad B_M = \frac{\sigma_v \beta_{vh}}{N_H} \quad (3)$$

which corresponds to NDM-system with $B_H = \frac{\beta_H}{N_H}$ and $B_M = \frac{\beta_M}{N_H}$, where $\beta_H = \sigma_v \beta_{hv}$ and $\beta_M = \sigma_h \beta_{vh}$.

But for N_H small and N_M considerable large we then get approximately

$$B_H = \frac{\sigma_h \beta_{hv}}{N_M}, \quad B_M = \frac{\sigma_h \beta_{vh}}{N_M}. \quad (4)$$

which is quite an opposite situation. As we interpret it, Chitnis et al suggested that dividing by small N_H in these cases will make an unrealistic big β -factor.

Chitnis et al has incidence terms with combinations $I_M S_H$, $I_H S_M$ and $R_H S_M$ as NDM-system has incidence terms for $I_M S_H$, $I_M R_H$, $I_{H1} S_M$ and $I_{H2} S_M$. NDM-system does not have the possibility for mosquitoes to get infectious from recovered class.

2.2.2 Recovery

The recovery rate is denoted by γ . Most models, except the NDM model have one type of recovery. The recovery terms are all linear. $\frac{1}{\gamma}$ is the average time spent in recovery if γ is the coefficient in the linear term. In the NDM-model there are two recovery rates, one of them representing the recovery from the infectious class is denoted by γ while the other representing the recovery from the re-infectious class is denoted by α . Also here the terms are linear. Usually after the recovery, the infectious are moved to a recovered class with some immunity but in Ross model the infectious move directly to the susceptible class while in the Ngwa et al model some of the infectious move to the susceptible while the rest move to recovered class.

2.2.3 Loss of Immunity

The loss of immunity is denoted by ω . It was observed that with the exception of the Ross model, all the other models have rates of loss of immunity. These terms are also linear. The quantity $\frac{1}{\omega}$ is the average time in losing immunity. Here ω is the coefficient of the linear term.

2.2.4 Birth, Death and Migration

The birth and death coefficients are $b, b_M, \mu_H, \mu_M, \delta_1, \delta_2$ and comes from linear terms in the NDM-system. The parameters b and μ_H are the birth and death rates for the host population respectively. The number $\frac{1}{\mu_H}$ is the average life expectancy of humans and $\frac{1}{b}$ is average time to give birth. Likewise the parameters b_M and μ_M are the birth and death rates for the mosquito population respectively.

In NDM-model we assume linear birth and death terms, whereas in Chitnis et al [8] and Ngwa et al [11] models, they assumed quadratic birth terms, whilst

death has both linear and quadratic terms. The disease-induced death rates δ_1 and δ_2 add an extra linear term for infectious classes. Chitnis et al also includes a migration factor into the susceptible host class which is a constant term.

2.2.5 Latency

The rate of becoming infectious in latent classes are denoted by ν_H and ν_M for the host and mosquito populations respectively. Some models have separate class for latency and is usually denoted by E , whereas in the NDM-model this latency class is accounted for by decreasing β values. Identifying how the latency values are included in the decreasing β values may be quite difficult. Nevertheless, latency can be included in the model in two ways, either with a latent population E , but if included more exact it should be included by making a delay system. Notwithstanding, there can be a lot of mathematical difficulties associated with this type of system. The need for having a latency term in the model becomes very important if the life span of the vector is relatively short and less important in the case of the host which has a longer life span. For individuals (e.g., host) with longer life span the latency term may often be excluded from the model.

In the case of malaria the latency period can be very different [9] and thus there is no clear latency period used in the delay equations but must be taken in average. This means that delay-equation are not so much better than models with a latent population included.

2.3 Typical values of parameters and their ranges

Some typical parameter values and the possible ranges of the parameters in the models are given in six tables below. Two of them give values for incidence parameters, two of them give values for transmission parameters between population classes and two tables give birth, death and migration parameter values.

The columns in the Tables 7 to 9 refer to different sets of parameter values used in different papers. Standard values of the NDM model are given in column 2 of the tables.

The C2006 refers to values in tables taken from Chitnis et al [6] and C2008 refers to values from Chitnis et al [7] with different sets for low and high transmission of the disease. Ngwa2000 refers to values from Ngwa et al [11]. RossMac refers to values from Ross model in May and Anderson [9]. The ranges for the parameter values are taken or calculated from the same references.

In Table 7 we see the values for the incidence parameters.

Table 7: Incidence Parameters

Parameters	NDM	C2006	C2008 Low	C2008 High	Ngwa2000	RossMac
β_H	0.06	0.011	0.0055	0.0088	-	0.055
β_M	0.05	0.48	0.06	0.19	0.4167	0.03
c	0.25	-	-	-	-	-
k	0.12	-	-	-	-	-
σ_h	-	18	4.3	19	-	-
σ_v, a	-	0.6	0.33	0.5	-	0.055
β_{hv}, C	-	0.02	0.022	0.022	-	0.5
β_{vh}, b	-	0.83	0.24	0.48	-	1
$\tilde{\beta}_{vh}, \tilde{C}_{hv}$	-	0.083	0.024	0.048	-	-
m	-	2	4	10	-	25

The parameters β_H and β_M are present in all models. In Chitnis et al model they are not constant and depend on human and mosquito population sizes. In this case we give the values of β_H and β_M for population sizes corresponding to disease free equilibrium. The following constants $\sigma_h, \sigma_v, \beta_{hv}, \beta_{vh}, \tilde{\beta}_{vh}$ are present in the incidence expressions in Chitnis et al model, while the constants c and k are present only in the NDM model. The parameters a, b, C are constants in the incidence expressions in the Ross model. The parameters $\tilde{\beta}_{vh}, \tilde{C}_{hv}$ are constants in the incidence expressions in the Ngwa et al model.

Finally $m = \frac{\mu_M}{\mu_H}$ is the ratio between the mosquito and human population used in the incidence expressions in the Chitnis et al and Ross models.

In Table 8 columns 2 to 7 are the values associated with transition parameters in column 1 (see, [13], [11], [7] and [6]).

We have constants for the rates of recovery, loss of immunity and transition from latency to infectious.

Table 8: Transition parameters

Parameters	NDM	C2006	C2008 Low	C2008 High	Ngwa2000	RossMac
$\gamma(I_H \rightarrow R_H)$	0.04	0.0037	0.0035	0.0035	0.0124	-
$\omega(R_H \rightarrow S_H)$	0.01	0.015	0.0027	0.00055	0.0146	-
$\alpha(I_{H_2} \rightarrow R_H)$	0.04	-	-	-	-	-
$\nu_H (E_H \rightarrow I_H)$	-	0.083	0.10	0.10	0.0833	-
$\nu_M (E_M \rightarrow I_M)$	-	0.1	0.083	0.091	0.10	-
$r_H(I_H \rightarrow S_H)$	-	-	-	-	0.00833	0.011

Table 9: Birth, death and migration parameters

Parameters	NDM	C2006	C2008 Low	C2008 High	Ngwa2000	RossMac
Λ_H	-	0.033	0.041	0.033	-	-
b	0.000055	0.000078	0.00011	0.000055	0.000077	-
b_M	0.05	0.4	0.13	0.13	0.04175	-
μ_H	0.000055	0.00012	0.00012	0.00016	-	-
μ_M	0.05	0.17	0.13	0.13	-	0.137
δ_1, δ	0.000018	0.00035	0.000018	0.00009	0.0000417	-
δ_2	0.00001	-	-	-	-	-
μ_{1h}	-	0.000042	0.0000088	0.000016	0.000056	-
μ_{1v}	-	0.1429	0.033	0.033	0.0417	-
μ_{2h}	-	0.0000001	0.0000002	0.0000003	-	-
μ_{2v}	-	0.00023	0.00004	0.00002	-	-

In Table 9 we see the values for the birth, death and migration parameters in the following: (see,[13],[11],[7] and [6]).

The parameters b and b_M are the birth rates for human and mosquito populations correspondingly. The parameters μ_H and μ_M are the death rates for human and mosquito populations correspondingly. The parameters $\delta_1, \delta_2, \delta$ are disease induced death rates for human population. In the Chitnis et al and Ngwa et al models, quadratic expressions are used for the death terms, with constants $\mu_{1h}, \mu_{2h}, \mu_{1v}, \mu_{2v}$ in the expressions.

From Tables 10 to 12 we now present possible realistic ranges for the various parameters.

In Table 10 we see the values for the ranges of the incidence parameters.

Ranges for $\sigma_h, \sigma_v, \beta_{hv}, \beta_{vh}, \tilde{\beta}_{vh}, a, b, C, m$ are taken directly from [7] , [11] and [9]. The maximal β_H, β_M , are calculated from [7]. The ranges for c and k are simply taken as the half and double values of the corresponding values in the standard parameter set.

Table 10: Ranges for incidence parameters

Parameters	Description	Range
β_H	Contact rate between susceptible humans and infectious mosquitoes	0-0.27
β_M	Contact rate between susceptible mosquitoes and infectious humans	0- 0.63
c	Constant of proportionality	0.125-0.5
k	Resistant factor	0.06-0.24
σ_h	The maximum number of mosquito bites a human can have per unit time	0.10-50
σ_v, a	Average number of bites given to humans by each mosquito per unit time, if humans were freely available	0.055-1.0
β_{hv}, C	The probability of transmission of infection from an infectious mosquito to susceptible human given that a contact between the two occurs	0.01-0.5
β_{vh}, b	The probability of transmission of infection from an infectious human to susceptible mosquito given that a contact between the two occurs	0.072-1.0
$\tilde{\beta}_{vh}$	The probability of transmission of infection from a recovered human to susceptible mosquito given that a contact between the two occurs	0.024-0.64
m	The ratio of number of mosquitoes to humans	2-40

Table 11: Ranges for transition parameters

Parameters	Description	Range
$\gamma (I_H \rightarrow R_H)$	Recovery rate due to clinical malaria	0.0014-0.04
$\omega (R_H \rightarrow S_H)$	Rate of loss of immunity	0.00055-0.0146
$\alpha (I_{H_2} \rightarrow R_H)$	Recovery rate due to re-infection	0.01-0.04
$\nu_H (E_H \rightarrow I_H)$	rate of progression of humans from the exposed state to the infectious state	0.067-0.20
$\nu_M (E_M \rightarrow I_M)$	rate of progression of mosquitoes from the exposed state to the infectious state	0.029-0.33
$r_H (I_h \rightarrow S_h)$	Recovery rate without any gain substantial immunity	0.008-0.011

In Table 11 depicts the values for the ranges of the transition parameters. The ranges are taken directly from [7] and γ is calculated from [7].

In Table 12 depicts the values for the ranges of the birth, death and migration parameters.

Table 12: Ranges for birth, death and migration parameters

Parameters	Description	Range
Λ_H	Immigration rate of humans	0.0027-0.27
b	Birth rate of humans	0.000027-0.00014
b_M	Birth rate of mosquitoes	0.020-0.4
μ_H	Natural death rate of humans	0.00003-0.00009
μ_M	Natural death rate of mosquitoes	0.02-0.12
δ_1, δ	Death rate due to clinical malaria	0-0.0001
δ_2	Death rate due to re-infection	0.000005-0.000015
μ_{1h}, μ_h	Density dependent part of the death (or emigration on) rate for humans	0.000001-0.001
μ_{2h}	Density independent part of the death (or emigration on) rate for humans	0.00000001-0.000001
μ_{1v}, μ_v	Density dependent part of the rate of mosquitoes	0.001-0.1
μ_{2v}	Density independent part of the rate of mosquitoes	0.000001-0.001

The ranges are taken directly from Chitnis et al [7] and [6] except the natural death rates which are taken as the inverse numbers of the average life expectancy.

2.4 Review of some known models

2.4.1 The NDM-model

In this section we review the NDM-model which is the main subject of investigation in this paper. In the paper published by R. Aguas et al [12], the authors identified an interesting phenomenon. This phenomenon was further investigated by the authors of the NDM model in [13]. R. Aguas et al claimed that a characteristic of *P. falciparum* is the gradual acquisition of clinical immunity, resulting from repeated exposures to the parasite. However any given infection produces a clinical outcome that depends on a combination of parasite, vector, host and environmental factors.

Also, in highly endemic regions, both prevalence of infection and incidence of severe malaria are high in young children and pregnant women, whereas in older children and adults, prevalence of infection is higher while incidence of severe cases is lower. Thus, even after many exposures, humans are not resistant to infection, but develop clinical immunity that prevents symptomatic disease which is not solely dependent on host intrinsic age factors.

In low endemic regions, however, malaria infection and morbidity shows less age dependence, with infections being commonly symptomatic even in adults, due to less frequent immunologic stimulation.

In the work done by the authors of the NDM model (see [13]), a model was created consisting of a system of ODE's for the host and vector populations.

The model divides the host populations into four classes: Susceptible, S_H , Infectious, I_{H1} , Recovered, R_H and Re-infectious, I_{H2} . Human beings enter the susceptible class either through birth (at a constant rate) or from the recovered class (at a constant rate). When an infectious mosquito bites a susceptible human, there is some probability that the parasite (in the form of sporozoite) will be passed on to the human and the person will move to the infectious class and become infectious. After some time the infectious humans recover and move to the recovered class. In our model a proportion of the recovered humans could move back into the susceptible class and the remaining become re-infectious and move to the re-infectious class. In addition, some of the re-infectious humans recover and return to the recovered class (at a constant rate). Humans leave the population through a density - dependent natural death rate δ_1 , and through a disease-induced death rate δ_2 .

In the NDM model, we divide the vector (mosquito) population into two classes: the Susceptible S_M , and the Infectious class, I_M . Female mosquitoes (we do not include male mosquitoes because only female mosquitoes bite human for blood meals) enter the susceptible S_M class through birth. The parasite (in the form of gametocytes) enters the mosquito, after biting an infectious human, with some probability. When this happens the mosquito then moves from the susceptible S_M class to the infectious I_M class. The mosquito remains infectious for life. Mosquitoes leave the population through a density-dependent natural death rate.

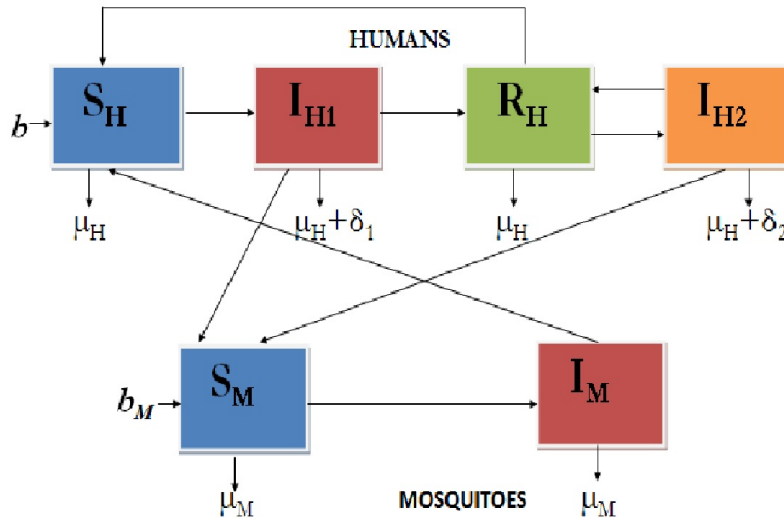


Figure 1: Flow diagram of malaria model

In Figure 1, we present a schematic diagram of the mathematical model for malaria transmission. Susceptible humans, S_H , get infectious at a certain probability, when they are bitten by an infectious mosquito. They then progress to infectious class, I_{H1} , and later into the recovered class R_H . These also progress from recovered to the re-infectious, I_{H2} or re-enter the susceptible S_H class.

Susceptible mosquitoes S_M get infectious at a certain probability when they come in contact with infectious I_{H1} or re-infectious I_{H2} humans and then progress to the infectious class I_M .

The equations for the malaria model in Figure 1 are shown in equation (5). The state variables and the parameters used in the model are described in section 2 and typical values are given in Tables 7, 8 and 9. All parameters are assumed to be strictly positive with the exception of the disease-induced death rate, δ_1 and δ_2 , which we assume to be nonnegative.

$$\begin{aligned}
\dot{S}_H(t) &= bN_H - \frac{\beta_H S_H I_M}{N_H} + \omega R_H - \mu_H S_H \\
\dot{I}_{H1}(t) &= \frac{\beta_H S_H I_M}{N_H} - \gamma I_{H1} - (\mu_H + \delta_1) I_{H1} \\
\dot{R}_H(t) &= \gamma I_{H1} + \alpha I_{H2} - \frac{c\beta_H R_H I_m}{N_H} - \omega R_H - \mu_H R_H \\
\dot{I}_{H2}(t) &= \frac{c\beta_H R_H I_M}{N_H} - \alpha I_{H2} - (\mu_H + \delta_2) I_{H2} \\
\dot{S}_M(t) &= b_M N_M - \frac{\beta_M S_M (I_{H1} + k I_{H2})}{N_H} - \mu_M S_M \\
\dot{I}_M(t) &= \frac{\beta_M S_M (I_{H1} + k I_{H2})}{N_H} - \mu_M I_M
\end{aligned} \tag{5}$$

2.4.2 Ross, Chitnis et al and Ngwa et al models

We hereby introduce and compare the NDM model with some known models which have important connections with the model we consider. We have chosen three very known models. The first one is the historical Ross model which is an SI-model with no recovery class, only two population classes for host and vector. The two other models are the Chitnis et al and Ngwa et al models which also have latency classes for both host and vector, but only one infectious class for host. We rewrite all the models in notations corresponding to the notations used in the NDM model. In section 2, we gave a list of ranges for parameters used in known publications and discuss the form of different transition terms between classes like incidence, latency, recovery and other terms.

Ross model

In this model we have only four population classes; the susceptible host

population S_H and mosquito population S_M and the infectious human population I_H and infectious mosquito population I_M . For details see [9].

We expect the total host and mosquito populations to be constant. Thus, the model is given by the equations for the infectious populations.

$$\begin{aligned} \dot{I}_H &= ab \frac{I_M S_H}{N_H} - \gamma I_H \\ \dot{I}_M &= aC \frac{I_H S_M}{N_H} - \mu I_M \end{aligned} \tag{6}$$

The equations for susceptible populations follow from the relations

$$S'_H = -I'_H \quad \text{and} \quad S'_M = -I'_M.$$

Parameters γ and μ are the host recovering rate and mosquitos death rate correspondingly. The incidence rates we described before as β_H and β_M are now represented by ab and aC respectively (we use C instead of c in the model described in [9] so as not to get confused with the constant c in the NDM model) and the meaning of a, b and C are given in the tables of parameter values in section 2.

Chitnis et al model

Here we introduce a known model of Chitnis et al [7] and discuss some connections with the NDM model.

In our notation the model takes the form:

$$\begin{aligned} \dot{S}_H &= \Lambda_H + bN_H + \omega R_H - \frac{\beta_H S_H I_M}{N_H} - \mu_H S_H \\ \dot{E}_H &= \frac{\beta_H S_H I_M}{N_H} - \nu_H E_H - \mu_H E_H \\ \dot{I}_H &= \nu_H E_H - \gamma I_H - \mu_H I_H - \delta I_H \\ \dot{R}_H &= \gamma I_H - \omega R_H - \mu_H R_H \\ \dot{S}_M &= b_M N_M - \frac{\beta_M S_M I_H + \tilde{\beta}_M S_M R_H}{N_H} - \mu_M S_M \\ \dot{E}_M &= \frac{\beta_M S_M I_H + \tilde{\beta}_M S_M R_H}{N_H} - \nu_M E_M - \mu_M E_M \\ \dot{I}_M &= \nu_M E_M - \mu_M I_M \end{aligned} \tag{7}$$

We have the following relations between our notations and Chitnis et al notations:

For Population Variables:

$$S_H = S_h, E_H = E_h, I_H = I_h, R_H = R_h, S_M = S_v, E_M = E_v \quad \text{and} \quad I_M = I_v \\ N_H = N_h = S_h + E_h + I_h + R_h \quad \text{and} \quad N_M = N_v = S_v + E_v + I_v.$$

The latency classes E_H and E_M are added in this model.

For the Parameters:

$$\Lambda_H = \Lambda_h, b = \psi_h, b_M = \psi_v, \omega = \rho_h, \nu_H = \nu_h, \nu_M = \nu_v, \gamma = \gamma_h, \\ \delta = \delta_h, \beta_H = \frac{\lambda_h N_h}{I_v} = \frac{\sigma_v \sigma_h \beta_{hv} N_h}{\sigma_v N_v + \sigma_h N_h}, \beta_M = \frac{b_v \beta_{vh} N_h}{N_v} = \frac{\sigma_v \sigma_h \beta_{vh} N_h}{\sigma_v N_v + \sigma_h N_h}, \\ \tilde{\beta}_M = \frac{b_v \tilde{\beta}_{vh} N_h}{N_v} = \frac{\sigma_v \sigma_h \tilde{\beta}_{vh} N_h}{\sigma_v N_v + \sigma_h N_h}, \mu_H = f_h(N_h) = \mu_{1h} + \mu_{2h} N_h, \quad \text{and} \\ \mu_M = f_v(N_v) = \mu_{1v} + \mu_{2v} N_v.$$

We have linear transmission terms from latency to infectious and quadratic death terms, except terms which are familiar from NDM model. We also have the possibility that mosquitoes can get the disease from recovered host. We observe that β_H, β_M and $\tilde{\beta}_M$ are not constant but have complicated form as explained in section 2 in connection to incidence.

Ngwa et al model

Here we introduce a known model of Ngwa et al [11] and discuss some connections with the NDM model.

In our notation the model takes the form:

$$\begin{aligned} \dot{S}_H(t) &= bN_H + \omega R_H + r_H I_H - \mu_H S_H - \frac{\beta_H S_H I_M}{N_H} \\ \dot{E}_H(t) &= \frac{\beta_H S_H I_M}{N_H} - (\nu_H + \mu_H) E_H \\ \dot{I}_H(t) &= \nu_H E_H - (r_H + \gamma + \delta + \mu_H) I_H \\ \dot{R}_H(t) &= \gamma I_H - (\omega + \mu_H) R_H \\ \dot{S}_M(t) &= b_M N_M - \mu_M S_M - \frac{\beta_M S_M I_H}{N_H} - \frac{\tilde{\beta}_M S_M R_H}{N_H} \\ \dot{E}_M(t) &= \frac{\beta_M S_M I_H}{N_H} + \frac{\tilde{\beta}_M S_M R_H}{N_H} - (\nu_M + \mu_M) E_M \\ \dot{I}_M(t) &= \nu_M E_M - \mu_M I_M \end{aligned} \tag{8}$$

We have the following relations between our notations and Ngwa et al notations:

For Population Variables:

$$S_H = S_h, E_H = E_h, H_H = I_h, R_H = R_h, S_M = S_v, E_M = E_v, \text{ and } I_M = I_v$$

$$N_H = N_h = S_h + E_h + I_h + R_h \text{ and } N_M = N_v = S_v + E_v + I_v$$

For parameters:

$$b = \lambda_h, \omega = \beta_h, \beta_H = c_{vh}a_v, \nu_H = \nu_h, r_H = r_h, \gamma = \alpha_h, \delta = \gamma_h, b_M = \lambda_v,$$

$$\nu_M = \nu_v, \beta_M = c_{hv}a_v, \tilde{\beta}_M = \tilde{c}_{hv}a_v, \mu_H = f_h(N_h) = \mu_h + \mu_{2h}N_h, \text{ and}$$

$$\mu_M = f_v(N_v) = \mu_v + \mu_{2v}N_v.$$

The model has the same population classes as in Chitnis et al. The term $r_H I_H$ for the transition from infectious directly to susceptible, with immediate loss of immunity is present in Ross equation but not present in NDM model nor in Chitnis et al model. The incidence terms are the same as in Chitnis et al but β_M and β_H do not depend on the population size. They also used logistic death terms.

2.5 Mathematical analysis

2.5.1 Simplified models

To carry out a serious mathematical investigation, it is usual to scale the equations to variables representing proportions of population classes, compared with total host or mosquitos classes. Sometimes after that, total host and mosquito populations are assumed constant. This often gives good approximations in short time behavior, even if not always, especially for the mosquito population which can change faster. Ngwa et al [11] and Chitnis et al [7] have pointed out this problem. Anyhow a lot can be obtained from simplified models assuming at least the host population is constant. The populations can be considered as slow variables thereby simplifying the general investigation.

Using the scaled variables $x = \frac{I_H}{N_H}, z = \frac{I_M}{N_M}$ the Ross model becomes:

$$\begin{aligned} x' &= \beta_H m z (1 - x) - \gamma x \\ z' &= \beta_M x (1 - z) - \mu z \end{aligned} \tag{9}$$

where $m = \frac{N_M}{N_H}$ and $\beta_H = ab, \beta_M = aC$. Also in Ngwa et al [11] and Chitnis et al [7] they have the same type of scaling before examining, even if they do

not assume constant populations, they still study equations for these relative population sizes.

In the NDM-model, we scale the population sizes in each class by the total population sizes to derive a scaled version of the model above, by introducing the following new variables:

$$s = \frac{S_H}{N_H}, x = \frac{I_{H1}}{N_H}, r = \frac{R_H}{N_H}, y = \frac{I_{H2}}{N_H}, u = \frac{S_M}{N_M}, z = \frac{I_M}{N_M}.$$

With these new variables, the equations become

$$\begin{aligned} s' &= b - \beta_H m s z + \omega r - \mu_H s - \varepsilon_s \\ x' &= \beta_H m s z - \gamma x - (\delta_1 + \mu_H)x - \varepsilon_x \\ r' &= -c\beta_H m z r + \alpha y + \gamma x - \omega r - \mu_H r - \varepsilon_r \\ y' &= c\beta_H m z r - \alpha y - (\delta_2 + \mu_H)y - \varepsilon_y \\ u' &= b_M - \beta_M u(x + ky) - \mu_M u - \varepsilon_u \\ z' &= \beta_M u(x + ky) - \mu_M z - \varepsilon_z \end{aligned} \quad (10)$$

where $m = \frac{N_M}{N_H}$ and $\varepsilon_j = \frac{jN'_H}{N_H}$ if $j = s, x, y, r$, and $\varepsilon_i = \frac{iN'_M}{N_M}$ if $i = u, z$, where $\frac{N'_H}{N_H} = (b - \mu_H) - \delta_1 x - \delta_2 y$, and $\frac{N'_M}{N_M} = b_M - \mu_M$. Assuming in system (11) $b_M = \mu_M$ and constant host population, we can derive a simplified system

$$\begin{aligned} x' &= \beta_H m s z - \gamma x - (\delta_1 + \mu_H)x \\ r' &= -c\beta_H m z r + \alpha y + \gamma x - \omega r - \mu_H r \\ y' &= c\beta_H m z r - \alpha y - (\delta_2 + \mu_H)y \\ z' &= \beta_M u(x + ky) - \mu_M z \end{aligned} \quad (11)$$

where $s = 1 - x - y - r$, and $u = 1 - z$.

We assume $b_M = \mu_M$ meaning the mosquito population is constant. Then ε terms seem to have no effect on the system in moderate time. In moderate time, the solution curves of system (11) are close to the solution curves of the simplified system (11) and after that, slowly move close to a curve of equilibria of the simplified system where parameter m changes.

3 Main Results

In this section we present and prove our main results. Before we do that,

we introduce the following notations.

Notations

$$\begin{aligned} r_x &= \frac{\gamma}{\omega + \mu_H}, \quad r_y = \frac{\mu_H + \delta_2}{\omega + \mu_H}, \quad \gamma_1 = \gamma + \mu_H + \delta_1, \\ \Delta b &= \frac{\delta_2}{1 + kc\gamma_1 r_y / \alpha_1 - r_y}, \quad B = \frac{\beta_H \beta_M}{\gamma_1 \mu_M}. \end{aligned} \quad (12)$$

We have the following main results:

Results for simplified system.

The simplified system has a unique endemic equilibrium for $m > \frac{1}{B}$ which is always a global attractor. For $m \leq \frac{1}{B}$ there is no endemic equilibrium and the disease-free equilibrium where $x = r = y = z = 0$ (and thus $s = u = 1$) is a global attractor. When m changes the endemic equilibria form a curve C_e in the phase space parameterized by m .

Results for original system.

For $\mu_H < b < \Delta b + \mu_H$ the original NDM-system has an equilibrium on the curve C_e which is a saddle with a four dimensional stable and one dimensional unstable manifold. The unstable manifold is well approximated by the curve C_e . On one side of the stable manifold of the saddle point the total host population slowly decreases to zero and on the other side, the population increases to infinity and getting to disease-free situation after the value of m has passed $\frac{1}{B}$. If $b \leq \mu_H$ the host population will decrease to zero near the curve C_e and if $b > \Delta b + \mu_H$ the host population will go to infinity near the curve C_e , becoming disease-free when m has passed $\frac{1}{B}$.

3.1 Calculations of endemic equilibrium for simplified system

(Existence of endemic equilibrium solution). We now show how to get the expressions for the curve C_e by solving for the equilibria for (11). We also prove that, this equilibrium is unique provided it exists.

From (11) we see that if; $x' = 0$, then

$$x = \frac{\beta_H}{\gamma_1} m s z, \quad (13)$$

$y' = 0$, then

$$y = \frac{c\beta_H}{\alpha_1}mrz, \quad (14)$$

where $\alpha_1 = \alpha + \mu_H + \delta_2$.

$r' + y' = 0$, then

$$r = r_x x - r_y y. \quad (15)$$

$z' = 0$ and using $u = 1 - z$, then

$$z = \frac{\beta_M(x + ky)}{\beta_M(x + ky) + \mu_M}. \quad (16)$$

Using these formulas we deduce an expression also for s . Some calculations give

$$s = \frac{1}{Bm} + C_1 x + C_2 y \quad (17)$$

where $C_1 = \frac{\gamma_1}{\beta_H m} - \frac{kc\gamma_1 r_x}{\alpha_1}$, and $C_2 = \frac{kc\gamma_1 r_y}{\alpha_1} + \frac{k\gamma_1}{\beta_H m}$.

From $s + x + r + y = 1$ using (15) and (17) we can solve for y as linear expression of x (that is, $y = L - Qx$) and substituting into (14) we get a second order equation for x as follows:

$$\eta_2 x^2 + \eta_1 x + \eta_0 = 0 \quad (18)$$

where

$$\begin{aligned} \eta_2 &= \beta_M(kQ - 1)(r_y A Q + Q + r_x A) \\ \eta_1 &= -2\beta_M k r_y A L Q - 2\beta_M k L Q - \mu Q + \beta_M r_y A L - \beta_M k r_x A L + \beta_M L \\ \eta_0 &= L(\beta_M k r_y A L + \beta_M K L + \mu_M) \end{aligned} \quad (19)$$

and where $Q = \frac{1 + C_1 + r_x}{1 + C_2 - r_y}$, $L = \frac{1 - \frac{1}{Bm}}{1 + C_2 - r_y}$, and $A = \frac{c\beta_H m}{\alpha_1}$.

Knowing x , we can easily calculate the other variables at equilibrium. Variable y is calculated from the linear expression in x and r from (15) and finally we have $s = 1 - x - r - y$, $u = 1 - z$.

(Uniqueness of endemic equilibrium solution). We now prove the uniqueness of the endemic equilibrium of the simplified system. Here we show that there is exactly one endemic equilibrium for the simplified system in the case $m > \frac{1}{B}$ and otherwise no endemic equilibrium.

For our range (see, Tables 7 to 12) of parameters Q must be positive. For y to be positive we need $x < \frac{L}{Q}$. For our range of parameters $L < Q$ and $\frac{L}{Q} < 1$.

We show that there is exactly one solution of equation (18) for $0 < x < \frac{L}{Q}$ when $m > \frac{1}{B}$. From $m > \frac{1}{B}$ follows $L > 0$. Equation (18) is quadratic or linear and as the value on the left hand side is positive for $x = 0$ and negative ($-\frac{\beta_M r_x A L^2}{Q^2}$) for $x = \frac{L}{Q}$ it must have exactly one solution in the interval from 0 to $\frac{L}{Q}$. For $m \leq \frac{1}{B}$ we get $L \leq 0$ and there is then no positive solution for y if $Q > 0$. Using the x value found for $m > \frac{1}{B}$ and calculating y and inserting these into the expressions for s, r, y, z and u , we see that all of them will be positive and less than one.

The solution considered as a function of m will be a parameter form for the curve C_e .

If we have parameters a little bit outside our parameter ranges, then Q might become negative and we have in the case $m < \frac{1}{B}$ the possibility of two endemic equilibria for the simplified system, one stable and the other unstable.

3.2 Calculations of the equilibrium for the original NDM system

In this section we take a look at equilibrium for the original system. In order to find the equilibrium we let $N'_H = 0$. For this equilibrium, the relations (13), (14), (15), (16) and (17) are valid. From (11) we see that if $N'_H = 0$, then

$$\delta_1 x + \delta_2 y = b - \mu_H. \quad (20)$$

From $x + y + r + s = 1$ using (15) and (17) we get

$$(1 + C_1 + r_x)x + (1 + C_2 - r_y)y = 1 - \frac{1}{Bm}. \quad (21)$$

Solving (20) and (21) with respect to x and y we get

$$\begin{aligned} x &= \frac{x_{n1}m + x_{n0}}{x_{d1}m + x_{d0}} \\ y &= \frac{y_{n1}m + y_{n0}}{x_{d1}m + x_{d0}} \end{aligned} \quad (22)$$

where $x_{n1}, x_{n0}, y_{n1}, y_{n0}, x_{d1}, x_{d0}$ do not depend on m and are given by the ex-

pressions below

$$\begin{aligned}
x_{n1} &= (c\gamma_1 k\mu_H r_y - \alpha_1 \mu_M y_y - bc\alpha_1 k r_y + \alpha_1 b r_y + \alpha_1 \mu_H + \alpha_1 \delta_2 - \alpha_1 b)\beta_H B \\
x_{n0} &= (\gamma_1 k\mu_H B - b\gamma_1 k B - \beta_H \delta_2)\alpha_1 \\
x_{d1} &= (c\delta_1 \alpha_1 k r_y - \alpha_1 \delta_1 r_y + c\delta_2 \gamma_1 k r_x - \alpha_1 \delta_2 + \alpha_1 \delta_1)\beta_H B \\
x_{d0} &= (\delta_1 k - \delta_2)\alpha_1 \gamma_1 B \\
y_{n1} &= (c\gamma_1 k\mu_H r_x - \alpha_1 \mu_H r_x - bc\gamma_1 k r_x + \alpha_1 b r_x - \alpha_1 \mu_H - \alpha_1 \delta_1 + \alpha_1 b)\beta_H B \\
y_{n0} &= (-\gamma_1 \mu_H B + b\gamma_1 B + \beta_H \delta_1)\alpha_1
\end{aligned} \tag{23}$$

By substituting (16) into (14) we get

$$y(\beta_M(x + ky) + \mu_M) = \frac{c\beta_H}{\alpha_1} \beta_M m(r_x x - r_y y)(x + ky). \tag{24}$$

Calculations show that $\beta_M(x_{n0} + ky_{n0}) + \mu_M x_{d0} = 0$ and thus substituting (22) into (24) the numerator gives a third order equations in m as follows:

$$q_3 m^3 + q_2 m^2 + q_1 m = 0, \tag{25}$$

where the coefficients

$$\begin{aligned}
q_3 &= \beta_H \beta_M c(ky_{n1} + x_{n1})(r_y y_{n1} - r_x x_{n1}) \\
q_2 &= \alpha_1 \beta_M k y_{n1}^2 + 2\beta_H \beta_M c k r_y y_{n0} y_{n1} + \alpha_1 \beta_M x_{n1} y_{n1} + \beta_H \beta_M c r_y x_{n0} y_{n1} \\
&\quad - \beta_H \beta_M c k r_x x_{n0} y_{n1} + \alpha_1 \mu_M x_{d1} y_{n1} + \beta_H \beta_M c r_y x_{n1} y_{n0} \\
&\quad - \beta_H \beta_M c k r_x x_{n1} y_{n0} - 2\beta_H \beta_M c r_x x_{n0} x_{n1} \\
q_1 &= 2\alpha_1 \beta_M k y_{n0} y_{n1} + \alpha_1 \beta_M x_{n0} y_{n1} + \alpha_1 \mu_M x_{d0} y_{n1} + \beta_H \beta_M c k r_y y_{n0}^2 \\
&\quad + \alpha_1 \beta_M x_{n1} y_{n0} + \beta_H \beta_M c r_y x_{n0} y_{n0} - \beta_H \beta_M c k r_x x_{n0} y_{n0} + \alpha_1 \mu_M x_{d1} y_{n0} \\
&\quad - \beta_H \beta_M c r_x x_{n0}^2.
\end{aligned} \tag{26}$$

Solving equation (25), we obtain three values of the ratio m between the mosquito and host population at equilibrium. We consider the positive value of m and substituting this value into (22) we get the values of x and y , after which we can calculate the values of the other variables from (15), (16) and from $s = 1 - x - y - r$ and $u = 1 - z$. The equations (20) and (21) have positive solutions only for $\mu_H < b < \Delta b + \mu_H$.

3.3 Numerical results

Extensive numerical experiments indicate that the endemic equilibrium for the simplified system is a global attractor when it exists and the disease-free equilibrium is globally attracting when there is no endemicity.

From numerical solutions of equation (25) we observe there is exactly one solution when $\mu_H < b < \Delta b + \mu_H$ and calculating the eigenvalues of the Jacobian matrix, we find that the equilibrium is a saddle with one dimensional unstable set.

For other systems (like Chitnis et al and Ngwa et al) there might be a stable equilibrium on the slow motion curve attracting all solutions. Whether this equilibrium can be reached in realistic time, depends on the concrete parameter values and the initial conditions. In Chitnis et al there is sometimes the possibility for more than one equilibria.

The ratio $K = \frac{\beta_H \beta_M m}{\gamma \mu_M}$ is an important approximative bifurcation parameter, so that there is a transcritical bifurcation for the simplified system at $K = 1$ and endemic solution exists only for $K > 1$. The proportion of susceptible population is approximately $1/K$. We can get the value of K analytically by requiring the determinant of the Jacobian matrix to be zero at the disease-free equilibrium.

Experiments show that by varying different parameters and initial conditions for the first 3 years, the simplified NDM model approximates well, to the original NDM model with a relative error of less than 2 percent. This situation occurs if the simplified model has an endemic equilibrium with a size not too small (i.e., the value of K is not too near to the bifurcation value) and in addition the sizes of some of the populations are not less than 1 percent of the total population.

Experiments also show that in the long term the dynamics follows the curve C_e which might have a saddle point on it. The Figures 2 and 3 depicts the long term behavior of the system.

By using the standard values of the NDM system and varying the b parameter, a saddle point is seen to exist in the interval for b and this is found to be approximately in the range $[0.000055, 0.000065]$. In Figure 2 we see the result of simulations of the NDM system with standard values but parameter $b = 0.00006$ for initial value a little bit above the stable set of the saddle point. The coordinates are in relative host populations. First there

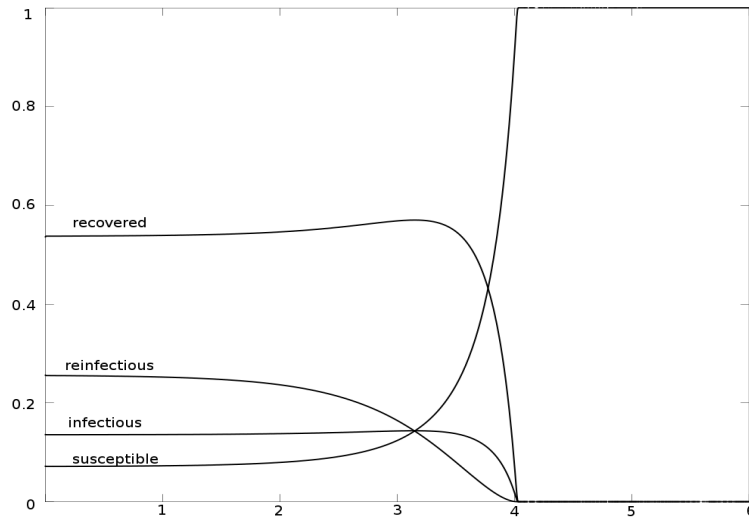


Figure 2: Relative coordinates on slow motion curve when host population grows

is slow movement out from the saddle point along the unstable set showing almost constant values of variables, but growing faster when population grows and then changing slowly until the population is so great that we have the disease-free situation. In this part of the unstable set, the relative size of the susceptible host population, starts from a low value near the saddle point and grows until it approaches a disease free situation.

The relative size of all other host populations decrease until they disappear for disease-free cases. Also the total host population is growing, implying a decrease in the mosquito-host ratio m , leading to disease-free in the long run.

In Figure 3 we see the result of simulations of the NDM system with standard values but parameter $b = 0.00006$ for an initial value a little bit below the stable set of the saddle point. We see slow movement to the situation when total population is zero and the mosquito-host ratio m grows to infinity. The relative size of all other host populations, except the re-infectious is decreasing and for small total host population the re-infectious class is dominating. The susceptible host population is always low.

In both of these cases there is a good agreement with the curve C_e and a

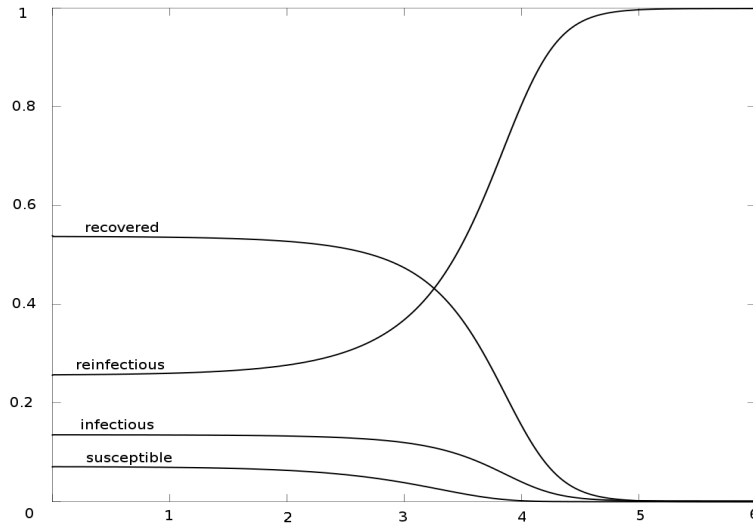


Figure 3: Relative coordinates on slow motion curve when host population decreases

point on that curve corresponds to the sizes of the populations at a given time in the figures.

4 Conclusion

Most mathematical models of malaria can be divided into two classes. Those simplified, assuming total host and vector population constant, and those allowing at least the host population to change. In general the change in the size of the total host populations are slow compared with the other developments and then the system can be very well approximated by a simplified system. An exception is when the migration factor is greater as in Chitnis [6] and [7], and then affecting essentially the dynamics for some initial conditions. Here we assumed the mosquito population constant and thus did not consider the interesting question of oscillating mosquito population.

In simplified models, we have at least one equilibrium that is the disease-free situation. Disease-free equilibrium points are steady state solutions where

there is no malaria in either the human or mosquito populations.

In most models for some parameter ranges we also have endemic equilibria, where the disease persists in the population (all state variables are positive). In some models (and this is usual in models with non-linear incidence terms) we can have more than one endemic equilibrium.

In the model where the host population changes, the motion can often be divided into fast motion and slow motion. First there is a fast motion as a result of coming near to an attracting point of a corresponding simplified system with constant host populations (often about 3 years). This fast motion is often very well approximated by the solution curve of the corresponding simplified system. After that there is a slow motion along approximately a curve of endemic equilibria for simplified systems for different total host populations. On this curve, the system with changing host population can have one or more equilibria which are saddles or attractors, or the motion will increase the host population to infinity or decrease it to zero. In reality only a small part of this curve is seen to be realized as it might take millions of days to move far away.

The equilibrium points are usually either stable or saddle points. If they are stable they have a basin of attraction determining global behavior. In the simplified Ross and NDM-model and the full Ngwa et al model we have only two possibilities. Either there is no endemic and the disease-free is a global attractor and we have no possibility for endemic or there is endemic and the endemic equilibrium is attracting everything except the disease-free equilibrium, so we will reach endemic independently of the initial situation.

In other models there is the possibility that both disease-free and endemic equilibria are stable. Between the stable equilibria there is usually a saddle endemic equilibria, determining the boundary of the basins of attractions of equilibria. In these cases it depends on the initial conditions whether we get endemic or disease-free situation.

Usually the endemic equilibrium appears at a transcritical bifurcation at the disease-free equilibrium. This is the case for the simplified Ross and NDM-model and full Ngwa et al model and usually also for the Chitnis et al model. There is also a possibility for saddle-node bifurcations where two endemic equilibria arise suddenly, one stable and the other of a saddle type. This can happen in the Chitnis et al model and is usually in models with non-linear incidence. In Chitnis et al [6], this sometimes happens on the slow

motion curve but never for the simplified versions. In the NDM-model the existence of a real endemic equilibrium depends approximately on the value of a quantity of four essential parameters and the ratio between mosquitos and host populations and this is also usual for many other models.

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References

- [1] S. Mandal, R.R. Sarkar and S. Sinha, Mathematical models of malaria - a review, *Malaria Journal*, **10**(202), (2011), 1475-2875.
- [2] R. Ross, *The Prevention of Malaria*, John Murray, London, 1911.
- [3] G. Macdonald, *The Epidemiology and Control of Malaria*, Oxford University Press, London, 1957.
- [4] K. Dietz, L. Molineaux and A. Thomas, A malaria Model Tested in the African Savannah, *Bull. World Health Organ*, **50**(3-4), (1974), 347-357.
- [5] J. Nedelman, Introductory Review: Some New Thoughts About Some Old Malaria Models, *Mathematical Biosciences*, **2**(73), (1985), 159-182.
- [6] N. Chitnis, J.M. Cushing and J.M. Hyman, Bifurcation Analysis of a Mathematical Model for Malaria Transmission, *SIAM J. Appl. Math.*, **67**(1), (2006), 24-45.
- [7] N. Chitnis, J.M. Hyman and J.M. Cushing, Determining Important Parameters in the Spread of Malaria Through the Sensitivity Analysis of a Mathematical Model, *Bulletin of Mathematical Biology*, **70**(5), (2008), 1272-1296.

- [8] N. Chitnis, *Using Mathematical Models in Controlling the Spread of Malaria*, PH.D. Thesis, Program in Applied Mathematics, University of Arizona, Tucson, AZ USA, 2005.
- [9] R.M. Anderson and R.M. May, *Infectious Diseases of Humans: Dynamics and Control*, Oxford University Press, Oxford, UK, 1991.
- [10] G.A. Ngwa, Modelling the Dynamics of Endemic Malaria in Growing Populations, *Discrete Continuous Dynamical Systems Series B*, **4**(4), (2004), 1173-1202.
- [11] G.A. Ngwa and W.S. Shu, A mathematical Model for Endemic Malaria with Variable Human and Mosquito Populations, *Mathematical and Computer Modelling*, **32**(7-8), (2000), 747-763.
- [12] Ricardo guas, Lisa J. White, Robert W. Snow, M. Gabriela and M. Gomes, Prospects for Malaria Eradication in Sub-Saharan Africa, *PLoS ONE*, **3**(3), (2008), e1767.
- [13] S. Nortey, E. Danso-Addo and T. Marijani, Reducing Severe Cases In Malaria In Low Endemic Area, *SACEMA-DIMACS, AIMS*, (2008).
- [14] B. Akoto, E.K. Essel and G. Soderbacka, On Behaviour of A Host-vector Epidemic Model with Non-linear Incidence, *Studies in Mathematical Sciences*, **4**(1), (2012), 6-17.
- [15] World Health Organization, World Health Organization Report on Malaria in Ghana, *WHO*, (2010).
- [16] H.W. Hethcote, The Mathematics of Infectious Diseases, *SIAM Review*, **42**(4), (2000), 599-653.
- [17] S. Owusu-Agyei, K.P. Asante, M. Adjuik, G. Adjei, E. Awini, M. Adams, S. Newton, D. Dosoo, D. Dery, A. Agyeman-Budu, J. Gyapong, B. Greenwood and D. Chandramohan, Epidemiology of Malaria in the Forest - Savanna Transitional Zone of Ghana, *Malaria Journal*, **8**(220), (2009).