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Modeling the complex hatching and development of *Aedes aegypti* in temperate climates

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ABSTRACT

Here, we present and discuss a compartmental stochastic model for *Aedes aegypti* conceived as a mathematical structure able to interpolate and extrapolate (predict) biological phenomena, and direct the attention to biological matters that need experimental elucidation. The model incorporates weather information in the form of daily temperatures and rain and pays particular attention to determining factors in temperate climates. Sufficiently large rains trigger egg hatching, which in turn leads to peaks in larval densities. Hatching is inhibited by the absence of bacteria (Gillett effect), a mechanism of relevance during the winter season and in seasons with isolated rains. The model also incorporates egg hatching independent of rains. Both egg hatching and larval development depend on the availability of food, which is modeled as bacteria produced at rates that depend on the temperature. Larval mortality and pupation rates depend on the larvae to bacteria ratio. The results of the model for egg laying activity were compared with field records during a normal season and a drought. Both the model and the records indicate that the egg laying activity of *Ae. aegypti* is not zero during the drought and recovers quickly when normal weather is reestablished. We studied the sensitivity of the model to different sets of physiological parameters published for a few different local populations of this species, and found that there is an important sensitivity to local characteristics that will affect some predictions of the model. We emphasize that if the information is going to be used to evaluate control methods, the life cycle of the mosquito must be studied for the local strain under the local environmental conditions (including food). We showed that the adult populations produced by the model are insensitive to certain combinations of parameters and that this insensitivity is related to the variability reported for different strains obtained from closely located places. When the model is considered in a larger biological context, it indicates that some standard procedures performed to measure the life cycle of *Ae. aegypti* in the laboratory might have a determining influence in the results.

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1. Introduction

Aedes aegypti is the main vector of dengue (Gubler, 1998) and other viral diseases (Dégallier et al., 1988). The origins of *Ae. aegypti* can be traced to tropical Africa but, since it is highly anthropophilic, it has dispersed around the world, thriving in tropical, subtropical and temperate urban ecosystems (Christophers, 1960).

Because of its relevance as a vector of deadly diseases, it has been the subject of numerous studies as well as of some modeling attempts. The best known model for *Ae. aegypti* is CIMSim (Focks et al., 1993a,b; Ellis et al., 2011). This model is conceived as "a mechanistic, comprehensive, and dynamic accounting of the multitude of relationships known to play a role in the life history of these mosquitoes" (Focks et al., 1993a). The model and its refinement, SkeeterBuster (Magori et al., 2009), are conceived as "important tool(s) in the fight against dengue". These models are not free from difficulties (Xu et al., 2010; Ellis et al., 2011), which are directly linked to their philosophy of design. The underlying idea of an accumulated knowledge from which reliable predictions can be produced closely resembles inductivism. Additionally, these models incorporate a structure of subsidiary models that greatly increases the number of parameters and effectively acts as a protective epistemological belt (Lakatos, 1978).

During the last years, we have developed another model named aedesBA (Otero et al., 2006, 2008). The design philosophy of aedesBA is one of a "developmental model", a term introduced by Leplin (Hartmann, 1995) for models that are used in the process of building theoretical knowledge. Although aedesBA is particularly concerned with *Ae. aegypti* populations in temperate climate, we expect it to be relevant (or at least adaptable) to other climates

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as well. Mathematically, aedesBA is built as a continuous-time Markov (jump) process (Kolmogoroff, 5794; Feller, 1940; Durrett, 2001), normally conceived as density-dependent Poisson processes with exponentially distributed times. However, we have shown that other (arbitrary) time distributions can be introduced without extraordinary efforts (Otero et al., 2011). The mathematical structure is such that it provides both the need to describe extinction processes of subpopulations (a problem where differential equations are bound to fail) and the convenience of having some analytical tools in addition to computational (simulations) tools. From an epistemological perspective, the model is simple in Popper's sense, i.e., it facilitates falsification attempts and its development follows the recently described epistemology of complex systems (García, 2006).

In a first confrontation with real data corresponding to egg-laying activity in Mataderos, a neighborhood of Buenos Aires city (Argentina), the model was able to produce an activity profile that corresponds well with the observations, although it overestimated the activity at the end of the season (Otero et al., 2008). Legros and co-workers noticed that the model SkeeterBuster has the same problem (Legros et al., 2011). However, this conclusion needs to be revised because a substantial part of the mismatch corresponds to an error. The database recovered for our study (Otero et al., 2008) corresponds to the summer 2000–2001 (Carbajo, 2003) but was erroneously attributed by us to the subsequent summer (2001–2002). Thus, for a year with regular weather, aedesBA produced results of egg-laying activity that correspond well with the observations available.

In a previous work, we used aedesBA to generate vector populations to analyze the possibility of dengue outbreaks in Buenos Aires (Otero and Solari, 2010). This work, submitted in late 2008, indicated the possibility of such occurrences and of non-epidemic (below threshold) circulation of the virus. Such a prediction was made just a short time ahead of the first report of transmission of dengue virus in the region and contradicted the expectations of local health authorities (Seijo et al., 2009) based on the use of CIMSim and DENSim (Focks et al., 1995).

Although this could be claimed as a remarkable success of aedesBA, we should be extremely cautious and list it as a possible false success, i.e., a success because of wrong reasons. In 2009, the virus began circulating after a historic drought in the region. It is well known that the eggs of *Ae. aegypti* hatch after being wetted, normally after rains (Gillett, 1955a,b; Christophers, 1960). Thus, expert knowledge indicates that low populations of the mosquito are expected during and after a drought. In contrast, aedesBA assumed a regular weather and made no use of rain records, i.e., it indicated the possibility of virus circulation by assuming a weather pattern different from the observed one. But then, why did it work? Are experts' opinions wrong? And if so, in which sense and why? We anticipate that populations can recover from the effects of a drought in a short time (Section 5), and that by the time the virus began to circulate, the activity of *Ae. aegypti* predicted by the old model and that predicted by the new model are in agreement.

Thus, the aim of this work is to re-formulate the hatching process built in aedesBA to account for normal hatching (prompted by rains) and abnormal hatching. By abnormal hatching we understand processes such as spontaneous hatching (Southwood et al., 1972; Christophers, 1960), eggs laid directly on top of the water, as well as hatching as a result of human intervention replenishing some breeding sites with water, etc. The hatching process cannot be considered without giving simultaneous consideration to other associated facts such as developmental times and their relation with the availability of food for the development of larvae. When introducing rains, the population-regulatory mechanism must be reconsidered, moving from an effective mechanism to a more

realistic one. We did so by introducing population (density-dependent) effects that have been recently described (Maciá, 2006, 2009). Since such mechanisms rely on the abundance of food, the incorporation of rains triggering egg hatching leads to the consideration of a new element in the (urban) ecology of *Ae. aegypti*, i.e., food dynamics. Starvation conditions induce a higher mortality of the larvae (Barrera, 1996), a complementary effect to delayed pupation, which plays a relevant role in the dynamics. This construction is presented in Section 2. In Section 3, we proceed to compare the predicted egg laying activity with experimental (field) records produced for the 2000–2001 and 2008–2009 seasons, the latter being the season of the drought. The sensitivity of the predicted populations to uncertainties and modeling decisions is explored in Section 4.

We consider different sets of physiological parameters reported in the literature and how, depending on the circumstances, only certain combinations matter; we also consider the sensitivity of the model to the assumptions of food production and mortality. In Section 5, we discuss the results obtained, what we have learned and what we need to learn. We emphasize how the uncertainty in the physiological parameters may lead to severe problems of predictions regarding population-control methods. We also make a case for the reconsideration of developmental (physiological) parameters in ecological terms as opposed to the prevailing individual view. We understand that the use of laboratory colonies reared for generations under (artificial) laboratory conditions to determine developmental parameters might introduce methodological bias to the model.

Beyond the general success of the new model, the results indicate that the model needs biological information that has not been measured so far. In the proposed dialog between the empirical world and the logical (abstract, conceptual, mathematical, theoretical) organization, we formulate some biological questions that need to be answered for further progress.

The last section corresponds to the summary and conclusions.

2. On the relation between hatching, developmental times, rain and food

2.1. The life cycle of Aedes aegypti

Ae. aegypti is a tree-hole mosquito currently adapted to urban ecosystems. It normally lays the eggs in relatively small containers holding water. The eggs hatch when proper conditions are met (Christophers, 1960). The mature (embryonated) eggs must be submerged in water, the temperature of the water must be sufficiently high (its lower temperature limits have been reported to range from 4 °C to 16 °C) and bacterial activity facilitates egg hatching (Gillett, 1955b,a; Gillett et al., 1977; Edgerly et al., 1993; Ponnusamy et al., 2011). The larvae of the mosquito develop in four instars separated by a molt until pupation. The adults emerge and, in the case of females, after completing a gonotrophic cycle (which in turn requires at least one blood meal), they lay eggs to begin the next gonotrophic cycle.

2.2. The original model

The original (aedesBA) model was developed for temperate climates, assuming the following: that the availability of blood meals is not a limiting resource; that rainfalls are regular; that total adult populations and total number of bites are the modeling target; and that the mechanisms that determine the carrying capacity are not relevant for the questions and circumstances addressed in the early works (Otero et al., 2006, 2008).

Populations are divided in compartments corresponding to eggs, larvae, pupae, adults-1 (non-parous), flyers -adults dispersing seeking oviposition sites- and adults-2 (parous). Only female adults are considered. Each population is located at a determined block and only flyers move from block to block. Populations and subpopulations are counted with non-negative integer numbers and evolve according to the occurrence of events. The waiting time between one event and the next is exponentially distributed, being its rate the sum of all the rates of the possible events. The event occurring is selected as the winner of a Poisson race (Durrett, 2001). In short, the model is expressed as a Kolmogorov Forward Equation for the jump process (Kolmogoroff, 5794) as discussed by Feller (1940) (see Appendix A). It is worth mentioning that the computer code associated with the model, instead of implementing Kendall's direct method (Kendall, 1950), uses an accelerated approximation method (Solari and Natiello, 2003) with fixed time increments usually taken as 2 h. The events considered are: egg-hatching, pupation, emergence, blood-meal (by parous and non-parous females), egg-laying and mortality events for each developmental stage. The only event with a non-linear rate (i.e., presenting population effects) is the mortality of the larvae, which increases linearly in the presence of other larvae with a coefficient that determines the carrying capacity of the environment and whose inverse was named BS, for "number of Breeding Sites".

2.3. Rains as a trigger for hatching

To implement the rains as a trigger for egg hatching, we divided the egg population in several compartments. Eggs are laid as immature, E_i, and evolve into mature eggs, E_m, with a temperature-dependent rate (already discussed in Otero et al., 2006). There is a probability of abnormal hatching, p_{ab}, for just matured eggs to proceed directly to the larval stage. The remaining just matured eggs are moved into the mature eggs compartment and their hatching will be triggered by rains (normal hatching). After a sufficiently large rain (exceeding a threshold set tentatively at 7.5 mm), the eggs are moved into the wet eggs compartment, E_w, with 0.8 probability (Christophers, 1960; Southwood et al., 1972), where they begin to hatch at a rate that depends on the temperature. Since the precise dependence is not known, for this work we adopted the same dependence as that of the embryonation rate, matching at 27 °C the rate reported by Southwood et al. (1972) for field studies in Thailand. Experiments to determine the temperature dependence of the hatching rate are in progress.

The life cycle implemented in the model is described in Fig. 1.

2.4. Rains, food and mortality

The incorporation of the rain as a trigger for egg hatching makes the effective form of introducing the mortality unsuitable. After a rain, the larval density would increase quickly and the non-linear mortality would kill larvae immediately until the probabilities of pupation and death are comparable for the individual larva. If this happened, the individual mortality rate would exceed the observed mortality rates by a factor of at least 100. Once the excess of larvae is whipped off, and until the next rain, the productivity of the breeding site would monotonously decrease with time. Thus, the average productivity would monotonically decrease with the interval between rains.

However, the way in which Ae. aegypti populations cope with high larval densities is different. Maciá (2009) showed that, in the presence of a constant amount of food, an increase in larval density (within a certain range of densities) results in an increase in the average time to pupation or, what is the same, in a decrease in the pupation rate. In fact, Moore and Whitacre (1972) indicated that the determining factor regulating pupation time was larval nutrition and not larval density. For higher densities, we interpret results from Barrera (1996) as indicative of an increase in the mortality rate.

We then consider a pupation rate as function of the produced (or available) food (see below) of the form

$$
\begin{cases}
l_p(T) = 0.37266 - \dfrac{0.3652}{1 + \exp((T - 25.189\,°C)/4.6456\,°C)} & L/P_f \le 1 \\[2ex]
\dfrac{l_p(T)}{1 + 0.6728 * (L/P_f - 1)} & 1 < L/P_f
\end{cases}
\tag{1}
$$

where $l_p(T)$ is the pupation rate as a function of temperature (expressed in Celsius) when food is in excess - usual laboratory feeding conditions-. The pupation rate (1) indicates that when food is scarce ($1 < L/P_f \le 4$) (see below), pupation proceeds at a lower rate. L/P_f stands for the ratio between larvae and available food.

The individual mortality rate assumed is

$$
\begin{cases}
d_{ll}(T) \equiv 0.01 + 0.97248 * \exp(-(T - 5\,°C)/2.70346) & \text{if } L/P_f < 4 \\[1ex]
d_{ll}(T) + M_{NL} * (L/P_f - 4)) & \text{if } 4 < L/P_f < 8 \\[1ex]
d_{ll}(T) + 4 * M_{NL} & \text{if } L/P_f > 8
\end{cases}
\tag{2}
$$

We refer to Appendix B for a discussion of the mortality and pupation rates in correspondence with the structure of the model and the experimental data. The coefficient of non-linear mortality (M_{ML}) is assumed to range between 0.01 and 0.023. For our calculation, we adopted a value of 0.023 unless otherwise stated. Eqs. (1) and (2) define three regions for feeding: abundance ($L < P_f$), scarcity ($P_f < L < 4 * P_f$), and deficit ($P_f * 4 < L$).

2.5. The Gillett effect

The first relation between food and development was probably that reported in the works by Gillett (1955b) and Gillett et al. (1977). Gillett established that the presence of bacteria regulates the hatching time of the eggs as well as the probability of hatching (Gillett et al., 1977). The inhibition of hatching by the presence of larvae was further studied in tree-hole mosquitoes (Livdahl et al., 1984; Livdahl and Edgerly, 1987) for Ochlerotatus triseriatus (then known as Aedes triseriatus) both in the laboratory and in the field. Experiments (Edgerly and Marvier, 1992) have shown that an increase from 4 to 24 larvae reduces bacterial colonies by two orders of magnitude in laboratory conditions when larvae are allowed to feed in the proximities of the eggs. Hatching inhibition by the presence of larvae in Ae. aegypti was studied as well (Edgerly et al., 1993). Hatching decreased almost ten-fold when the number of larvae increased from 4 to 12 and then further decreased in the presence of 24 larvae. The relation between bacterial populations and hatching probability has been recently studied in Ponnusamy et al. (2011). The hatching probability for bacterial colonies presents a transition: when the density of bacteria increases from 10^6 to 10^8, the hatching probability changes from about 0.1 to 0.8. These figures are well aligned with the numbers reported for Ochlerotatus triseriatus in Edgerly and Marvier (1992). Hatching probabilities measured in the laboratory as a function of bacterial density range from 0.02 to 0.95.

We thus introduced a reduction of the hatching probability after a rain from 0.8 to 0.04 under scarcity conditions when there is no "leftover food" (food not consumed by the existing larvae). Hence, eggs are less likely to hatch in an already crowded site. We will explore the sensitivity to this parameter in Section 4. In practical terms, we assume that mature eggs hatch after a rain with a probability of 0.8 if there is leftover food, but they hatch with a probability of $0.8 * G$ with $0 \le G \le 1$ when there is no leftover food. The value of G was kept as $G = 0.05$, except when exploring the influence of this coefficient.
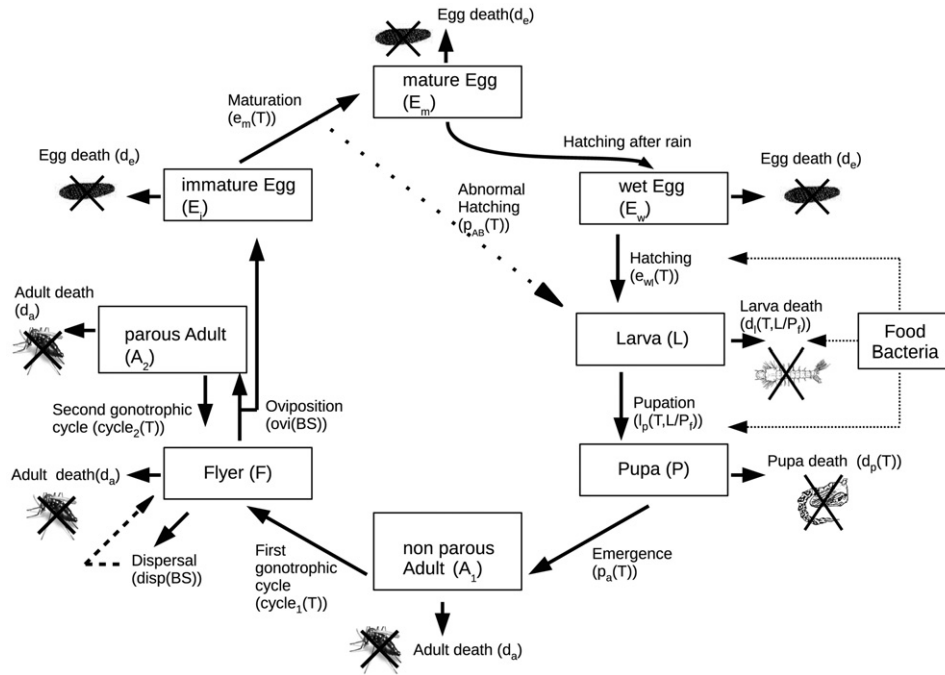
Fig. 1. Scheme of the model. The population compartments are indicated in boxes. The arrows indicate transitions. The dashed arrow stands for a transition to a different cell/block. The labels of the transitions indicate the transition rates per individual and their functional dependence (*BS* for breeding sites, *T* for temperature and P_f for the available food) (see also Tables A1 and A2).

2.6. Food production and consumption

While the construction of the previous paragraphs regarding the relations between food, mortality and developmental time is supported by experimental data, it says nothing about the food and its dynamics. Indeed, not much is known about the food of the larvae of *Ae. aegypti* outside the laboratory. The larvae of *Ae. aegypti* feed on bacteria or yeast associated with the decomposition of organic matter, mainly by filtering water (Merritt et al., 1992). Correspondingly, we assume that the larvae forage on stranded bacteria, without altering the decomposition process. For food, we used a continuous variable, *f*, which is produced at a rate $f_{pr}(T)$ that depends on the temperature, since the reproduction of bacteria and yeast is well known to depend strongly on the temperature. While food is available, it evolves with the following equation:

$$\frac{df}{d(u*t)} = f_{pr}(T) - f - L \tag{3}$$

where *u* is a characteristic decay time for the food. The equation integrates into

$$f(u*t) = \exp(-u*(t-t_0)) * (f(u*t_0) + \int_{t_0}^{t} \exp(s)*(f_{pr}(T(s)) - L(s))ds) \tag{4}$$

$$f(u*t) = P_f(t) - C_f(t)$$

$$P_f(t) = \exp(-u*(t-t_0)) * (f(u*t_0) + \int_{t_0}^{t} \exp(s)*f_{pr}(T(s))ds)$$

$$C_f(t) = \exp(-u*(t-t_0)) * \left(\int_{t_0}^{t} \exp(s)*L(s)ds\right)$$

Here, P_f and C_f stand for produced and consumed food respectively and *L* is the number of larvae. Since it is not possible to consume more food than that available, Eqs. (3) and (4) are valid provided that $P_f(t) \geq C_f(t)$; otherwise, the remaining food is set to zero. When $P_f(t) \geq C_f(t)$, we define the leftover food as: $f(u*t) = P_f(t) - C_f(t) \geq 0$. Notice that the transition rates depend on the quotient between P_f and *L*, which is the ratio between available food rations and larvae.

The dependence of the food production rate f_{pr} and the temperature adopted corresponds to a Ratkowsky-2 model (Zwietering et al., 1991) with $T_{min} = 11\,°C$ and $T_{max} = 40\,°C$.

$$f_{pr}(T) = L_{opt} * ((T - T_{min}) * \exp(T - T_{max}))^2 \text{ for } T_{min} \leq T_{max} \tag{5}$$

$$f_{pr}(T) = 0 \text{ if } T < T_{min} \text{ or } T > T_{max}$$

The influence of these choices will be discussed in Section 5. The parameter L_{opt} indicates the productivity of the breeding site in optimal conditions (density $L/P_f = 1$) and normalizes the food to the number of larvae than can be fed in optimal conditions at 27 °C (a temperature chosen arbitrarily).

3. Egg laying activity: comparison between field data and simulations

One of the standard methods used to detect the presence and monitor the activity of *Ae. aegypti* is the use of ovitraps (Schweigmann et al., 2002; Micieli and Campos, 2003; Vezzani et al., 2004; Carbajo et al., 2006; Chadee, 2002; Estallo et al., 2011; Bergero et al., 2011). We will briefly describe the method; the details can be consulted in the references. In particular, mathematical details can be found in Bergero et al. (2011). Let us consider an urban patch which can be thought from an urbanistic and ecological point of view as homogeneous. A set of N ovitraps is distributed in the patch and the number of positive ovitraps (and other data) is recorded periodically (weekly in the cases discussed here), resetting all ovitraps to the negative state. If $K(t)$ is the number of positive ovitraps recorded on day *t*, the oviposition activity is $-\log(1 - (K(t)/N))$ (Bergero et al., 2011). However, here we used the exponential scale because it is used more often. Hence, we define

$$ova = \frac{K(t)}{N} \tag{6}$$

which is a statistical measure of the egg-laying activity of mosquitoes and as such is subject to statistical fluctuations even when the conditions are ideal. Such fluctuations are distributed
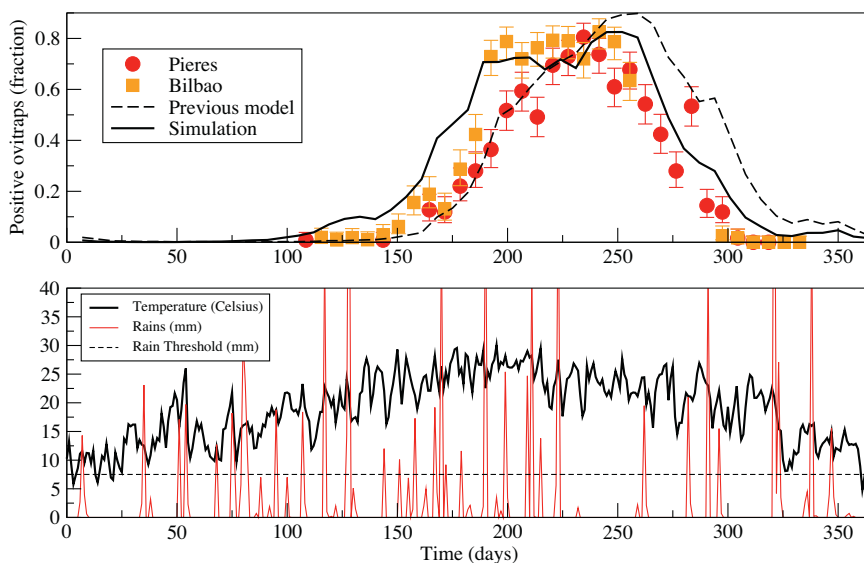
Fig. 2. Summer 2000–2001. Field-measured egg laying activity in the Bilbao patch and the Pieres patch, and simulated egg laying activity averaged over 20 runs (food parameter L_{opt} = 2.5) performed with the present model (full lines) and the previous model (dashed lines). Error bars correspond to 90% confidence intervals (upper panel). Weather data used for the simulations provided by the SMN (lower panel). The first day corresponds to July 1st 2000.

according to a binomial distribution, as it has been discussed in the appendix of Otero et al. (2008) (see Bergero et al., 2011 as well).

To simulate the oviposition activity, we delimit a patch that corresponds with the experimental patch (composed of several city blocks). Using the number of egg laying events, *elev*, in the blocks, we determine representative results considering that each trap has a probability p_{trap} of being positive. A given trap is chosen at each egg-laying event with a probability $q_t = a/(BS + a*n)$, competing with the breeding sites and the other traps. Each trap has a quality factor of a as compared to 1 for the breeding sites and there are n traps. In what follows, we have set a = 0.5.

A trap will turn negative if all the females choose any of the other options. Since this happens with probability $(1 - q_t)^{elev}$, the probability of finding a positive trap is given by $p_{trap} = 1 - (1 - q_t)^{elev} = 1 - (1 - a/(BS + a*n))^{elev}$. In the model, BS is a parameter and *elev* is produced by the simulations for each block accumulating egg laying events during a week. Since *elev*, and then p_{trap}, is a random variable, p_{trap} is averaged over the study area and over several realizations (20 realizations have shown to be enough to obtain stable averages).

Four field studies from Buenos Aires city, performed during two summer seasons (September–June), are available to us. Two of these studies correspond to the 2000–2001 season and were performed in two adjacent patches of 5 × 5 blocks in the neighborhood of Mataderos (Carbajo, 2003) and are labeled Bilbao (record of 120 ovitraps placed by pairs, which is incomplete because the sampling was interrupted for some weeks) and Pieres (120 ovitraps placed by pairs). The remaining two studies correspond to the 2008–2009 summer, and were conducted in the neighborhoods of Mataderos and Belgrano. The patches considered were approximately 3 × 3 blocks, and 26 ovitraps were placed in each patch regularly distributed. Hourly temperature records were taken at each site with a HOBO® Pendant Temperature Data Logger placed in an ovitrap (De Majo, 2011). Additionally, in all cases, weather records of the Villa Ortúzar (WMO #87585 SABA) station in Buenos Aires city were obtained from the Servicio Meteorológico Nacional (Argentina) SMN-ar.

We show the results in three figures. In all the cases, we show the measured values and the 90% (statistical) confidence band (which accounts only for statistical fluctuations of an ideal experiment), the average results from the simulations of the present model

(solid lines) and the average results obtained with the simulations performed with the previous model (Otero et al., 2008). The only parameter adjusted is the Lopt (see Eq. (5)) in the food model. The number of breeding sites has been kept fixed in BS = 15 for all the cases. In Fig. 2, observe that although Pieres and Bilbao field studies were performed at adjacent patches of the same urbanization, they display some differences beyond the statistical expectation, particularly at the beginning of the season. It is also a constant feature in the simulations that the opening of the favorable mosquito season is more variable than the closing of the season. We will turn to this matter in the discussion, Section 5.

In Fig. 3 we can see the performance of the model during the 2008–2009 summer as compared to the field results in Belgrano and Mataderos. The differences in the simulations between both patches result from the differences in the local temperatures and the food parameter L_{opt} (Eq. (5)) that take the values L_{opt} = 4 and L_{opt} = 6 respectively.

4. Do all the parameters matter?

Situations can be found which are sensitive to every parameter in the model. Yet, at the time of predicting particular features, they might be sensitive only to some parameter combinations depending on the circumstances (the climate for example). Thus, when describing the numbers of mosquitoes, we may find that what really matters is not the duration of the gonotrophic cycle and the fecundity separately but rather the average number of eggs per day laid by each female. We illustrate this idea in Fig. 4.

Notice, however, that the number of bites will be proportional to the number of cycles completed. Thus, from an epidemiological point of view, the situations are completely different for each value of ϕ in Fig. 4.

Similarly, other parameters will influence the adult population in regular situations only as combinations. For example, pupation and death of pupae compete as events, and what matters most is the success in pupation. Variation in pupation times is less important. Hence, keeping the ratio $p_a(23\,°C)/d_p(23\,°C)$ constant (the temperature T = 23 °C was chosen to match the experiments in Grech et al. (2010)), the adult population was found not to be sensitive to the values of the product $p_a(23\,°C) * d_p(23\,°C)$.
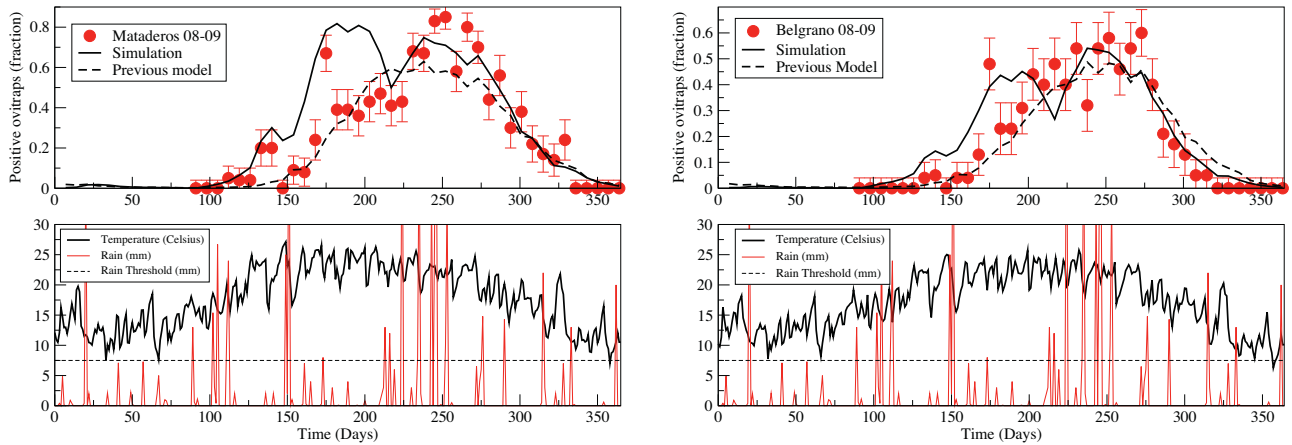
Fig. 3. Summer 2008–2009. Left: Field-measured egg laying activity in Mataderos and simulated egg laying activity averaged over 20 runs (upper panel) (food parameter L_{opt} = 6). Right: Field-measured egg laying activity in Belgrano and simulated egg laying activity averaged over 20 runs (upper panel) (food parameter L_{opt} = 4). Simulations performed with the present model are represented by full lines, whereas simulations with the previous model are represented by dashed lines. Error bars correspond to 90% confidence intervals (upper panel). Lower panels: temperature data were recorded in situ and rainfall data from Villa Ortúzar station (SMN; lower panel). The first day corresponds to July 1, 2008.

Since the parameters in the model are assumed to be measured independently of the model, as opposed to a free set of parameters to be adjusted, in what follows we preferred to show the sensitivity of the model to different sets of developmental parameters measured.

4.1. Sensitivity to Aedes aegypti types

Grech et al. (2010) measured developmental times and mortality in the laboratory under the same food and climatic conditions starting from eggs collected in three wild (urban) locations in Argentina (Córdoba, San Javier and Orán) distant hundreds of kilometers one from each other and a fourth laboratory strain (Rockefeller). The laboratory strain showed a fecundity per day 5 times larger than the wild strains, a fact that might indicate mis-adaptation of the wild strains to the new environment (the laboratory). We ran simulations using these four parameter sets as well as the set used in Focks et al. (1993a) and the weather data

corresponding to Buenos Aires 2001–2002. The results are shown in Fig. 5. We observe that most differences correspond to the beginning of the season and are not important between Rockefeller, Focks and San Javier. In particular, the apparent reproductive advantage of the Rockefeller strain is not reflected in the adult population. Instead, the mis-adaptation of the Oran strain to the laboratory is evident and significant. When the use of food is considered, all except the Oran strain are consuming all the food available most of the time, whereas the Oran strain produces significant food leftovers.

4.2. Sensitivity to the Gillett effect

Sensitivity to the value of the Gillett parameter was observed only in the simulations corresponding to the 2008–2009 summer associated with the lack in rains. A decrease of the hatching rate from 0.8 to 0.04 was necessary to reproduce the lower values of egg laying activity recorded during the summer (see Fig. 6).
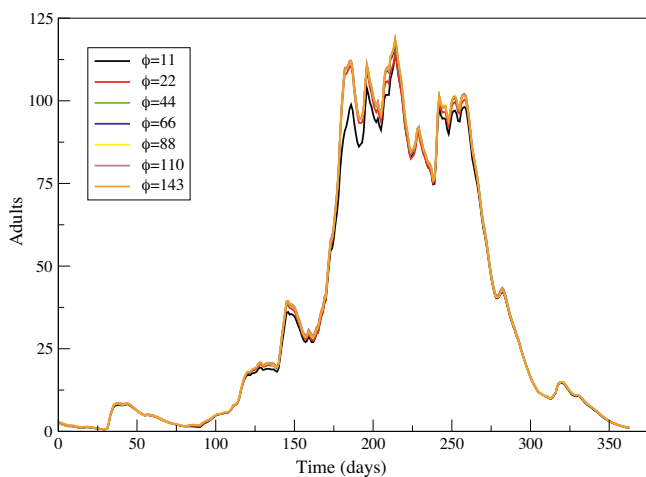

Fig. 4. Dependence of the population on the duration of gonotrophic rate, α_{cy1}, and the number of eggs laid after each gonotrophic cycle, ϕ, when the product ($\alpha_{cy1} * \phi$) (see Table A2) is kept constant. The adult population corresponds to simulations for the 2001–2002 season. The remaining parameters are kept constant at the default values specified in the text and in Otero et al. (2008). The first day corresponds to July 1, 2001. Plots are averages over 20 runs. Temperature and rainfall data are from Villa Ortúzar station (SMN).
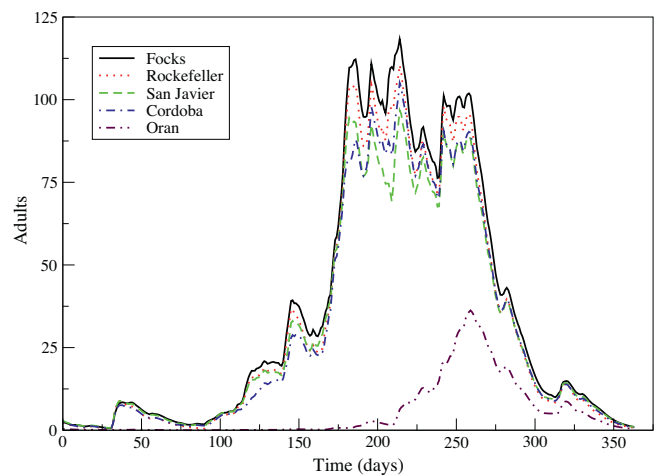

Fig. 5. Adult females per block simulated for the 2001–2002 season for Buenos Aires with parameters obtained in the laboratory for *Ae. aegypti* strains from Córdoba, San Javier, Orán, Rockefeller strain and Focks data. Temperature and rainfall data are from Villa Ortúzar station (SMN). The first day corresponds to July 1, 2001. Plots are averages over 20 runs.
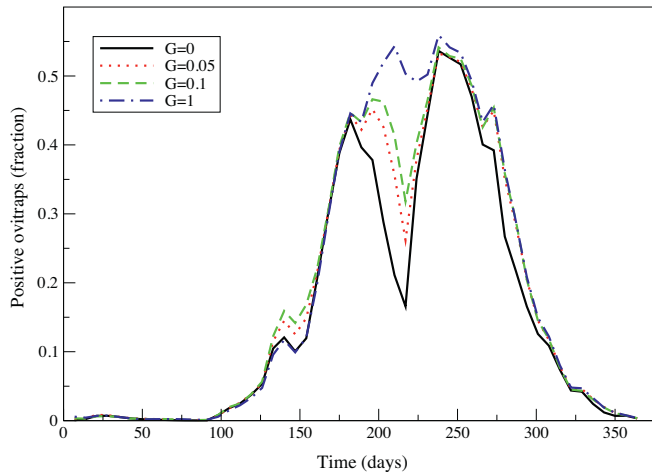
Fig. 6. Sensitivity of the simulated egg laying activity to the Gillett factor (G), during the 2008–2009 season in Belgrano. Temperature data were measured in Belgrano and rainfall data are from Villa Ortúzar station (SMN). Plots are averages over 20 runs.

4.3. Sensitivity to density-dependent mortality

Likewise the Gillett effect, the 2008–2009 season was the most sensitive to density-dependent mortality. We present simulations on the effect of changing the value of the food-dependent (non-linear) mortality term M_{NL} in Eq. (2).

Fig. 7 shows that the ability to reproduce the decrease in egg laying activity by the end of the drought (days 200–240) depends on having a non-linear mortality large enough, since otherwise the long survival time of the larvae allows some larvae (hatched long before) to reach pupation during the worst part of the drought. Yet, the sensitivity is not linear, and increases beyond $M_{NL} \sim 0.019$ do not introduce important changes.

4.4. Sensitivity to abnormal hatching

Small values of abnormal hatching, such as 2% of the eggs, are able to sustain the populations during the 2008–2009 season. During years with normal weather, no significant differences are obtained.
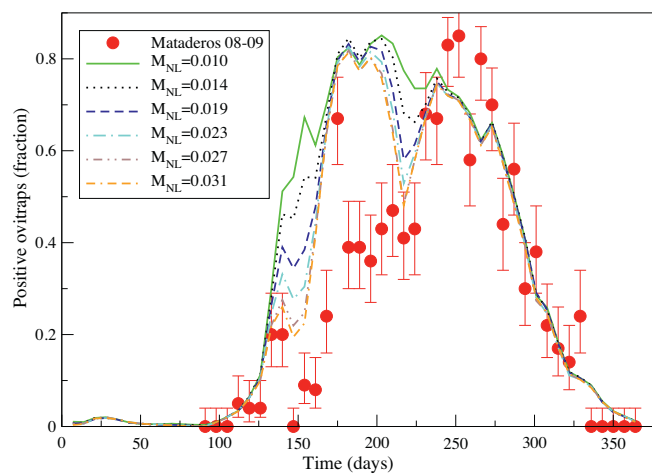

Fig. 7. Sensitivity of the simulated egg laying activity to the non-linear mortality, M_{NL}, in Eq. (2), during the simulation of the 2008–2009 season compared with the data from Mataderos. Plots are averages over 20 runs ($p_{ab} = 0.01$, $G = 0.05$). Temperature data were measured in situ and rainfall data are from Villa Ortúzar station (SMN).
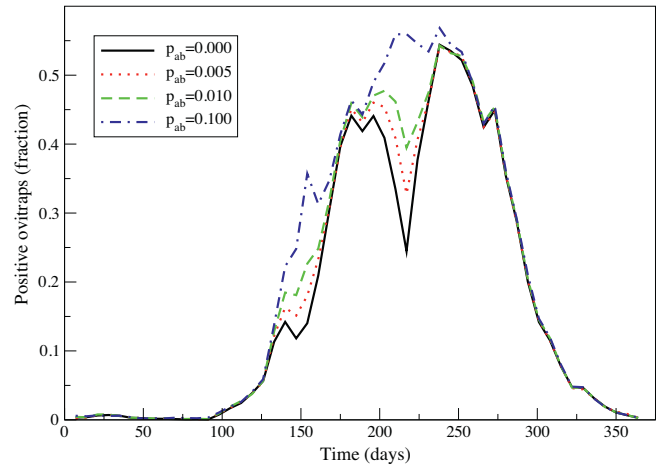

Fig. 8. Sensitivity of the egg laying activity to the abnormal hatching probability p_{ab} during the 2008–2009 season. Temperature data were measured in Belgrano and rainfall data are from Villa Ortúzar station (SMN). Plots are averages of 20 runs.

Actually, sufficiently high abnormal hatching ($p_{ab} \geq 0.02$) or the lack of Gillett effect have the same ability of sustaining populations during the drought (Fig. 8).

4.5. Sensitivity to the food production model

The sensitivity to the parameters and to the form of the food production model (Eq. (5)) is relatively important. The selection of higher values for T_{min} will cause the activity season to begin later and end earlier. The dependence on T_{max}, in contrast, is not important as long as T_{max} is beyond the range of temperatures recorded. In fact, Ratkowsky models (Zwietering et al., 1991) present an important range of temperatures in which they do not qualitatively differ from a quadratic form (Ratkowsky-1 model) depending only on T_{min}. If a different kind of model is used, for example

$$f_{pr}(T) = \begin{cases} L_{OPT} * \left(\dfrac{(T - T_{min})}{(27\,°\mathrm{C} - T_{min})} \right)^2 \exp\left(-2 * \dfrac{(T - 27\,°\mathrm{C})}{(27\,°\mathrm{C} - T_{min})} \right) & \text{for } T \geq T_{min} \\ 0 & \text{for } T \leq T_{min} \end{cases} \tag{7}$$

which presents the same productivity at 27 °C as the model in Eq. (5) as well as the same leading dependence around T_{min} but a different behavior at high temperatures, we can observe different population profiles (Fig. 9). Furthermore, if a model producing constant food (independent of the temperature) is used, winter adult populations, as well as longer favorable seasons and higher overall populations, are present, even during the summer time when all food production models are roughly equivalent (Fig. 9).

In addition, we found little to no sensitivity with respect to the decay time assigned to food when it varied between hours and several days. The reason for this is that most food is consumed immediately.

5. Discussion

Expanding the scope of the aedesBA model requires moving away from the simplifying-hypothesis regarding the weather and the effective nonlinearities implemented. The more realistic hatching and pupation mechanisms implemented are successful in this task. The new model adapts to the dry and normal seasons and is particularly good by the end of the season. However, it has difficulties following isolated rains as they happened during the 2008–2009 drought, a more demanding test than the 2000–2001 season. The difficulties presented consist in that adult population and egg laying activity peaks associated with isolated events
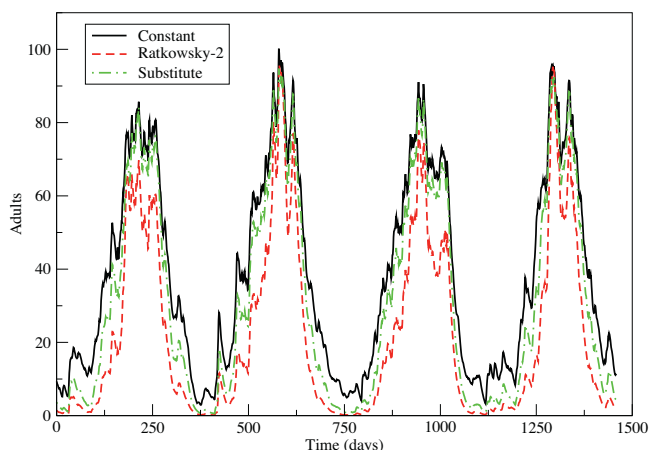
Fig. 9. Sensitivity of the simulated egg laying activity to the bacterial-growth model using temperatures and rains recorded at Villa Ortúzar station (SMN) during 2001–2005. The first day corresponds to July 1, 2001. Parameter values are: $L_{OPT} = 5$, $T_{min} = 11\,°C$, $BS = 5$, $M_{NL} = 0.025$. Ratkowsky corresponds to Eq. (5) and Substitute to Eq. (7). Plots are averages over 20 runs.

are much wider in the simulation than in the actual records. We attribute this disagreement to important differences in the statistic of pupation times between the model and the natural case. Results of studies of cohort maturation under field conditions (Southwood et al., 1972) and in the laboratory (Rueda et al., 1990) are strikingly different. The ratios reported between standard deviation and average time (the coefficient of variation) from hatching to emergence are ~0.30 and ~0.06 respectively, whereas the present model has a ratio of ~0.71. The work in the laboratory is consistent with the idealization of cohorts developing synchronously (Focks et al., 1993a). However, the field results show substantial dispersion, although in lesser amount than our model. The matter requires further study. We are currently working theoretically and experimentally in such direction. Cohort (synchronization) effects are more noticeable at the beginning of the season than at the end because at the beginning of the season the population is represented mainly by eggs, while at the end we expect mosquitoes in all the development stages.

Fig. 2 suggests that the previous model performed better than the new model at predicting the starting of the season. A close examination of this matter indicates that the pool of eggs that survived the winter in the previous model is substantially smaller than in the present model. The previous model allowed hatching during the winter, even without rains and into an environment without food, resulting in very small adult populations, reproductively inefficient, during the winter. The more realistic hatching mechanism implemented results into a larger number of eggs at the beginning of the favorable season and hence a faster take off of the population. In the previous model, a large fecundity attributed to the mosquito was compensated by a hatching mechanism that, in essence, represented additional mortality during winter. Thus, the difference observed is that the large fecundity is not longer compensated. If the physiological parameters used turn to be correct, then the model could be indicating that egg mortality during the winter must be reconsidered. However, several features, when studied with the model, appear to indicate that the fecundity attributed to the mosquito is unrealistic for the local populations.

The results concerning parameter sensitivity indicate that differences between *Ae. aegypti* strains can be adaptive as well as neutral (Stearns, 1989). According to the model, adaptation has to be considered at least as a triad (strain, food, weather). In this sense, our results are only exploratory and indicate that attention must be paid to this matter. It is not surprising that with the parameters obtained in their environment (the laboratory) and under

the feeding conditions they are adapted to, the domestic strains (Rockefeller and data from Focks) perform better (in the sense of exploiting more exhaustingly the resources available) than wild strains taken to the lab. Food may represent a strong selective pressure. Adaptation to food in *Drosophila* for example, occurs in a few generations (Robertson, 1960, 1966). Hence, experiments regarding the physiological characteristics of *Ae. aegypti* populations in natural conditions (including natural food) are needed. This matter is particularly relevant when several (for profit) projects are engineering genetically modified mosquitoes. Claims for modified mosquitoes, showing the same developmental parameters as laboratory strains under laboratory conditions, as equally fitted than wild mosquitoes (Lee et al., 2009) are precarious. Domesticated (lab) mosquitoes are not proper substitutes for wild ones unless the environment is reproduced in the laboratory as well.

Significant fluctuations in fecundity associated with almost identical (within experimental fluctuations) values of daily fecundity reported for strains obtained at four different locations within a radius of 150 km (Tejerina et al., 2009) appear in qualitative agreement with the model that does not identify advantages for lower or higher fecundity as long as the daily fecundity is kept constant, and as such, fecundity might experience genetic (or phenotypic) drift (Lande, 1976).

The insensitivity of the model to certain combination of parameters displayed by adult populations under normal weather may reflect biological facts (as opposed of being modeling artifacts or over-parameterization). In mathematical language, this implies that there are manifolds in parameter space which represent biological situations of equal adaptation. Having no selective forces tangent to the manifold one would expect a dispersion of values along the manifold.

Abnormal hatching may represent human intervention by replenishing containers as reported in Morrison et al. (2004) for Iquitos (Peru) and in Kearney et al. (2009) for Australia. In Iquitos, pupal production for rain-filled containers amounts to 88% of the pupae (Morrison et al., 2004), thus leaving 12% as a lower limit for abnormal hatching (some larvae could have been produced in rain-filled containers independently of rains). Considering the regularity of the rains in Iquitos (rains almost daily), which would imply an almost daily wetting of embryonated eggs by rain and considering that the probability of emergence as adults starting from larvae makes no difference for the hatching method in the model, such observation would be in line with a choice of $p_{ab} \sim (0.12 * 0.8/0.88)G$, which for $G = 0.05$ gives $p_{ab} \sim 0.0054 < 0.02$ meaning that the numbers acceptable for aedesBA in Buenos Aires during the drought are consistent with those just deduced from the observations in Iquitos. We recall for comparison that "newly embryonated eggs hatch spontaneously without flooding" corresponding to 19.7% of all eggs in CIMSim (Focks et al., 1993a), a figure taken from Southwood et al. (1972). Human intervention is in turn the result of urbanistic infrastructure (for example the existence of reliable tap water and sewage) and cultural factors as those related to gardening. The egg laying activity studied corresponds to neighborhoods that have reliable sources of running (tap) water and sewage system, no wells (the first water horizon is salty) and no cisterns.

The response of the model to non-linear mortality, Gillett effect and abnormal hatching indicate that these effects are most important when rains are well separated in time and all of them have a similar (or reciprocal) influence. The relatively high mortality and the relevance of the Gillett effect, as well as the small abnormal hatching tolerated to achieve (some) compatibility with the field observations, must be considered in relation to the large fecundity of the Focks strain. The model is sensitive mainly to the product of these parameters with the subpopulation of mature eggs, which is greatly influenced by fecundity. The fecundity of domestic strains

of *Ae. aegypti* might have been selected in the laboratory and not be present in the field. Laboratory-dependent traits in *Ae. aegypti* are not a novelty (Craig et al., 1961). The insensitivity of adult populations to daily fecundities above a range of 2–3 eggs per female per day indicates either that wild strains are mis-adapted to the laboratory or that the selective forces in the wild differ from those in the laboratory.

The model and the data support the idea that a drought such as the one that took place in Buenos Aires during the 2008–2009 season has little lasting effects since populations do not dramatically decrease and recover as soon as the rains recover regularity. The circulation of dengue virus in Buenos Aires started after the end of the drought, when the populations had recovered and the results of the present model are consistent with the old aedesBA model used in Otero and Solari (2010).

According to the model, strategies to prevent dengue by lowering the daily fecundity, for example releasing sterile males (Lee et al., 2009), would have to sustain populations of sterile males in excess of a 1:3 (optimistic) or 17:3 (pessimistic) ratio with respect to the local males to produce a decrease to 5/6 of the population using parameters corresponding to the Córdoba strain (optimistic) or Rockefeller strain (pessimistic). Such large uncertainty between optimistic and pessimistic would disappear if the physiological parameters of the local mosquitoes and the characteristics of their food and environment were known.

6. Conclusions

The development of the model under the epistemology of complex systems (García, 2006) has led us to present new inquiries to nature to be answered by the empirical method. The aedesBA model is constructed as a statistical description which emphasizes dynamical effects at the population level more than at the level of individuals. To attain a better and broader description of the hatching and development dynamics, we have introduced a new element of description consisting of the bacteria that are consumed by developing larvae. There are several features in the development of immature mosquitoes (hatching (Gillett effect), statistics of developmental times and larval mortality) that appear to be sensitive to food, and hence to food dynamics. Incorporating all these effects to the model requires further experimental inquiries at the ecological level.

Contrasting with the prevailing intuition that *Ae. aegypti* abundance and consequently dengue risk is determined by individual (physiological or entomological) characteristics that are homogeneous at the species level, the results obtained support the idea that *Ae. aegypti* presents large amounts of genetic plasticity (Craig et al., 1961), evidenced by the different performances of the "native" mosquitoes (those whose characteristics are measured in their environment, the laboratory) and those collected in the wild. It should be kept in mind that "considerable genetic plasticity in *Ae. aegypti*" in the form of morphological and physiological variations has been recognized (Craig et al., 1961). Here, we indicated that such differences are large enough to be relevant when modeling and cannot be ignored. The construction of the model from an ecological point of view stresses the relations between the environment and the individuals and suggests experiments that could shed some light on the matter of adaptation. However, not all matters are sensitive to physiological differences between mosquito strains. Such differences are important when interventions are considered or dengue propagation is the problem of concern, and the matter becomes crucial at the time of estimating the effort needed when using sterile male techniques as control methods. Yet, other matters as mosquito abundance are not so sensitive.

We have further shown that mosquito abundance is linked by the model to a daily fecundity concept (average number of eggs laid by female and day) but it is insensitive to the quotient between the number of eggs laid per oviposition and the duration of the gonotrophic cycle. Yet, vector capacity is sensitive to the latter. Hence, if the required parameters are not properly determined, models may produce correct populations but incorrect vector capabilities at the same time.

When considered from an individual point of view, the strains simulated in this work display a range of net-reproductive-rate, NRR, going from 10 to 134 (Grech et al., 2010). Yet, when it comes to the adult numbers, strains with NRR around 10 present substantial differences among them, while the differences between some strains with NRR 10 and the Rockefeller strain (NRR 134) are not significant, evidencing important non-linearities. These results indicate that the life-history approximation to fitness and the ecological approximation are in conflict. When fitness is approached from the point of view of the individual, an infinite environment placing no limits to the population is implicitly assumed.

The model also suggests that some observed differences between mosquito strains obtained from different places located at relatively short distances (about 100 km) may play no important adaptive role.

Acknowledgement

Appendix A. Model formula

The model produces realizations of the process described by the Kolmogorov Forward Equations for the events. Let X_i be the populations $i = 1, \ldots, N$, which evolve by jumps of δ_i^α when the event $\alpha = 1, \ldots, E$ occurs, i.e., if the event α occurs at $t = 0$ the populations jump from $X_i(0^-)$ to $X_i(0^+) = X_i(0^-) + \delta_i^\alpha$. Then, the probability, $P(\mathbf{n}, t)$, of $\mathbf{n} = \{n_\alpha\}$ events that have happened up to the time t is ruled by the following equation:

$$\frac{dP(\mathbf{n}, t)}{dt} = \sum_\alpha w_\alpha(\mathbf{X} - \boldsymbol{\delta}^\alpha, t) * P(\mathbf{n} - \mathbf{1}_\alpha, t)$$

$$- \left(\sum_\alpha w_\alpha(\mathbf{X}, t) \right) * P(\mathbf{n}, t) \tag{A.1}$$

where $w_\alpha(\mathbf{X}, t)$ stands for the rate of occurrence of event α, which depends on the time and the populations (the vector $\mathbf{1}_\alpha$ is a vector with all the entries equal to zero, except the α entry, which is one).

It is important to realize that, in mathematical terms, two different events (say α and β) are different if and only if $\delta^\alpha \neq \delta^\beta$. For example, two different causes of larval mortality constitute one event with a rate that is composed of two different contributions (causes). It is possible, for convenience, to split the event in terms of the various causal contributions. Thus, there is a mapping of many to one events from biological causes to mathematical events. This is particularly relevant for the discussion of abnormal hatching, since, by definition, abnormal hatching is "all hatching not triggered by the rain". Thus, it describes several biological contributions, such as sites refilled with water by human action, spontaneous hatching, and eggs oviposited on top of the water, in a single event. The mathematics then explains that such sources of hatching cannot be distinguished by the effects on populations except when the dependences of their rates are significantly different.

Table A1
Variable names and symbols.

Variable	Name
Egg	
Immature	E_i
Mature	E_m
Wet	E_w
Larva	L
Pupa	P
Adult	
Non parous	A_1
Flyer	F
Parous	A_2
Produced food	P_f
Leftover food	f
Temperature	T
Breeding sites	BS

Random sequences distributed with the probabilities given by Eq. (A.1) are sequences of jumps in the populations at time intervals distributed exponentially with rate $W = \sum_\alpha w_\alpha(X, t)$ and probability of the event given by $p(\alpha) = w_\alpha(X, t)/W$, as originally discussed in Feller (1940). Monte Carlo implementations for these types of processes rely on the generation of random variables distributed with exponential and multinomial probabilities and were first implemented in Kendall (1950). An efficient algorithm to proceed with population updates at fixed time intervals (taken as 2 h in our simulations) was presented in Solari and Natiello (2003).

The use of exponentially distributed times is not a limitation on the type of distributions for biological processes that can be implemented. By introducing intermediate steps, it is possible to generate any desired time statistics as discussed in Otero et al. (2011). Thus, the method does not impose a limitation on the biology.

Additionally, it is worth having into account that by defining $x = (X/BS)$ and taking the limit for large carrying capacities ($BS \to \infty$) with x finite, a deterministic limiting process that corresponds to the standard heuristic ordinary differential equations for this family of mathematical problems is defined (Kurtz, 1970; Ethier and Kurtz, 1986).

The populations, events and rates considered in this work are listed in Table A1.

The computer code of aedesBA is written in C, is distributed under GNU license and a copy can be obtained from the corresponding author.

Appendix B. Model interpretation of the experimental results of Macia and Barrera

In his work, Macia reports the average time for pupation (in days), D, and the survival probability, S, in experiments performed at 26 °C under natural conditions (natural, self-sustained feeding) at different densities (4, 8, 16, 32, 64, 128, and 256 larvae). Each experiment was replicated four times. The experiment was considered complete when either there were no more larvae in the replica or there was no pupation for a period of 7 days. We summarize the values extracted from Macia in Table B1. The 7-day rule was not applied to the densities 4–64 but it may be influencing the 128 larvae density and definitely influences the 256 larvae density. Thus, because of this reason we will limit our elaboration of the results to the densities 4–64.

Similarly, mortality depends on the relation between larvae and food. While the daily survival is usually considered in the range between 0.99 and 0.96 under laboratory conditions (Grech et al., 2010), such values are obtained in the competition between the events pupation and death. Such competitions are won by pupation under laboratory conditions in about seven days.

Resistance to starvation was studied by Barrera (1996). Larvae of *Ae. aegypti* that were starved after 3.5 days of being naturally fed showed a survival rate that quickly decreased towards zero at 15 to 20 days of starvation. Barrera indicates that "no pupa was produced during starvation in any of the experiments with natu-

Table B1
Results from Maciá (2009).

Density	Individuals	D (days)	Survival
4	4×4	5.45	1
8	4×8	5.78	1
16	4×16	5.41	1
32	4×32	7.14	1
64	4×64	11.75	0.97
128	4×128	10.39	0.45
256	2×256	7.42	0.065

Table A2
Events actions and rates.

Event	Action	Individual rate Ω	w
Maturation	$E_i \to E_m$	$e_m(T) = -0.017 + 0.039 * e^{(T+7.260)/16.479}$	$(1 - p_{ab}) * e_m(T) * E_i$
Abnormal hatching	$E_i \to L$		$p_{ab} * e_m(T) * E_i$
Rain	$E_m \to E_w$	$Prob = 0.8 * G$	
	Gillett effect	$G = \begin{cases} 1 & f > 0 \\ 0.05 & f = 0 \end{cases}$	
Hatching	$E_w \to L$	$e_{wl}(T) = \alpha_{ewl} * e_m(T)$	$e_{wl}(T) * E_w$
Pupation	$L \to P$	$l_p(T, L/P_f)$ (Eq. (1))	$l_p(T, L/P_f) * L$
Emergence	$P \to A_1$	$p_a(T) = \alpha_{pa} * e^{(T-4.765)/11.106}$	$p_a(T) * L$
Oviposition	$F \to A_2$	$ovi(BS) = \begin{matrix} BS < 150 & 0.029 * BS \\ BS \geq 150 & 4.35 \end{matrix}$	$ovi(BS) * F$
	$E_i \to E_i + \phi$		
Dispersal rate		$migr$	$0.664 * F$
Dispersal direction	$F_{ij} \to F_{i'j'}$	$dire = \begin{cases} 0.165 & \text{straight flight} \\ 0.085 & \text{diagonal flight} \end{cases}$	
First g. cycle	$A_1 \to F$	$cycl_1(T) = \alpha_{cy1} * e^{(T-4.751)/10.580}$	$cycl_1(T) * A_1$
Later g. cycle	$A_2 \to F$	$cycl_2(T) = cycl_1(T) * 1.721$	$cycl_2(T) * A_2$
	$E_i \to \emptyset$		
Egg death	$E_m \to \emptyset$	$d_e = 0.01$	$d_e * E$
	$E_w \to \emptyset$		
Larva death	$L \to \emptyset$	$d_l(L/P_f, T)$ (Eq. (2))	$d_l(L/P_f) * L$
Pupa death	$P \to \emptyset$	$d_p(T) = \alpha_{dp} * (0.01 + e^{-(T-5)/2.703})$	$d_p(T) * P$
	$A_1 \to \emptyset$		$d_a * A_1$
Adult death	$A_2 \to \emptyset$	$d_a = 0.09$	$d_a * A_2$
	$F \to \emptyset$		$d_a * F$

ral food". The experiments were performed in three replicas of 100 larvae each and no larvae survived more than 25 days of starvation. In contrast, 36%-78% survival would have been expected extrapolating the constant mortality found when food is in excess, a fact that clearly indicates an increase in the mortality due to starvation.

B.1. Pupation

In the current model, there are only two competing events for larvae: death and pupation. The probability of pupation for a larva is

$$p(T, L/P_f) = \frac{l_p(T, L/P_f)}{l_p(t, L/P_f) + d_l(L/P_f)} \tag{B.1}$$

The average survival is then

$$LS \equiv L * S = \sum_{i=1}^{L} p(T, i/P_f) \approx 1.4 + 0.96839 * L \tag{B.2}$$

The average time of pupation computed for L larvae in competition is

$$D(T, L/P_f) = \sum_{i=1}^{L} \frac{1}{\Omega_{l_p}(T, i/P_f)} \tag{B.3}$$

when all the larvae reach pupation and

$$D(T, L/P_f) = \frac{1}{LS} \sum_{i=1}^{L} \frac{p(T, L/P_f)}{\Omega_{l_p}(T, i/P_f)} \tag{B.4}$$

considering the mortality.

Hence, if we consider the values reported by Macia (see Table B1), we can adjust a linear relation between LS and L. The slope of the line corresponds to the survival rate (Fig. B.1).

We then obtain an approximately constant survival rate of 0.97.

For the average time to pupation, we can proceed similarly. $LSD \equiv LS * D$ as a function of L can be adjusted with a quadratic function.

Fig. B.2.

Hence, we obtain

$$LSD(L) \approx 14.237 + 2.2965 * L + 0.13867 * L^2 \tag{B.5}$$

$$1/\Omega_{l_p}(T, L/P_f) = 0.97 * (LSD(L) - LSD(L - 1)) \tag{B.6}$$

However, this fit does not take into account the fact that for $L = 4, 8, 16$ the pupation time is almost constant. Hence, we consider that Macia's experiment shows that there was food in excess

Fig. B.1. Total survival as a function of the initial number of larvae and linear fit.
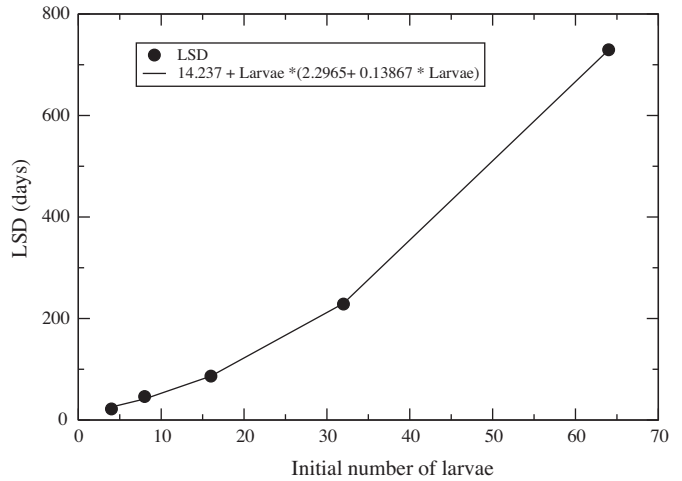
Fig. B.2. *LSD* plot against the initial number of larvae, and quadratic fit.

for 16 larvae and that pupation was maintained up to 64 larvae with a decreasing rate which is the multiplicative inverse of a linear function. For higher densities, the long pupation times result in a prevalence of death events over pupation. We will account for it as an increase in the mortality rate.

These considerations lead us to propose the pupation rate as a function of the relation between larvae and food (Eq. (1)).

B.2. Mortality

Mortality rates are more difficult to establish from the experiments. While a constant mortality probability suggests a proportionality between pupation and death rates, the difference with an accepted constant mortality rate of 0.01 reflected in $S(L)$ lies within the uncertainty of the data. We prefer adopting a constant mortality rate at low densities.

Starvation imposes a limit time to the mortality rate (Barrera, 1996). With no food, a larva fed in the 3.5 previous days with natural food will last about 15 to 25 days. Additionally, starving larvae do not reach pupation. In Macia's experiment, the mortality increases significantly for the 128-larvae density and even further for the 256-larvae density, although these data are influenced by the 7-day rule of the experiment. We take these data as an indication that starvation conditions begin to appear at densities of 128 larvae and linearly interpolate an increase in the mortality to an average survival time of 18 days.

$$W_{dl}(L) = \begin{cases} 0.01 & \text{if } L < 64 \\ 0.01 + \dfrac{M_{NL} * (L - 64)}{16} & \text{if } 64 < L < 128 \\ 0.01 + M_{NL} * 4 & \text{if } 128 < L \end{cases} \tag{B.7}$$

The coefficient of non-linear mortality is expected to range between 0.010 and 0.023, corresponding to an average survival under starvation conditions between 10 and 20 days. The lower limit accounts for a shorter period of sufficient feeding before starvation than the one studied by Barrera. Eq. (B.7) results in the dependence on the Larvae to available food relation of Eq. (2).

Appendix C. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ecolmodel. 2012.12.004. These data include Google maps of the most important areas described in this article.
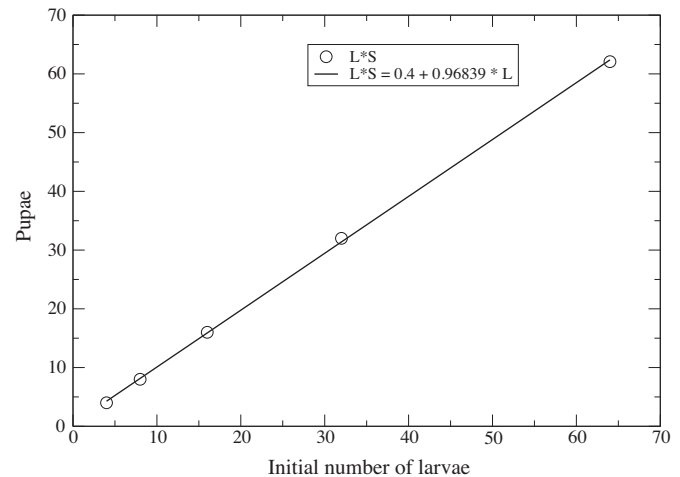
References

Barrera, R., 1996. Competition and resistance to starvation in larvae of container-inhabiting *Aedes* mosquitoes. Ecological Entomology 21 (1), 17–127.

Bergero, P., Ruggerio, C., Lombardo, R., Schweigmann, N., Solari, H., 2011. Dispersal of *Aedes aegypti*: field study in temperate areas and statistical approach, preprint available from the authors.

Carbajo, A. E., 2003. Distribución espacio-temporal de *Aedes aegypti* (Diptera: Culicidae): su relación con el ambiente urbano y el riesgo de transmisión del virus dengue en la Ciudad de Buenos Aires. Ph.D. thesis. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, director: Susana I Curto.

Carbajo, A.E., Curto, S.I., Schweigmann, N., 2006. Spatial distribution pattern of oviposition in the mosquito *Aedes aegypti* in relation to urbanization in Buenos Aires: southern fringe bionomics of an introduced vector. Medical and Veterinary Entomology 20, 209–218.

Chadee, D.D., 2009. Oviposition strategies adopted by gravid *Aedes aegypti* (L.) (Diptera: Culicidae) as detected by ovitraps in Trinidad, West Indies (2002–2006). Acta Tropica 111, 279–283.

Christophers, R., 1960. *Aedes aegypti* (L.) the yellow fever mosquito. Cambridge University Press, Cambridge.

Craig Jr, G.B., Vandehey, R.C., Hickey, W.A., 1961. Genetic variability in populations of *Aedes aegypti*. Bulletin of the World Health Organization 24, 527–539.

De Majo, M.S., 2011. Asociación de la temperatura y de la mortalidad invernal de los huevos con la dinámica poblacional de *Aedes aegypti* en Buenos Aires. Master's thesis. Departamento de Ecología, Genética y Evolución, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Sylvia Fischer (supervisor).

Durrett, R., 2001. Essentials of Stochastic Processes. Springer Verlag, New York.

Dégallier, P.N., Hervé, J.P., Rosa, A.F.A.T.D., Sa, G.C., 1988. *Aedes aegypti* (L.): importance de sa bioécologie dans la transmission de la dengue et des autres arbovirus. Bulletin de la Societe de Pathologie Exotique 81, 97–110.

Edgerly, J.S., Marvier, M.A., 1992. To hatch or not to hatch? egg hatch response to larval density and to larval contact in a treehole mosquito. Ecological Entomology 17, 28–32.

Edgerly, J.S., Willey, M.S., Livdhal, T.P., 1993. The community ecology of *Aedes* egg hatching: implications for mosquito invasion. Ecological Entomology 18, 123–128.

Ellis, A.M., Garcia, A.J., Focks, D.A., Morrison, A.C., Scott, T.W., 2011 Aug. Parameterization and sensitivity analysis of a complex simulation model for mosquito population dynamics, dengue transmission, and their control. American Journal of Tropical Medicine and Hygiene 85, 257–264.

Estallo, E.L., Ludueña-Almeida, F.F., Visintin, A.M., Scavuzzo, C.M., Introini, M.V., Zaidenberg, M., Almirón, W.R., 2011. Prevention of dengue outbreaks through *Aedes aegypti* oviposition activity forecasting method. Vector-Borne and Zoonotic Diseases 11, 543–549.

Ethier, S.N., Kurtz, T.G., 1986. Markov Processes. John Wiley and Sons, New York.

Feller, W., 1940. On the integro-differential equations of purely discontinuous Markoff processes. Transactions of the American Mathematical Society 48, 488–515.

Focks, D.A., Haile, D.C., Daniels, E., Keesling, D., 1995. A simulation model of the epidemiology of urban dengue fever: literature analysis, model development, preliminary validation and samples of simulation results. American Journal of Tropical Medicine and Hygiene 53, 489–505.

Focks, D.A., Haile, D.C., Daniels, E., Moun, G.A., 1993a. Dynamics life table model for *Aedes aegypti*: analysis of the literature and model development. Journal of Medical Entomology 30, 1003–1018.

Focks, D.A., Haile, D.C., Daniels, E., Mount, G.A., 1993b. Dynamic life table model for *Aedes aegypti*: simulations results. Journal of Medical Entomology 30, 1019–1029.

García, R., 2006. Sistemas Complejos. Conceptos, métodos, y fundamentación epistemológica de la investigación interdisciplinaria, Gedisa, Barcelona, Spain.

Gillett, J.D., 1955a. The inherited basis of variation in he hatching response of *Aedes* eggs (Diptera: Culicidae). Bulletin of the World Health Organization 46, 255–265.

Gillett, J.D., 1955b. Variation in the hatching-response of *Aedes* eggs (Diptera: Culicidae). Bulletin of the World Health Organization 46, 241–255.

Gillett, J.D., Roman, E.A., Phillips, V., 1977. Erratic hatching in *Aedes* eggs: a new interpretation. Proceedings of the Royal Society London B 196, 223–232.

Grech, M.G., Ludueña-Almeida, F., Almirón, W.R., 2010. Bionomics of *Aedes aegypti* subpopulations (Diptera: Culicidae) from Argentina. Journal of Vector Ecology 35, 277–285.

Gubler, D.J., 1998. Dengue and dengue hemorrhagic fever. Clinical Microbiology Review 11, 480–496.

Hartmann, S., 1995. Models as a tool for theory construction: some strategies of preliminary physics. In: Herfel, W.E. (Ed.), Theories and Models in Scientific Processes: Proceedings of AFOS '94, vol. 44. Poznarí Studies in Phylosophy and Humanities, pp. 49–67.

Kearney, M., Porter, W.P., Williams, C., Ritchie, S., Hoffmann, A.A., 2009. Integrating biophysical models and evolutionary theory to predict climatic impacts on species' ranges: the dengue mosquito *Aedes aegypti* in Australia. Functional Ecology 23, 528–538, http://dx.doi.org/10.1111/j.1365-2435.2008.01538.x.

Kendall, D.G., 1950. An artificial realization of a simple "birth-and-death" process. Journal of the Royal Statistical Society, Series B: Statistical Methodology 12, 116–119.

Kolmogoroff, A., 1931. Über die analytischen methoden in der wahrscheinlichkeitsrechnung. Mathematische Annalen 104, 415–458.

Kurtz, T.G., 1970. Solutions of ordinary differential equations as limits of pure jump Markov processes. Journal of Applied Probability 7, 49–58.

Lakatos, I., 1978. Mathematics, Science and Epistemology. Cambridge University Press, Cambridge, UK.

Lande, R., 1976. Natural selection and random genetic drift in phenotypic evolution. Evolution 30, 314–334.

Lee, H.L., Jokob, H., Naznia, W.A., Vasanc, S.S., 2009. Comparative life parameters of transgenic and wild strain of *Aedes aegypti* in the laboratory. Dengue Bulletin 33, 103–144.

Legros, M., Magori, K., Morrison, A.C., Xu, C., Scott, T.W., Lloyd, A.L., Gould, F., 2011. Evaluation of location-specific predictions by a detailed simulation model of *Aedes aegypti* populations. PLoS ONE 6, e22701.

Livdahl, T.P., Edgerly, J.S., 1987. Egg hatching inhibition: field evidence for population regulation in a treehole mosquito. Ecological Entomology 12, 395–399.

Livdahl, T.P., Koenekoop, R.K., Futterweit, S.G., 1984. The complex hatching response of *Aedes* eggs to larval density. Ecological Entomology 9, 437–442.

Maciá, A., 2006. Differences in performance of *Aedes aegypti* larvae raised at different densities in tires and ovitraps under field conditions in Argentina. Journal of Vector Ecology 31, 371–377.

Maciá, A., 2009. Effects of larval crowding on development time, survival and weight at metamorphosis in *Aedes aegypti* (Diptera: Culicidae). Revista de la Sociedad Entomológica Argentina 68, 107–114.

Magori, K., Legros, M., Puente, M.E., Focks, D.A., Scott, T.W., Lloyd, A.L., Gould, F., 2009. Skeeter Buster: a stochastic, spatially explicit modeling tool for studying *Aedes aegypti* population replacement and population suppression strategies. PLOS Neglected Tropical Diseases 3, e508, http://dx.doi.org/10.1371/journal.pntd.0000508.

Merritt, R.W., Dadd, R.H., Walker, E.D., 1992. Feeding behavior, natural food, and nutritional relationships of larval mosquitoes. Annual Review of Entomology 37, 349–376.

Micieli, M.V., Campos, R.E., 2003 Jul. Oviposition activity and seasonal pattern of a population of *Aedes (Stegomyia) aegypti* (L.) (Diptera: Culicidae) in subtropical Argentina. Memorias do Instituto Oswaldo Cruz 98, 659–663.

Moore, C.G., Whitacre, C.H., 1972. Competition in mosquitoes. 2. Production of *Aedes aegypti* larval growth retardant at various densities and nutritional levels. Annals of the Entomological Society of America 65, 915–918.

Morrison, A.C., Gray, K., Getis, A., Astete, H., Sihuincha, M., Focks, D., Watts, D., Stancil, J.D., Olson, J.G., Blair, P., Scott, T.W., 2004. Temporal and geographic patterns of *Aedes aegypti* (Diptera: Culicidae) production in iquitos, peru. Journal of Medical Entomology 41, 1123–1142.

Otero, M., Barmak, D.H., Dorso, C.O., Solari, H.G., Natiello, M.A., 2011. Modeling dengue outbreaks. Mathematical Biosciences 232, 87–95.

Otero, M., Schweigmann, N., Solari, H.G., 2008. A stochastic spatial dynamical model for *Aedes aegypti*. Bulletin of Mathematical Biology 70, 1297–1325.

Otero, M., Solari, H.G., 2010. Mathematical model of dengue disease transmission by *Aedes aegypti* mosquito. Mathematical Biosciences 223, 32–46.

Otero, M., Solari, H.G., Schweigmann, N., 2006. A stochastic population dynamic model for *Aedes aegypti*: formulation and application to a city with temperate climate. Bulletin of Mathematical Biology 68, 1945–1974.

Ponnusamy, L., Böröczky, K., Wesson, D.M., Schal, C., Apperson, C.S., 2011. Bacteria stimulate hatching of yellow fever mosquito eggs. PLoS ONE 6, e24409.

Robertson, F.W., 1960. The ecological genetics of growth in *Drosophila*. 1. Body size and developmental time on different diets. Genetic Research 1, 288–304.

Robertson, F.W., 1966 Oct. The ecological genetics of growth in *Drosophila*. 8. Adaptation to a new diet. Genetic Research 8, 165–179.

Rueda, L.M., Patel, K.J., Axtell, R.C., Stinner, R.E., 1990. Temperature-dependent development and survival rates of *Culex quinquefasciatus* and *Aedes aegypti* (Diptera: Culicidae). Journal of Medical Entomology 27, 892–898.

Schweigmann, N., Orellano, P., Kuruc, J., Vera, M.T., Vezzani, D., Méndez, A., 2002. Distribución y abundancia de *Aedes aegypti* (Diptera: Culicidae) en la ciudad de Buenos Aires. In: Salomón, D.S. (Ed.), Actualizaciones en Artropodologí a Sanitaria Argentina. Revista Sociedad Entomológica Argentina. Fundación Mundo Sano, pp. 155–160.

Seijo, A., Romer, Y., Espinosa, M., Monroig, J., Giamperetti, S., Ameri, D., Antonelli, L., 2009. Brote de dengue autóctono en el area metropolitana Buenos Aires. experiencia del Hospital de enfermedades infecciosas F. J. Muñiz. Medicina 69, 593–600.

Solari, H.G., Natiello, M.A., 2003. Stochastic population dynamics: the Poisson approximation. Physical Review E 67, 031918.

Southwood, T.R.E., Murdie, G., Yasuno, M., Tonn, R.J., Reader, P.M., 1972. Studies on the life budget of *Aedes aegypti* in Wat Samphaya Bangkok Thailand. Bulletin of the World Health Organization 46, 211–226.

Stearns, S.C., 1989. The evolutionary significance of phenotypic plasticity. BioScience 39, 436–445.

Tejerina, E.F., Almeida, F.F.L., Almirón, W.R., 2009. Bionomics of *Aedes aegypti* subpopulations (Diptera: Culicidae) from Misiones province, northeastern Argentina. Acta Tropica 109, 45–49.

Vezzani, C., Velázquez, S.T., Schweigmann, N., 2004. Seasonal pattern of abundance of *Aedes aegypti* (Diptera: Culicidae) in Buenos Aires city, Argentina. Memorias do Instituto Oswaldo Cruz 99, 351–356.

Xu, C., Legros, M., Gould, F., Lloyd, A.L., 2010. Understanding uncertainties in model-based predictions of *Aedes aegypti* population dynamics. PLOS Neglected Tropical Diseases 4 (9), e830.

Zwietering, M.H., de Koos, J.T., Hasenack, B.E., de Witt, J.C., van't Riet, K., 1991. Modeling of bacterial growth as a function of temperature. Applied and Environment Microbiology 57, 1094–1101.