Uncertainties Regarding Dengue Modeling in Rio de Janeiro, Brazil

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Dengue fever is currently the most important arthropod-borne viral disease in Brazil. Mathematical modeling of disease dynamics is a very useful tool for the evaluation of control measures. To be used in decision-making, however, a mathematical model must be carefully parameterized and validated with epidemiological and entomological data. In this work, we developed a simple dengue model to answer three questions: (i) which parameters are worth pursuing in the field in order to develop a dengue transmission model for Brazilian cities; (ii) how vector density spatial heterogeneity influences control efforts; (iii) with a degree of uncertainty, what is the invasion potential of dengue virus type 4 (DEN-4) in Rio de Janeiro city. Our model consists of an expression for the basic reproductive number (R_0) that incorporates vector density spatial heterogeneity. To deal with the uncertainty regarding parameter values, we parameterized the model using a priori probability density functions covering a range of plausible values for each parameter. Using the Latin Hypercube Sampling procedure, values for the parameters were generated. We conclude that, even in the presence of vector spatial heterogeneity, the two most important entomological parameters to be estimated in the field are the mortality rate and the extrinsic incubation period. The spatial heterogeneity of the vector population increases the risk of epidemics and makes the control strategies more complex. At last, we conclude that Rio de Janeiro is at risk of a DEN-4 invasion. Finally, we stress the point that epidemiologists, mathematicians, and entomologists need to interact more to find better approaches to the measuring and interpretation of the transmission dynamics of arthropod-borne diseases.

Key words: dengue modeling - uncertainties - vector density spatial heterogeneity - control measures of arthropod-borne diseases - Rio de Janeiro - Brazil

In the end of 1981, dengue fever (DF) reemerged in Brazil after 58 years of absence (Osanai et al. 1983). Coming from Central America and the Caribbean Islands, dengue virus type 1 and 4 (DEN-1 and DEN-4) caused 11,000 confirmed cases of DF in Boa Vista, Roraima. In 1986, DF emerged in Ceará (Northeast of Brazil) and Rio de Janeiro (Southeast), triggering large outbreaks. By the year 2000, all 26 Brazilian states had reported DF cases. In recent years, outbreaks have increased in frequency, with a higher proportion of dengue hemorrhagic fever cases (DHF). DF is the most important arthropod-borne viral disease in the country, being responsible for more than 2 million accumulated cases and 200 deaths. The success of DF invasion has two main reasons: (i) re-infestation of the country by its mosquito vector *Aedes aegypti*, and (ii) unplanned urbanization (Tauil 2001).

Rio de Janeiro city (RJC) has reported the largest numbers of DF cases in Brazil. Five large epidemics have occurred since 1986 (Fig. 1), when the virus was first detected. In the 1986/1987 epidemics, 93 thousand cases of DEN-1 were notified, the actual number of infected individuals might have reached 1 million (Guia de doenças - dengue 2002). In April 1990, the second epidemic was triggered by the arrival of DEN-2 through Niterói, a neighbor city. In the 1995 and 1998 epidemics, both DEN-1 and DEN-2 were responsible for more than 30 thousand cases each virus (Nogueira et al. 1999). In 2001, DEN-3 was identified in the neighbor city of Nova Iguaçu (Nogueira et al. 2001).

Despite the effort, dengue control has been a difficult task. The overall dissemination of the mosquito is evident (Travassos Da Rosa et al. 2000, Teixeira et al. 2001), and traditional (chemical) vector control measures do not seem to make a real difference. Failure of the *Ae. aegypti* eradication goal has prompted a change in the paradigm of dengue control from a chemical-oriented strategy to a more systemic approach that includes population awareness, appropriate garbage disposal, surveillance and vector control (Programa nacional de controle da dengue 2002).

As control strategies become more complex, appropriate assessment of risk, evaluation of control efforts, and comparison of alternative strategies become more dependent on mathematical models (Focks et al. 1995, Esteva & Vargas 1998). A dengue mathematical model would be very useful for the evaluation of the Brazilian dengue control effort. To be used in decision-making, however, a mathematical model must be carefully parameterized and validated with epidemiological and entomological data. Unfortunately, despite the research effort on dengue in Brazil, information required for model parameterization still lacks.

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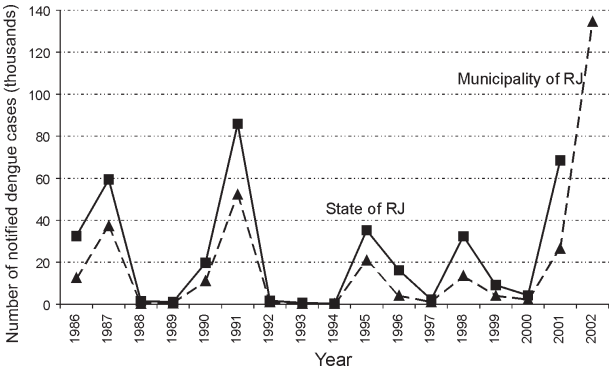

Fig. 1: number of reported cases of dengue in the state and municipality of Rio de Janeiro, from 1986 to 2001. Source: Centro Nacional de Epidemiologia, Fundação Nacional de Sáude, Ministério da Saúde and Secretaria Municipal de Saúde do Rio de Janeiro.

The first aim of this work is to determine which parameters are worth pursuing in the field in order to develop a dengue transmission model for Brazilian cities. Secondly, we analyze how much vector density spatial heterogeneity influences control efforts. Finally, we estimate, with a degree of uncertainty, the invasion potential of DEN-4 in RJC.

The invasion potential of a new pathogen is expressed by the basic reproductive number (R_0). R_0 is understood as the number of secondary infections that would be generated by an index case, after its introduction into a large susceptible population (Anderson & May 1991, Massad et al. 2001). Considering homogeneous mixing of the human population, we can restate R_0 as the expected number (or average number) of contacts that an infectious individual has during its entire infectious period (Hernandez-Suarez 2002). If $R_0 > 1$, more than one individual is infected on average by the index case. How large the outbreak will be depends upon the magnitude of R_0. Knowledge of R_0 is important for the assessment of control strategies.

The model - Risk of dengue transmission between humans is directly related to the density of infected vectors. Although the vector is a necessary element of the chain, state models can be used to represent the dynamics without clear mention of the vector, assuming that vector density is constant. In classical epidemic state models, the population is subdivided into susceptible (X), infected (Y), and recovered (R) states. The transition of individuals between states occurs at a constant rate, and individuals in the same state interact homogeneously.

Considering that vector density, in reality, varies geographically, we opted for developing a simple model with spatial heterogeneity of transmission risk. The areas are classified into two types: one with high transmission risk due to high vector density (*h*) and another with low transmission risk due to low vector density (*l*). Infectious individuals in area *h* are "more infectious" than individuals in *l* areas because the risk of infecting a mosquito is greater in area *h*. Geographical commutation of individuals between areas *h* and *l* is implicitly modeled as the movement of individuals between the two infectious states.

The outbreak potential, R_0, is computed as follows: the index case starts its infectious period in either area *h* or *l*. During this period, he commutes between the two areas with daily probability δ. The expected number of secondary cases produced by this person during the entire infectious period (R_0) is estimated as the expected daily number of secondary cases produced in area *h* (λ_h), times the time spent in *h* (D_h), plus the expected number of cases produced daily in area *l* (λ_l), times the time spent in that area (D_l). In mathematical notation: $R_0 = \lambda_h D_h + \lambda_l D_l$.

Estimating D_h and D_l - Hernandez-Suarez (2002) proposed an algorithm to estimate the time spent by an infectious individual within different infectious states. Our model is equivalent to case B described in his paper. In this paper, we give a brief description of the method; we refer the reader to the cited reference for further details.

Consider a continuous-time Markov chain model with state space $\Omega = \{X, Y_h, Y_l, R, \Lambda\}$ where X, Y_i and R are the susceptible, infected and recovered populations, and $i = l$ or h. Λ represents the individuals who die from dengue. Now, let Ω be partitioned into two subsets: $\omega = \{Y_h, Y_l\}$ is the set of infective states and $\Delta = \{X, R, \Lambda\}$ is the set of reflecting states. An individual starts his infectious period when he leaves Δ to enter ω. He remains in ω for a certain period of time until he recovers or die, returning to Δ. The embedded Markov chain, T, for this model is:

$$T = \begin{array}{c} \begin{matrix} Y_h & Y_l & \Delta \end{matrix} \\ \begin{pmatrix} 0 & \frac{\delta}{\delta+r} & \frac{r}{\delta+r} \\ \frac{\delta}{\delta+r} & 0 & \frac{r}{\delta+r} \\ \Gamma_h & \Gamma_l & 0 \end{pmatrix} \end{array}$$

Where δ is the daily probability of commutating, r is the daily probability of infection recovery, Γ_h and Γ_l are the probabilities of the index case starting his infectious period in *h* or *l*, respectively. The expected times spent in Y_h and Y_l are defined as (Hernandez-Suarez 2002, equation 4):

$$D_h = \frac{\pi_{Y_h}}{\pi_\Delta(\delta+r)}; D_l = \frac{\pi_{Y_l}}{\pi_\Delta(\delta+r)} \quad \text{where } \pi_{Y_h}, \pi_{Y_l}, \pi_\Delta$$

are elements of the stationary distribution of matrix T (Hernandez-Suarez 2002):

$$\begin{pmatrix} \pi_{Y_h} \\ \pi_{Y_l} \\ \pi_\Delta \end{pmatrix} = \begin{pmatrix} A[\Gamma_L(\delta - r) + r + 2\delta + \Gamma_H(2r+\delta)] \\ A[\Gamma_L(2r - \delta) + r + 2\delta + \Gamma_H(\delta - r)] \\ r/(2r+\delta) \end{pmatrix}$$

$$\text{where } A = \frac{(\delta+r)}{3(2\delta+r)(2r+\delta)}$$

After substituting the expressions above for π_{Yh}, π_{Yl} and some algebraic simplifications, we obtain D_h and D_l:

$$D_h = \frac{\delta + h/D}{1/D(2\delta + 1/D)}, \quad D_l = \frac{\delta + (1-h)/D}{1/D(2\delta + 1/D)}$$

Note that $D_h + D_l = D$.

Estimating λ_h and λ_l – R_0 for vector-borne diseases has traditionally been defined as (Anderson & May 1991, Massad et al. 2001):

where $R_0 = \lambda \times D$ (1)

$$\lambda = a\frac{M}{H}a\frac{e^{-\mu\tau}}{\mu}bc \quad (2)$$

In this formulation, *M* and *H* are the densities of female adult mosquitos and humans, respectively. *M/H* is the average number of female mosquitos per person. *a* is the daily bitting rate of female mosquitos, which makes $a \times M/H$ the daily average number of bites received by an individual. The probability of virus transmission from human to mosquito is *c*, so the expected number of infected mosquitos is $a \times M/H \times c$. Mosquitos, after taking an infected blood meal, spend a period of time during which they cannot transmit the virus to humans. This is called the extrinsic incubation period τ. This period is long compared to the mosquito life expectancy ($1/\mu$), and only a small fraction $\exp(-\mu t)$ of the initially infected mosquitos survives this latency period. The fraction of infected mosquitos that survives the incubation period will remain infectious for the rest of their lives. These infectious mosquitos will bite and infect humans at a daily rate of $a \times b$, where *b* is the probability of virus transmission from an infected mosquito to susceptible human per blood meal. In addition to the mosquito acquisition of the virus through the bite on an infected human host, the virus may also be passed on to other mosquito generations through transovarial transmission. However, there is no estimate in the literature of how efficient this transmission is; we opted to not include this form of virus transmission in our model.

The final model - The final model is a composition of the time spent in each area multiplied by the local force of infection:

$$R_0 = \lambda_h \times D_h + \lambda_l \times D_l \quad (3)$$

where the local force of infection for each area (λ_h and λ_l) is:

$$\lambda_h = a\frac{M_h}{H}a\frac{e^{-\mu\tau}}{\mu}bc, \quad \lambda_l = a\frac{M_l}{H}a\frac{e^{-\mu\tau}}{\mu}bc \quad (4)$$

The assumption is that the two regions are similar in all aspects but the vector-to-host relative density, which is higher in *h*. This implies that, $\lambda_h > \lambda_l$. Note that the condition for an epidemic in the presence of vector density spatial heterogeneity remains the same: $R_0 > 1$. Moreover, note that the model assumes that mosquito-to-person ratio is constant. This is a reasonable assumption if only short term dynamics is of interest (approximately 1 month).

Parameter values - Similarly to humans, mosquitos differ among themselves in terms of their life history traits. Besides individual variations, the environment (temperature and humidity) also has strong effect on the life history. Another source of uncertainties regarding appropriate parameter values is the scarcity of the data available for the Brazilian mosquito population, and the diversity among the international data. These uncertainties and variations can be incorporated into the model by associating a range of possible values to the parameters. Probability density functions (pdf) were specified for each parameter. The shape of each pdf represents our current knowledge about an aspect of the disease natural history (Blower & Dowlatabadi 1994). The bibliographical review we performed for the choice of the pdf was not comprehensive and it is likely that more information could be used to design less uncertain pdf. However, the aim was not to propose the most adequate pdf, but to indicate parameters that should be targeted by field research in Brazil. In the Table, we briefly describe the parameters, the information available in the literature and the pdfs used for each parameter. Please refer to original articles for any further information.

Estimating vector density spatial heterogeneity - In Brazil, urban vector infestation is expressed as the percentage of edifications positive for immature forms of the vector (the house index). The RJC health department publishes regularly a map classifying the neighborhoods, by the house index, into three groups: 0.01-2%, 2-5%, and 5-12%. In 2001, the house index of RJC per neighborhood varied from 0.01% to 12%, with most neighborhoods not exceeding the 5% level (Combate à dengue - Índice de pendência dos imóveis 2002). Based on the maps, we classified the neighborhoods of RJC into two classes, according to their level of mosquito infestation. The areas classified as *h* in the model correspond to neighborhoods with house index exceeding 2%. Areas classified as *l* in the model correspond to neighborhoods with house index less than 2%. A person with dengue in *h* will generate more secondary cases than one staying in *l*. I.e., a person restricted to *h* would generate R_{0h} new infections. A person restricted to *l*, would generate R_{0l} cases. Since the force of infection is greater in *h*, the following relationship holds: $R_{0h} > R_{0l}$.

Uncertainty analysis - For the uncertainty analysis, we used a Monte Carlo sampling procedure, the Latin Hypercube Sampling (Mckay et al. 2000). This sampling procedure has been described and used in deterministic models of disease transmission (Blower & Dowlatabadi 1994, Porco & Blower 1998). The procedure is as follows: each probability density function created for the parameters is divided into 1000 intervals of equal marginal probability (1/1000). Then, one value from each of these intervals is randomly sampled. This approach produces 1000 sets of different parameter values, which are mixed at random to produce input parameters for 1000 different calculations of R_0. As a result, we obtain 1000 different values of R_0. For each scenario proposed, the parameters were re-sampled from their distributions. The distribution of the output can be used to indicate the parameter space in which the R_0 assumes the characteristics of interest (values above unity).

RESULTS

Infectious person stays in the h area - Suppose that an individual infected with DEN-4 arrives in an *h* area of RJC and stays there during his entire infectious period (i.e., $\delta = 0$, $h = 1$). After *D* days of infection, he will have produced R_{0h} new human infections. Although uncertainty regarding the true ranges of the parameters of dengue transmission in RJC precludes a precise estimation of R_{0h}, we can use the a priori pdf to find a

TABLE

Description of the parameters used in the model, information gathered in the literature regarding parameters values and probability density functions used in the model

Parameter	Symbol	Information gathered in the literature	A priori probability density function
Duration of infectious period in humans (days)	D	Focks (1995): 5 days Newton & Reiter (1992): 3 days	Uniform probability density function within the interval [3, 5]
Biting rate (bites/female day^{-1})	a	Scott et al. (2000): 0.76 in Thailand and 0.63 in Puerto Rico Newton & Reiter (1992): 0.5 and 1 Focks (2000): 0.75 at 26ºC and 1.2 at 32ºC, considering three blood meals per gonothropic cylcle	Uniform probability density function within the interval [0.6, 1.2]
Mosquito to human transmission efficiency (*ad*) Human to mosquito transmission efficiency (*ad*)	b c	Focks (1995): 0.9 for b Watson & Kay (1999): 0.9 for b We found no information regarding parameter c	Uniform probability density function within the interval [0.5, 0.9] for each parameter
Extrinsic incubation period (days)	τ	Focks (1995): 8 days at 30ºC Watts et al. (1987): 7 days at 32 to 35ºC. At 30ºC: 12 days for high viral doses and 25 days for low viral doses	Triangular probability density function within [7, 25] with mode at 12
Death rate of adult female mosquitos estimated based on the daily survival probability (S), exponential model (days^{-1})	μ	Focks (1993): $S = 0.91$ Watson & Kay (1999): $S = 0.85$ Harrington et al. (2001): $S = 0.73$ (Puerto Rico) and $S = 0.82$ (Thailand) Trpis & Hausermann (1986): $S = 0.85$ Muir & Kay (1998): $S = 0.91$ Costero (1998): $S = 0.96$	Uniform probability density function within [0.04, 0.17], which corresponds to the interval [0.83, 0.96] for S
Mosquito per person density in the high density area (h) and in the low density area (l). Using the relationship proposed by Focks (2000) to estimate mosquito per person as a function of pupae per person	h l	Focks (2000): 0.34 to 2.75 pupae per person	Uniform probability density function within [0.12, 11.2] for area h [0.09, 1.02] for area l

confidence interval for this number. We calculated the value of R_{0h} for all set of parameters sampled from the a priori pdfs, and found a 95% CI for R_{0h} of [0.66-22.4]. Fig. 2 shows the results comparing the parameter values that lead to prediction of outbreak ($R_0 > 1$) and disease extinction ($R_0 < 1$). Successful transmission was obtained for an average lifespan of at least 7.7 days, i.e. a mosquito death rate of less than 0.13 day^{-1}, and an extrinsic incubation period of at most 17 days. Since low mortality and short extrinsic incubation period are associated with warm temperatures (Costero et al. 1998), this may well be the situation in the h area of RJC. Parameters a, b and D did not differ between the two qualitatively different predictive scenarios.

Infectious person stays in the l area - Now, let's suppose that the DEN-4 index case starts of in an area of type l and stays there during his infectious period (i.e., $\delta = 0$, $h = 0$). After D days, he will have produced R_{0l} new human cases. Calculating the R_{0l} for all set of parameters sampled from the a priori pdf, we found a 95% CI for R_{0l} of [0.03-14.4]. Almost half of the parameter space (48.6%) resulted into an $R_0 > 1$. This 48% of the parameter space corresponds to a probability of 48%, given the sampling algorithm used. Fig. 3 shows the results comparing the parameter values that lead to prediction of outbreak ($R_0 > 1$) and disease extinction ($R_0 < 1$). Similarly to the h scenario, outbreak in area l was related to a low mosquito death rate and short extrinsic incubation period. Parameters a, b, c and D did not differ between the two qualitatively different predictive scenarios.

Infectious person commutes between h and l areas - At last, let's suppose that the index case arrives at either the l or h area and commutes, at a rate δ, between areas during his infectious period. The number of secondary cases he will produce will be the sum of cases generated in l and in h. If the index case initiates his infectious period in l, and $\delta = 5$, the 95% CI for R_0 is [0.05 17.9]. If the index case starts in h, and $\delta = 5$, the 95% CI for R_0 is [0.05 18.1]. The longest the time spent in h, the greater the number of secondary cases produced, resulting in a greater parameter space with $R_0 > 1$ (Fig. 4). When commutation is high, a steady state situation is achieved where the index case stays 50% of his time in h and 50% in l. At this point, $R_0 > 1$ was observed in approximately 58% of the parameter

space. These 58% were, again, characterized by low mosquito death rate ($\mu < 0.09$ day^{-1}) and low extrinsic incubation period ($\tau < 13$ days) (data not shown).

DISCUSSION

The importance of the parameters μ (mortality rate) and τ (extrinsic incubation period) can be inferred from equation 3 since they enter the equation exponentially. Our work shows that these two parameters continue to be the most important parameters even in the presence of vector density spatial heterogeneity and, therefore, are worth estimating in field works. These parameters greatly influence the number of secondary cases produced by an index case, i.e. the basic reproductive number. At this point it is important to bring attention to the fact that the parameter values used in the model were not measured for the current mosquitos infesting Brazil. It is extremely necessary that we analyze our *Ae. aegypti*, its survival and incubation period in the climate of RJC. In addition, the other parameters which compose equation 4 also need to be estimated in field works. Analysis of the spatial variation of the vector capacity and biting rate of our mosquito strains would greatly aid the modeling of the disease. At last, we believe that other forms of virus transmission in the mosquito population, such as transovarial transmission, also need to be quantified in field works since they may play a role in the dynamics of the infected mosquito population.

For the second question, we conclude that the vector density spatial heterogeneity affects the dynamics of dengue since the commuting between areas with different vector densities promotes the dissemination of the disease. The reason is that the commuting exposes the infected individual to different environments, and, as a result, an epidemic has a greater chance of occurring. This conclusion is extremely important when analyzing dengue control strategies for large urban centers, as RJC. RJC is heterogeneous, vector density varies within the city, and its population does commute among different neighborhoods. The surveillance and control programs regarding the mosquito need to be done in large scale, and with the aid of the population.

Another very important aspect of vector control programs regards with the type of information gathered. In 2001, the Brazilian Ministry of Health proposed the Plan for Intensification of Actions for Dengue Control.

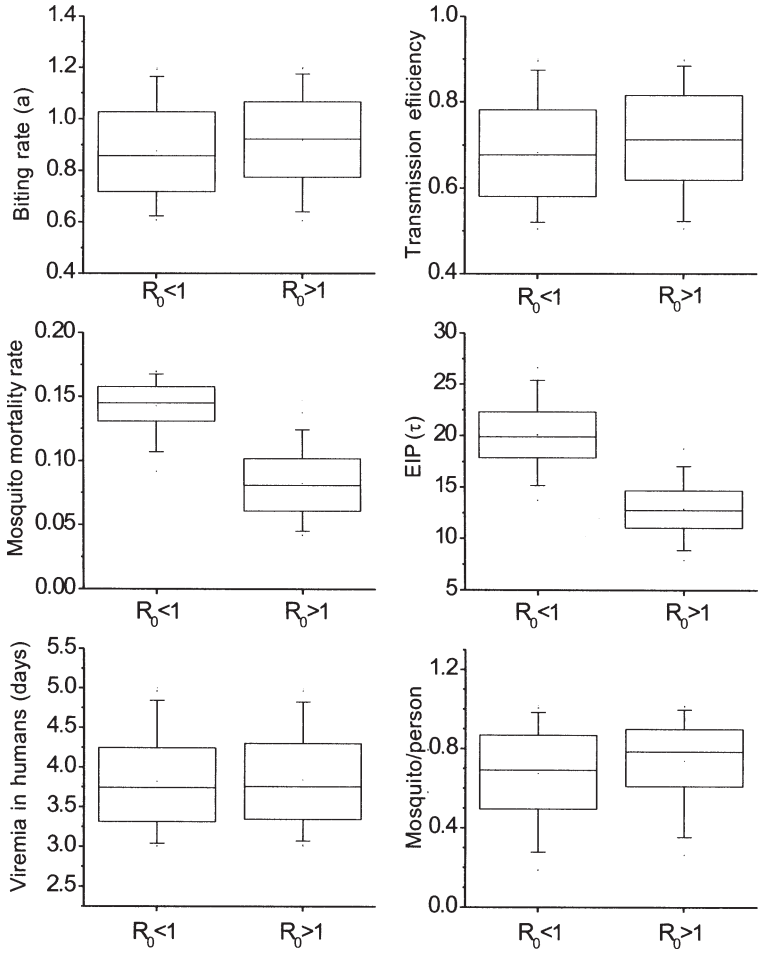

Fig. 2: box plots comparing parameter values that lead to prediction of outbreak ($R_0 > 1$) and disease extinction ($R_0 < 1$) in the scenario where an infective person arrives and stays in area *h*. Boxes indicate 25-75 percentiles; whiskers indicate the 5-95 percentiles. EIP is the extrinsic incubation period. We bring attention to the difference between the box plots for the mortality rate and the extrinsic incubation period.

One of the actions proposed in this plan is the improvement of the entomological and epidemiological surveillance in order to increase the ability to predict and detect outbreaks of the disease (Programa nacional de controle da dengue 2002). For the entomological part, the Plan proposes the surveillance of the house index as well as the proportion of permanent breeding sites per neighborhood. The goal of the control plan is to reduce the infestation index to less than 1%. However, estimates of house infestation do not translate directly into the density of the mosquito population since it does not take into account the size and larval capacity of the breeding sites. For this work, we used the pupae-to-mosquito relationship proposed by Focks et al. (2000) to estimate the standing crop from the density of pupae. Fieldwork would be necessary to validate this relationship in Brazil or to propose other estimates of standing crop.

In a study carried out in a RJC adjacent municipality, pupae were surveyed monthly, from Nov 1997 to Oct 1998, in a set of tires (Honorio & Lourenco-De-Oliveira 2001). They reported an average production of 0.08 to 5.08 pupae per tire (all tires positive for larvae and eggs). Using the relationship proposed by Focks et al. (2000), each tire should produce from 0.028-20.7 females. If we consider the relationship proposed by Focks et al. (2000) as valid for RJC, then the standing crop produced by tires is quite above the levels used in our model, suggesting that the situation might be even more complicated. There is an urgent need for a better analysis of the mosquito density: number of breeding sites, their sizes and capacities.

At last, we found that RJC is prone to a DEN-4 epidemic. Our model shows that, even regions considered as having a "low" infestation rate (1% infestation index), can bear an epidemics. In RJC, most of the mosquito breeding sites are located in houses. A large fraction of the population does not allow access of vector control professionals to their houses. We must rely strongly on population education and hope that residents take responsibility regarding the control of breeding sites at their own houses.

Using ecology terminology, we can say that *h* and *l* neighborhoods are source and sink habitats for the dengue virus. In source-sink structured environments, some habitats allow a positive net growth rate of a population (sources) and a negative net growth rate in the other fraction (sinks). A population may persist in a sink habitat

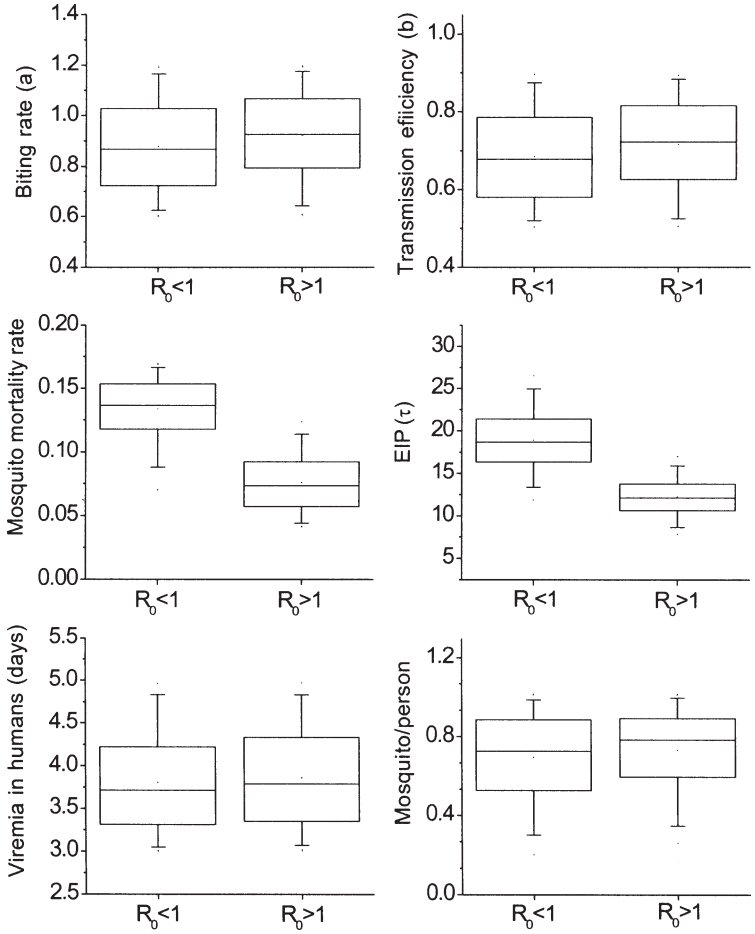

Fig. 3: box plots comparing parameter values that lead to prediction of outbreak ($R_0 > 1$) and disease extinction ($R_0<1$) in the scenario where an infective person arrives and stays in area *l*. Boxes indicate 25-75 percentiles; whiskers indicate the 5-95 percentiles. EPI is the extrinsic incubation period. We bring attention to the difference between the box plots for the mortality rate and the extrinsic incubation period.

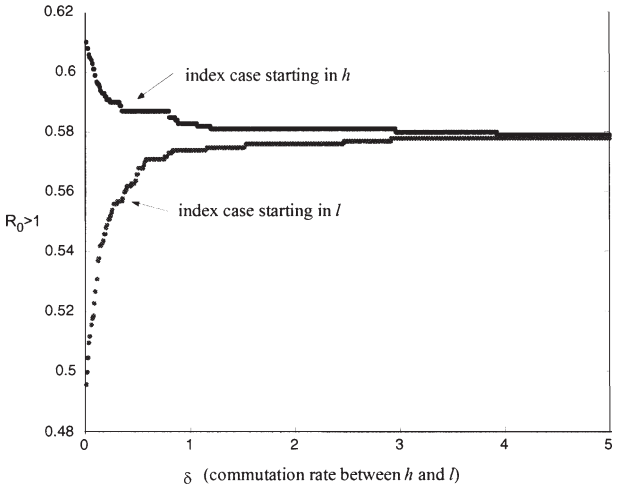

Fig. 4: proportion of the parameter space that resulted into a $R_0 > 1$ as a function of the commutation rate of the index case, between *h* and *l* areas. Upper curve is derived from the scenario where the index starts at *h*. The lower curve was obtained for the case where the index starts at *l*.

if there is sufficient migration from the source. Theoretical models with spatial variation suggest that dispersal may have a strong stabilizing effect on population dynamics and species interaction, promoting coexistence of competitors, preventing extinction in host-parasitoid and predator-prey systems.

We conclude this work stressing the need for a closer interaction between mathematicians, epidemiologists and entomologists in order to find better approaches to the measuring and interpretation of the transmission dynamics of arthropod-borne diseases. Parameters estimation in field works will greatly aid the modeling of the disease, making it more realistic and useful. We believe that the surveillance and control policies based on careful scenario analysis will benefit from this interaction.

REFERENCES

Anderson RM, May RM 1991. *Infectious Diseases of Humans: Dynamics and Control,* Oxford University Press, Oxford.

Blower SM, Dowlatabadi H 1994. Sensitivity and uncertainty analysis of complex - Models of disease transmission - An HIV model, as an example. *Int Stat Rev 62*: 229-243.

Combate à dengue - Índice de pendência dos imóveis 2002. Secretaria Municipal de Saúde, Prefeitura da cidade do Rio de Janeiro, http://saude.rio.rj.gov.br/.

Costero A, Edman JD, Clark GG, Scott TW 1998. Life table study of *Aedes aegypti* (Diptera : Culicidae) in Puerto Rico fed only human blood versus blood plus sugar. *J Med Entomol 35*: 809-813.

Esteva L, Vargas C 1998. Analysis of a dengue disease transmission model. *Math Biosci 150*: 131-151.

Focks DA, Brenner RJ, Hayes J, Daniels E 2000. Transmission thresholds for dengue in terms of *Aedes aegypti* pupae per person with discussion of their utility in source reduction efforts. *Am J Trop Med Hyg 62*: 11-18.

Focks DA, Daniels E, Haile DG, Keesling JE 1995. A simulation model of the epidemiology of urban dengue fever: literature analysis, model development, preliminary validation, and samples of simulation results. *Am J Trop Med Hyg 53*: 489-506.

Focks DA, Haile DG, Daniels E, Mount GA 1993. Dynamic life table model for *Aedes aegypti* (Diptera: Culicidae): analysis of the literature and model development. *J Med Entomol 30*: 1003-1017.

Guia de doenças - dengue 2002. Fundação Nacional de Saúde, Ministério da Saúde, http://www.funasa.gov.br/.

Harrington LC, Buonaccorsi JP, Edman JD, Costero A, Kittayapong P, Clark GG, Scott TW 2001. Analysis of survival of young and old *Aedes aegypti* (Diptera: Culicidac) from Puerto Rico and Thailand. *J Med Entomol 38*: 537-547.

Hernandez-Suarez CM 2002. A markov chain approach to calculate r(0) in stochastic epidemic models. *J Theor Biol 215*: 83-93.

Honorio NA, Lourenço-de-Oliveira R 2001. Frequency of *Aedes aegypti* and *Aedes albopictus* larvae and pupae in traps, Brazil. *Rev Saúde Pública 35*: 385-391.

Massad E, Coutinho FA, Burattini MN, Lopez LF 2001. The risk of yellow fever in a dengue-infested area. *Trans R Soc Trop Med Hyg 95*: 370-374.

Mckay MD, Beckman RJ, Conover WJ 2000. A comparison of three methods for selecting values of input variables in the analysis of output from a computer code. *Technometrics 42*: 55-61.

Muir LE, Kay BH 1998. *Aedes aegypti* survival and dispersal estimated by mark-release-recapture in Northern Australia. *Am J Trop Med Hyg 58*: 277-282.

Newton EA, Reiter P 1992. A model of the transmission of dengue fever with an evaluation of the impact of ultra-low volume (ULV) insecticide applications on dengue epidemics. *Am J Trop Med Hyg 47*: 709-720.

Nogueira RM, Miagostovich MP, de Filippis AM, Pereira MA, Schatzmayr HG 2001. Dengue virus type 3 in Rio de Janeiro, Brazil. *Mem Inst Oswaldo Cruz 96*: 925-926.

Nogueira RM, Miagostovich MP, Schatzmayr HG, dos Santos FB, de Araujo ES, de Filippis AM, de Souza RV, Zagne SM, Nicolai C, Baran M, Teixeira Filho G 1999. Dengue in the state of Rio de Janeiro, Brazil, 1986-1998. *Mem Inst Oswaldo Cruz 94*: 297-304.

Osanai CH, Travassos da Rosa AP, Tang AT, do Amaral RS, Passos AD, Tauil PL 1983. Dengue outbreak in Boa Vista, Roraima. Preliminary report. *Rev Inst Med Trop São Paulo 25*: 53-54.

Porco TC, Blower SM 1998. Quantifying the intrinsic transmission dynamics of tuberculosis. *Theor Popul Biol 54*: 117-132.

Programa nacional de controle da dengue 2002. Vigilância Epidemiológica, Fundação Nacional de Saúde, Ministério da Saúde, http://www.funasa.gov.br/epi/dengue/pdfs/pncd_2002.pdf.

Scott TW, Amerasinghe PH, Morrison AC, Lorenz LH, Clark GG, Strickman D, Kittayapong P, Edman JD 2000. Longitudinal studies of *Aedes aegypti* (Diptera: Culicidae) in Thailand and Puerto Rico: Blood feeding frequency. *J Med Entomol 37*: 89-101.

Tauil PL 2001. Urbanization and dengue ecology. *Cad Saúde Pública 17* (Supl.) 99-102.

Teixeira MG, Costa MC, Barreto ML, Barreto FR 2001. Epidemiology of dengue in Salvador-Bahia, 1995-1999. *Rev Soc Bras Med Trop 34*: 269-274.

Travassos da Rosa AP, Vasconcelos PF, Travassos Da Rosa ES, Rodrigues SG, Mondet B, Cruz AC, Sousa MR, Travassos Da Rosa JF 2000. Dengue epidemic in Belém, Pará, Brazil, 1996-97. *Emerg Infect Dis 6*: 298-301.

Trpis M, Hausermann W 1986. Dispersal and other population

parameters of *Aedes aegypti* in an African village and their possible significance in epidemiology of vector-borne diseases. *Am J Trop Med Hyg 35*: 1263-1279.

Watson TM, Kay BH 1999. Vector competence of *Aedes notoscriptus* (Diptera: Culicidae) for Barmah Forest virus and of this species and *Aedes aegypti* (Diptera: Culicidae) for dengue 1-4 viruses in Queensland, Australia. *J Med Entomol 36*: 508-514.

Watts DM, Burke DS, Harrison BA, Whitmire RE, Nisalak A 1987. Effect of temperature on the vector efficiency of *Aedes aegypti* for dengue 2 virus. *Am J Trop Med Hyg 36*: 143-152.