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Analysis of the vectorial capacity of vector-borne diseases using moment-generating functions

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ABSTRACT

The vectorial capacity of a mosquito species that is a disease-vector indicates the expected number of infectious bites given by all mosquitoes infected from biting a single infected human individual, assuming perfect transmissions between humans and vectors. Assessing this number for different transmitting species of the same disease, such as dengue or malaria, expresses how capable these species are of spreading the disease. We describe the vectorial capacity as a random process and present a model for analyzing its probability distribution. Our stochastic model permits us to obtain the moment-generating function for the distribution of the vectorial capacity and, under reasonable assumptions, the probability distribution itself. A stochastic modeling framework is helpful for analyzing the dynamics of disease spreading, such as when performing sensitivity analysis.

1. Introduction

Seminal works by Ross [1] and MacDonald [2] analyzed the dynamics of malaria transmission under mathematical models. These works built a framework for modeling diseases caused by pathogens transmitted by vectors, in particular by mosquitoes such as several species of *Anopheles* (malaria vectors), as well as *Aedes* mosquitoes (dengue vectors). Garrett-Jones [3–5] proposed the concept of vectorial capacity (Garrett-Jones' vectorial capacity): the number of infectious inoculations by a given vector to humans, per unit of time, that arise from an index case, assuming perfect transmission between humans and vectors.

Such modeling framework has been applied not only for comparing malaria vectors, but also for comparing vectors of other diseases such as dengue, already well-known for regularly causing epidemics throughout the world, and also emerging infections, such as Chikungunya. For different species of vectors of a disease, their vectorial capacities indicate how capable the species are of transmitting the disease. Conversely, they can also be used to evaluate strategies for controlling the disease spreading. In the case of malaria, multiple *Anopheles* species transmit the malaria parasite (also multiple *Plasmodium* species). The vectorial capacity permits us to compare their respective rates of transmitting the infection in purely entomological parameters. Also, different populations of the same species can be compared using this metric, for instance if using strategies such as transgenic mosquitoes versus wild ones.

In order to estimate the expected number of infectious bites, epidemiologists and entomologists measure several parameters that describe the vector's biological behavior and also the interaction between the vector and both pathogens and humans. Let the density of vectors in a given area be m (vectors per humans). Mosquitoes transmit (or receive) pathogens

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to (from) humans when having human-blood meals for which they need to bite human individuals. For the mosquito to become infectious, i.e., being able to infect humans, the viremia levels need to be sufficient at their salivary glands. The necessary parameters are the biting rate λ (bites per time unit), mortality rate g, and the time ν required by pathogens for a vector to become infectious, i.e., to enter a disease-transmitting state. Garrett-Jones vectorial capacity C is[1]:

$$C = \frac{m\lambda^2 e^{-g\nu}}{g}. \tag{1}$$

The vectorial capacity differs from the basic reproduction number R_0, which quantifies the disease transmission dynamics from humans to humans, therefore considering transmission from human to vector, and from vector to other humans (incorporating for instance the vectorial competence), and the recovery rate as well. By considering the recovery rate, the basic reproduction number R_0 also determines whether an epidemic might occur by the condition $R_0 > 1$. Aron and May [26] derived the reproduction number as $R_0 = \frac{mb\lambda^2 e^{-g\nu}}{gr}$, where b gives the vectorial competence and the recovery rate is given by r. Clearly, the vectorial capacity is an important factor in deriving R_0.

As helpful as an expected number, the vectorial capacity metric has been reviewed using deterministic models in several works. Anderson and May in [6] provided a comprehensive literature review of this modeling framework. Smith and McKenzie [7] revisited the formulae involved in the statics and the dynamics of malaria infections. Smith et al. [8] described the history behind the contributions of Ross and MacDonald. Massad and Coutinho [9] derived a formulation to explain the dimensionless property of the number. As deterministic analyzes, these works focus on the mean value formula presented by Garrett-Jones.

The average-based vectorial capacity has been used and even extended using deterministic approaches and considering other factors that impact one or various of its parameters. For instance, Jansen et al. [10] used the concept to evaluate risks by different *Aedes* species of introducing chikungunya in Australia. Novoseltsev et al. [11] derive the vectorial capacity assuming age-structured population model. Liu et al. [12] propose estimations of temperature-dependent vectorial capacity.

Bailey [13,14] analyzed epidemics using stochastic models, including using moment-generating functions, which provided a seminal body of work in its own right. Also, for a general epidemic process, Ball and Donnelly [15] present approximations results, using moment-generating functions.

Nevertheless, the treatment presented here using moment-generating functions to describe the vectorial capacity has not appeared elsewhere, to the best of our knowledge, and can be quite important to advance the study of the vectorial capacity. We demonstrate the derivation of the probability distribution and the mean value formula given by Eq. (1) as an expected number from the vectorial capacity distribution.

The Methods section contains our model description, assumptions, and the definition of moment-generating functions. In the Results section we derive the moment-generating function for the vectorial capacity process. In our results, we demonstrate using the moment-generating function the moments of the vectorial capacity process. We also illustrate the probability distribution as a numerical example by considering parameters that describe density, survival, biting rate, and incubation period, which were estimated from other works in the literature. We end with discussion about other stochastic models and their possibilities.

2. Models and methods

2.1. Moment-generating functions

For any generic random variable X the moment-generating function (MGF) is defined by $X^*(\theta) = E[e^{\theta X}]$.[2] Therefore,

$$X^*(\theta) = \int_0^\infty e^{\theta x} P(X = x)dx. \tag{2}$$

For discrete distributions, which is the case of the variable that describes the vectorial capacity is convenient to work with the z-transform:

$$X^*(z) = \sum_{k=0}^{\infty} z^k P(X = k), z = e^\theta, \text{ if } X \text{ is discrete.}$$

Two properties of MGFs are important in our derivations. First, since a MGF is unique for any given probability distribution, once a MGF is known we can obtain either analytically by an inverse transformation or at least numerically the distribution itself. Second, for a sum of random variables, the MGF is the product of the individual MGFs [16]. This property frequently helps obtaining the MGF and the probability distribution is then derived from the MGF.

MGFs, as the name suggests, are also helpful to determine moments. For instance, if applying a derivative of the MGF, $\frac{dX(z)}{dz} = \sum_{k=1}^{\infty} kz^{k-1}P(X = k)$, and $z = 1$, we find $\sum_{k=1}^{\infty} kP(X = k) = E[X]$.

[1] The original formula in [4] used a as the biting rate.

[2] The Laplace transform is the case when there is a variable replacement from θ to $-s$, i.e. $E[e^{-sX}]$.