

An Agent-Based Model of Host Odor-Mediated Host-Seeking Behavior of Mosquitoes

Ricardo Cortez

Mathematics Department
Tulane University

Angela Gallegos

Mathematics Department
Occidental College

Cavin Ward-Caviness

Mathematics Department
Tulane University

Ivo M. Foppa

Department of Epidemiology
Tulane University

June 15, 2009

1 Introduction

As most mosquitoes depend for their reproduction on a blood meal, it must be assumed that they evolved to be very well adapted to the difficult task locating suitable feeding-hosts. This premise implies that the spatial distribution of hosts informs the spatial distribution of feeding mosquitoes and thus their distribution relative to hosts. As the female mosquito’s blood meal is the driver of horizontal mosquito-borne transmission, the process of host location as important to the epidemiology of mosquito-borne diseases as it is to the survival of mosquitoes. All hematophagous insects use olfaction to locate their feeding-hosts [12]. In night-time active mosquitoes, such as *Cx. quinquefasciatus*, this is likely to be the most important modality. It therefore seems surprising that a recent comprehensive text on the biology of disease vectors [13] devotes less than half a page to the subject of olfaction and host-seeking and states that

“[l]ittle is known about the exact behaviors involved during this process [of bringing mosquitoes in contact with their host] and how specific stimuli may activate them.”
[11]

This substantial lacuna in our understanding of host-seeking by mosquitoes may seem surprising, but likely has to do with the complexity of the odor plume associated with a host. Odor plumes are defined by the distribution of odor molecules once they are released from their source and result from the physical interaction between odor molecules and the “fluid” environment (to include air) [14]. Odor plumes have complex spatiotemporal structure and cannot easily be physically characterized. Equally importantly, technology for tracking mosquito flight is only starting to emerge (see, e.g. ??) The development of flexible models of odor-plume mediated mosquito behavior is therefore ... Here we describe a detailed agent-based simulation model of mosquito host seeking behavior

1.1 The Mathematical Model

The model can be described in terms of three components: (1) the evolution of a concentration plume used by the mosquitoes to seek out hosts, (2) the behavior of the hosts, and (3) the behavior of the mosquitoes. The transmission dynamics is assumed to occur in a two-dimensional rectangular region whose sides are of length L_x and L_y . A population of N_v mosquitoes (e.g. *Cx. quinquefasciatus*) are initially placed in a subregion that can be selected by the user. Similarly, there are initial populations of N_h hosts (e.g. birds), placed in several subregions.

The odor plume. The first component of a transmission dynamics model is the mosquito-host interaction, including the mechanisms that mosquitoes use to find hosts. Our model is based on the assertion that hosts release a fixed amount of CO_2 (or some other gaseous clues) per host per unit time. This concentration plume is then diffused and possibly convected by wind within the two-dimensional region. The convection velocity of the wind is assumed to be represented by the known velocity vector $\vec{U}(x, y, t)$. The concentration $C(x, y, t)$ satisfies the advection-diffusion equation

$$\frac{\partial C}{\partial t} + \vec{U} \cdot \nabla C = D \nabla^2 C + S(x, y), \quad (1)$$

where t is time, and (x, y) are spatial coordinates. D is the (constant) diffusion coefficient and can be adjusted to reflect the speed at which the particular substance of interest diffuses in air. The transport velocity \vec{U} can be used to introduced drifts or relatively large features produced by the air, but in this case it does not represent small scale turbulence. The last term represents the source of CO_2 concentration at the host locations. In our model, we will consider this term to be $S(x, y) = S_0 \sum \delta(x - x_h, y - y_h)$ where S_0 is a constant concentration per unit time and the delta function reflects the fact that the CO_2 occurs only at the host locations. Although Eq. (1) is continuous in space and time, to simulate this spread computationally, we use a discrete grid of spacing h that covers the two-dimensional domain $L_x \times L_y$. We use $x_j = jh$ and $y_k = kh$ (with $hN_x = L_x$ and $hN_y = L_y$). Then $C_{j,k}^n$ approximates $C(x_j, y_k, t_n)$ and its derivatives are approximated using center-differences:

$$\frac{\partial C}{\partial x}(x_j, y_k, t_n) \approx \frac{C_{j+1,k}^n - C_{j-1,k}^n}{2h}, \quad \frac{\partial^2 C}{\partial y^2}(x_j, y_k, t_n) \approx \frac{C_{j,k+1}^n - 2C_{j,k}^n + C_{j,k-1}^n}{h^2}, \quad \text{etc.}$$

The host behavior. The principal opportunities for host-mosquito interaction are during roosting periods in which hosts are relatively stationary. This assumption is based on the crepuscular and nocturnal feeding habits of *Culex quinquefasciatus*. Our model allows the hosts a small random motion about their roosting location. At fixed time intervals, the steps of this random walk are selected from a Gaussian distribution with zero mean and adjustable variance. The direction of each step is given by a random angle θ taken from a uniform distribution between 0 and 2π . Currently, the random steps in all directions are equally likely; however, enhancements to this component such as biasing the random walk to account for preferred motion of the hosts can easily be included.

The mosquito behavior. A random walk with zero mean and its own variance is also applied to the mosquitoes to describe small-scale behavior not accounted for in other parts of the model. In addition, the mosquito behavior includes a host-seeking component that allows them to find hosts. Neither the host nor the mosquito locations are restricted to the CO_2 grid. We assume that the mosquitoes can sense the direction of the concentration gradient of the CO_2 with an accuracy depending on the magnitude of the gradient. Larger gradients are sensed with better accuracy than lower ones. This sensing mechanism is accounted for by introducing a second random walk

of the mosquitoes in a direction approximately equal to that of the concentration gradient. For example, we assume that the concentration gradient at the mosquito location (x, y) is $\nabla C(x, y)$ in the direction of an angle θ (see Figure 1). The mosquito at that location takes a step of fixed size in a direction given by a random angle in the interval $[\theta - \alpha, \theta + \alpha]$. The size of this window, represented by α , is smaller when the concentration gradient magnitude $|\nabla C|$ is large. Specifically, we use

$$\alpha = \alpha_{min} + \frac{\alpha_{max} - \alpha_{min}}{1 + \beta|\nabla C|}$$

so that the extreme cases of $|\nabla C| = \infty$ and $|\nabla C| = 0$ give α_{min} and α_{max} , respectively. In this equation, β is a constant with the appropriate units to make the expression dimensionless.

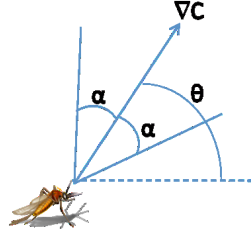


Figure 1: Schematic of the mosquito host-seeking model based on the concentration gradient direction.

The biting rate. Once a mosquito comes in contact with a host, there is a possibility of a blood meal and transmission of the infection. In our model, the mosquitoes and hosts are represented by points moving in space; thus, they do not actually come into contact. However, we define a “biting radius” around each mosquito. If a mosquito is within the biting radius of the host, it has a possibility of biting it. The biting radius is a purely computational parameter so there is a need to determine its appropriate range of values through numerical tests. Once a host is within the biting radius of a mosquito, we assign both a probability of a blood meal and a probability of transmission (in the case that the encounter involves one infectious and one susceptible agent). The mosquito-to-host transmission and the host-to-mosquito transmissions occur with different probabilities. Hosts recover from infection at a given rate and no host mortality was assumed to occur.

In summary, the model consists of the following equations for the hosts locations (x_h, y_h) , the mosquito locations (x_m, y_m) and the CO_2 concentration C :

$$\begin{aligned} \text{Hosts:} \quad & \frac{dx_h}{dt} = \ell_h \cos(\phi_u), \quad \frac{dy_h}{dt} = \ell_h \sin(\phi_u) \\ \text{Mosquitoes:} \quad & \frac{dx_m}{dt} = \ell_m \cos(\psi_u) + d_m \cos(\alpha_u), \quad \frac{dy_m}{dt} = \ell_m \sin(\psi_u) + d_m \sin(\alpha_u) \\ \text{Concentration:} \quad & \frac{\partial C}{\partial t} + U_1 \frac{\partial C}{\partial x} + U_2 \frac{\partial C}{\partial y} = D \left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2} \right) + S_0 \sum \delta(x - x_h, y - y_h) \end{aligned}$$

where ℓ_h , ℓ_m and d_m are fixed distances, all angles with a subscript u are random variables with uniform distribution; ϕ_u and ψ_u take values in $[0, 2\pi)$ and α_u takes values in $(\theta - \alpha, \theta + \alpha)$ as described earlier. The wind transport is represented by \vec{U} and is assumed to be known, D is the diffusivity of the concentration C in air, and S is the CO_2 source (constant per host per unit of time) at the host locations.

The equations are coupled together since the host locations affect the concentration gradient, which in turn, affects the motion of mosquitoes. Once a mosquito is within the biting radius R_b of a host,

there is a probability P_b of biting. After biting, there is a probability P_t of transmission to the host. Both of these probabilities are assumed to be constant. Once a mosquito has bitten a host, it no longer participates in the dynamics (one blood meal per mosquito).

1.1.1 Dimensionless representation of the model

In order to reduce the number of parameters in the model, we define dimensionless versions of all variables by choosing appropriate scalings. We choose the velocity scale to be d_m , the mosquito host-seeking speed, and the length scale to be the size of the domain L . Together they define a time scale given by $T = L/d_m$. We also choose a concentration scale based on the rate of CO_2 production per host per time, $S_0 T$. In this way, the dimensionless concentration is related to the dimensional concentration by $\hat{C} = C/(S_0 T)$. Similarly, all variables with units of length are divided by L . The equations in dimensionless form are

$$\begin{aligned} \text{Hosts:} \quad & \frac{dx_h}{dt} = \xi \cos(\phi_u), \quad \frac{dy_h}{dt} = \xi \sin(\phi_u) \\ \text{Mosquitoes:} \quad & \frac{dx_m}{dt} = \gamma \cos(\psi_u) + \cos(\alpha_u), \quad \frac{dy_m}{dt} = \gamma \sin(\psi_u) + \sin(\alpha_u) \\ \text{Concentration:} \quad & \frac{\partial C}{\partial t} + V_1 \frac{\partial C}{\partial x} + V_2 \frac{\partial C}{\partial y} = \mu \left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2} \right) + \sum \delta(x - x_h, y - y_h) \\ & \alpha = \alpha_{min} + \frac{\alpha_{max} - \alpha_{min}}{1 + \rho |\nabla C|} \end{aligned}$$

where the dimensionless groups are,

$$\xi = \frac{\ell_h}{d_m}, \quad \gamma = \frac{\ell_m}{d_m}, \quad \mu = \frac{D}{d_m L}, \quad \rho = \frac{\beta S_0}{d_m}, \quad V_i = \frac{U_i}{d_m}$$

1.1.2 Example: Parameter study

We begin with an example that will help gain insight into the effect of the parameters in host-seeking behavior. In this case, the hosts will be stationary, so we set $\xi = 0$, and we assume there is no advection ($V_1 = V_2 = 0$). We fix the value of μ and study the effect of γ and ρ . The setup consists of two groups of hosts containing 90% and 10% of the hosts, respectively, placed initially at the same distance from the release location of the mosquitoes. As we vary the parameters, we record the number of mosquitoes that bite hosts in each of the groups.

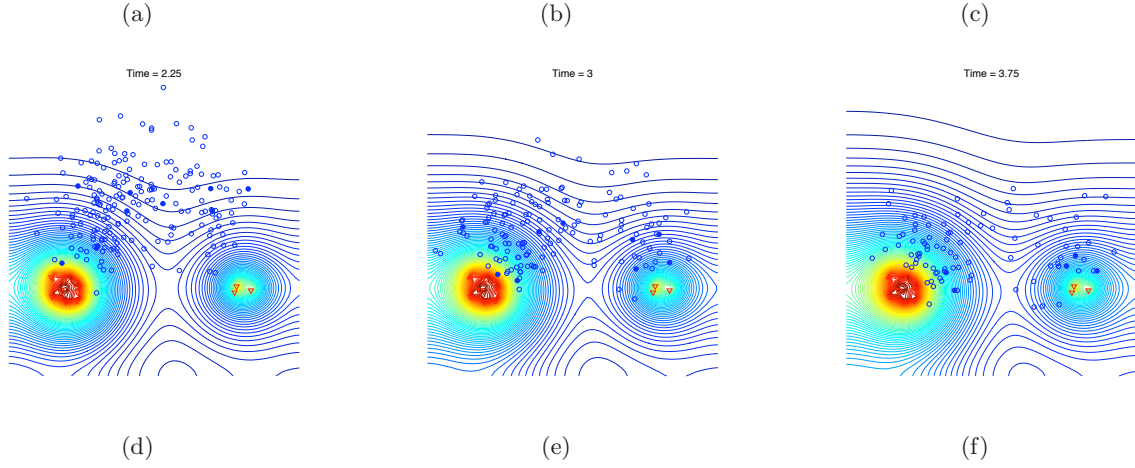


Figure 2: Mosquito and host spatial distribution at various times. The initial host population was given by two equal groups at equal distances from the mosquito release location. Vectors seek hosts by moving in the direction of a concentration gradient plus the random walk. The number of vectors infected by the larger group is larger but not proportional to the group size.

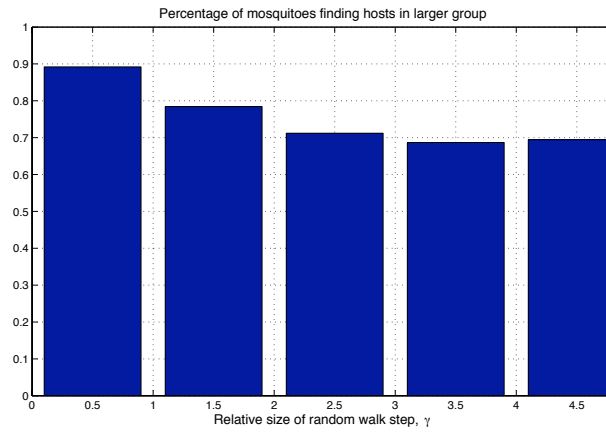


Figure 3: Percentage of mosquitoes that find hosts in the larger group as a function of γ . Since γ is the ratio of the random walk speed of mosquitoes to the speed of mosquitoes due to the gradient sensing, the smaller values of γ correspond to less dispersion of mosquitoes during the process. This leads to a larger percentage of them reaching the larger group of hosts.

2 Preliminary studies

2.1 Host mortality and transmission dynamics

By inspection of a simple expression for the R_0 of enzootic WNV transmission and by simulation we showed that an acute die-off of reservoir hosts may substantially boost transmission of an agent like WNV [8]. We found that very high reservoir mortality increased the resulting number of infectious mosquitoes by the end of the epizootic by roughly 50% compared to an avirulent situation (Figure 4. This was, however, only true if no alternative, reservoir incompetent hosts were locally available. The presence of only few such hosts substantially mitigated the transmission boosting effect of reservoir mortality. This work relied on a set of assumptions that have yet to be verified. Most importantly, it assumed frequency dependence and host number independence of the biting rate; i.e. the mosquito feeding rate is entirely determined by intrinsic factors (or constant). However, these results pointed out the potential epidemiological importance of the mosquito-host ratio and the somewhat counterintuitive role host mortality may play to promote an agent like WNV.

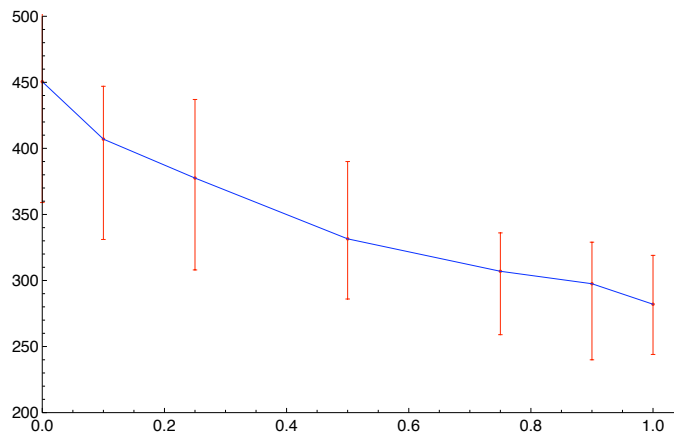


Figure 4: Final distribution of the number of infectious mosquitoes after epizootics according to various levels of virulence. The x-axis represents the level of virulence (% in terms of reservoir host mortality) and the y-axis the number of infectious mosquitoes at the end of an epizootic. The crosses represent median numbers of infectious mosquitoes at the end of the epizootic, at different levels of virulence, expressed as cumulative mortality. Error bars correspond to the 2.5th and the 97.5th percentile, respectively (From [8]).

2.2 Host density and feeding density in the olfactometer

To examine host choice of mosquitoes (colonized *Cx. pipiens*) in dependence of host density, we used a modified y-tube olfactometer in a pilot experiment (Figure 5, upper left). The two chambers of the apparatus were baited with ten chickens (*Gallus gallus*) between 2 and 9 days old and variably distributed among the two chambers. Invariably, more mosquitoes (65%; 95% C.I. 51%, 78%) were retrieved from the chamber with fewer chickens. As these results did not appear meaningful in the context of our hypothesis and due to olfactometers being notoriously cumbersome we abandoned this experimental setup in favor of a more realistic field-based or field-like approach.

2.3 Host density and feeding density in the field

To examine the impact of host density on feeding density of ornithophilic mosquitoes in the field we conducted a field study, using chickens as bait. Briefly, during October 2008, we exposed ten adult Longhorn chickens in wire surveillance cages overnight to the resident mosquito fauna of a rural site (Tulane University's Hébert Research Center in northern Plaquemines Parish, LA) (Figure 5, right). The chickens were distributed such that in one location nine chickens were exposed, while the remaining chicken was exposed at a distance of approx. 90 ft. Malaise traps (BioQuip Products, Rancho Dominguez, CA) were draped over the cages. The next morning, mosquitoes were retrieved from the collection jars of the malaise traps (Figure 5, upper right) and brought to the laboratory. Mosquitoes were identified to species and sorted into engorged and non-engorged mosquitoes. More than 95% of all engorged mosquitoes were *Culex nigripalpus*. Relative feeding rates per chicken per night were calculated for the two host densities. Although, on average, the number of mosquitoes at the location with the higher number of hosts was double the number from the location with only one chicken, the relative feeding density was four times there the feeding density the larger group of chickens experienced.

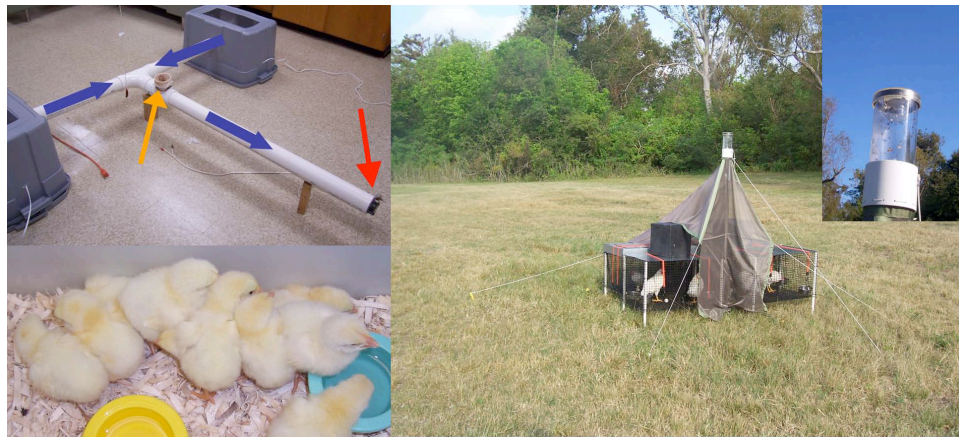


Figure 5: Left-hand panel, upper part: T-tube olfactometer with blue arrows indicating the direction of the airflow; orange arrow pointing to the release chamber and red arrow pointing to the fan. Lower part: Young chicks (*Gallus gallus*) used in the experiment. Right-hand panel: Malaise trap with 5 wire cages, each holding up to 2 chickens. Two resting boxes are placed on top of the cages. The insert shows a collection jar after overnight exposure.

No. of chickens	No. of fed <i>Cx. nigripalpus</i> (exact 95% C.I.) [†]	Biting rate per chicken
1	16 (9.2, 26.0)	8.0 (4.6-13.0) [‡]
9	33 (22.7, 46.3)	1.8 (1.3-2.6)

[†] Daly L., Simple SAS macros for the calculation of exact binomial and Poisson confidence limits. Comput. Biol. Med. (1992) 22:351-361.

[‡]As the numbers are based on two experiments, the second column was divided by 2 times the first column to obtain the rate (third column).

Table 1: The number of blood-fed *Cx. nigripalpus* collected by malaise trap and the resulting per host feeding rates. The presented numbers were collected in two experiments.

References

- [1] Petersen, L. R. and Roehrig, J. T. *Emerging Infectious Diseases* **7**(4), 611–614 (2001).
- [2] Ross, R. *The Prevention of Malaria*. E.P. Dutton & Company, New York, (1910).
- [3] Macdonald, G. *Trop Dis Bull* **49**(9), 813–29 (1952).
- [4] Cruz-Pacheco, G., Esteva, L., Montano-Hirose, J. A., and Var-gas, C. *Bull Math Biol* **67**(6), 1157–72 (2005).
- [5] Bowman, C., Gumel, A. B., van den Driessche, P., Wu, J., and Zhu, H. *Bull Math Biol* **67**(5), 1107–33 (2005).
- [6] Wonham, M. J., de Camino-Beck, T., and Lewis, M. A. *Proc Biol Sci* **271**(1538), 501–7 (2004).
- [7] Diekmann, O., Heesterbeek, J. A. P., and Metz, J. A. J. *Journal of Mathematical Biology* **28**(4), 365–382 (1990).
- [8] Foppa, I. M. and Spielman, A. *Theor Biol Med Model* **4**, 17 (2007).
- [9] Wonham, M. J., Lewis, M. A., Renclawowicz, J., and van den Driessche, P. *Ecol Lett* **9**(6), 706–25 (2006).
- [10] Kilpatrick, A. M., Kramer, L. D., Jones, M. J., Marra, P. P., and Daszak, P. *PLoS Biol* **4**(4), e82 (2006).
- [11] Klowden, M. J. and Zwiebel, L. J. In *Biology of disease vectors*, Marquardt, W. C., editor, 277–87. Elsevier Academic Press, Burlington, MA 2nd edition (2005).
- [12] Lehane, M. J. *Biology of blood-sucking insects*. HarperCollins Academic, London, (1991).
- [13] Marquardt, W. C. and Kondratieff, B. C. *Biology of disease vectors*. Elsevier Academic Press, Burlington, MA, 2nd edition, (2005).
- [14] Vickers, N. J. *Biological Bulletin* **198**(2), 203–212 (2000).