

Parallel Session
Epidemiology X

MODELLING THE ROLE BETWEEN
ANTIBODY-DEPENDENT ENHANCEMENT AND
HETEROLOGOUS SECONDARY INFECTION IN
SEVERE DENGUE

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Keywords: Antibody-dependent enhancement, Severe dengue.

We develop a mathematical model to explore the effects of antibody-dependent enhancement (ADE) on heterologous secondary infections due to a previous infection with one serotype of dengue virus. The model has a virus-free equilibrium which is locally asymptotically stable under certain conditions, but not globally stable (it is not an attracting point depending on the initial inoculation of viral load by infected mosquitoes). This stability arises due to the interplay between basic reproduction number of virions and ADE weakening factor. Other locally asymptotically stable virus-presence equilibrium can exist, depending on the trade-off between the strength of proliferation of memory immune cells and apoptosis of infected macrophages. However, ADE must be accounted in the initial stage of infection (a window of time of few days), period of time elapsed from the heterologous infection until the immune system mounting an effective response against the secondary infection. We apply the results yielded by model to evaluate ADE phenomenon in heterologous dengue virus infection. We also hypothesize the occurrence of ADE *in vitro* in Zika virus infection, but not *in vivo*.

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References

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COMPARATIVE ANALYSIS OF DENGUE VERSUS CHIKUNGUNYA OUTBREAKS IN COSTA RICA

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Keywords: Dengue, Chikungunya, Mathematical Epidemiology, Parameter Estimation, Genetic Algorithm.

For decades, dengue virus has been a cause of major public health concern in Costa Rica, due to its landscape and climatic conditions that favor the circumstances in which the vector, *Aedes aegypti*, thrives. The emergence and introduction throughout tropical and subtropical countries of the chikungunya virus, as of 2014, challenged Costa Rican health authorities to provide a correct diagnosis since it is also transmitted by the same vector and infected hosts may share similar symptoms. We study the 2015-2016 dengue and chikungunya outbreaks in Costa Rica while establishing how point estimates of epidemic parameters for both diseases compare to one another. Longitudinal weekly incidence reports of these outbreaks signal likely misdiagnosis of infected individuals: underreporting of chikungunya cases, while overreporting cases of dengue. Our comparative analysis is formulated with a single-outbreak deterministic model that features an *undiagnosed* class. Additionally, we also used a *genetic algorithm* in the context of weighted least squares to calculate point estimates of key model parameters and initial conditions, while formally quantifying misdiagnosis.

References

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A FIRST GLIMPSE ON INSECTICIDE RESISTANCE DEVELOPMENT

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Keywords: Modelling, *Aedes aegypti*, Population Control, Genes.

The 5-stage structured population model proposed by Schechtman and Souza[1] was modified to comprise insecticide resistance as a recessive trait and allow for additional death rates at the larval and imago stages.

Insecticide at the larval stage was considered to affect all genotypes equally. Insecticide at the two imago stages, *i.e.* immature and mature sexually, did not affect the resistant homozygous genotype. In other words, insecticide affected both the homozygous susceptible and the heterozygous genotypes.

Insecticide resistance was assessed by evaluating the total fraction of the gene for resistance present in the population, which is a natural index choice when the dynamics is in a quasi-Hardy-Weinberg equilibrium.

Two insecticides policies were evaluated. For both policies larval insecticide was applied throughout the year with an efficacy of 90%.

The first policy comprised of 6 single applications of adult insecticide, with a resting interval of 4 days between any two consecutive applications, at the beginning of the summer season. The efficacy of the insecticide was 10% and a fitness cost of 0.005.

A second, very intense, policy comprised of 18 blocks of applications of adult insecticide, with a resting interval of 2 days between any two consecutive blocks of applications, during the summer season. Each block of application consisted of two daily applications of insecticide for 5 consecutive days. The efficacy of the insecticide was 6% and a fitness cost of 0.05.

For the two scenarios here presented, insecticide resistance as expressed by an increase in the fraction of the gene for resistance only occurred for the very intensive policy.

References

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MATHEMATICAL MODELLING OF MOSQUITO MOVEMENT FOR MALARIA VECTOR CONTROL

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Keywords: Malaria vector control, Individual-based modelling, Stochastic modelling.

Since the year 2000, considerable reduction in malaria transmission and disease burden has been achieved via mosquito control. But the rates of decline in malaria cases and deaths have stalled globally since 2014, and therefore new mosquito control tools are urgently needed both to address coverage gaps and increasing insecticide resistance. Mathematical models play a key role in designing control interventions, but usually operate without explicit notion of space or only in large scale discrete space. Modelling the movement of Anopheles mosquitoes on a fine spatial scale and coupling these models with early trial data of new mosquito control tools could help to design and assess new tools.

Here we present a new continuous space, individual-based, stochastic model for the movement of Anopheles mosquitoes while foraging. We define basic rules comprising random perturbations for the behaviour of a single mosquito in response to inputs of environmental factors like wind, attractants, repellents and physical barriers. This model is highly flexible and can predict entomological outcomes such as biting rates and mosquito survival rates for arbitrary combinations of different mosquito control tools being placed at various places in the study area. The model is parameterized to data from semi-field mark-release-recapture experiments testing odour-baited traps (pull) and spatial repellents (push). As a result, we recommend spatial configurations of push and pull devices placed in the given experimental setup at the same time. Hence we contribute to the development of a working push-pull system targeting outdoor transmission of malaria.

In the future, the inclusion of breeding sites and mosquito life cycle could further improve the understanding of mosquito behaviour and facilitate the development of other new vector control tools as well.

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ESTIMATION OF THE EXPECTED NUMBER OF CASES OF MICROCEPHALY IN BRAZIL AS A RESULT OF ZIKA

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Keywords: Zika virus, Microcephaly, Dengue Ω *Aedes aegypti*.

In this talk we shall describe a delayed dengue model adapted to zika. By assuming that the epidemic starts by a single infected individual entering a disease-free population at some initial time t_0 we have used the least squares parameter estimation technique in R to estimate the initial time t_0 using observed zika data from Brazil as well as the transmission probabilities of zika in Brazil between humans and mosquitoes and vice-versa. Different values of *Aedes aegypti* (*A. aegypti*) biting rate are used throughout the talk.

We have estimated the value of the basic reproduction number for zika in Brazil and calculated the expected number of cases of microcephaly in newborns as a result of women infected with zika during pregnancy. We started off with a non-age-structured model then introduced age-structure into the model.

However in reality seasonality, in particular temperature and rainfall, have a great impact on the population size of *A. aegypti*. Hence we repeat both the non-age-structured and age-structured analyses introducing seasonality into the *A. aegypti* birth function to model the effect of these environmental factors.