

## HOST RESPONSE PROFILES: A NEW THEORY TO HELP US UNDERSTAND WHY AND HOW ATTRACTANTS ATTRACT

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**ABSTRACT.** Much insect behavior is better described in terms of response profiles than by classical stimulus-response patterns; the response to a particular stimulus may vary with changing internal and external conditions, making it important to qualify statements such as "compound X is an attractant." Because of the large number of conditions that may affect responses, it is crucial to develop a theoretical basis to direct the collection of field and experimental data, and their interpretation. A theory-driven model can help us predict response profiles over a wide range of such conditions. We describe an example of such a model, the assumptions upon which it is based, how the model is constructed, and the types of results that a computer implementation of the model can produce.

### INTRODUCTION

Evidence has accumulated over the past several decades that supports the notion that insects (including mosquitoes) are complex organisms that respond in a variety of ways to different ecological parameters. For example, Scott and Traniello (1990) showed that the amount of parental care provided by female burying beetles was dependent upon carcass size and Roitberg et al. (1992, 1993) demonstrated that highly plastic egg-laying behaviors are mediated by changes in life expectancy. What these and other studies suggest is that the simple ethologically based approach of describing insect behavior by means of stimulus-response patterns is not broad enough to help us predict how expression of behavior will change under varying exogenous and endogenous states (Roitberg 1992). As pointed out by Huntingford (1993), research programs that stress causes of behavior and ignore their function tend to become increasingly fragmented and stale. Here, we adopt a balanced approach that employs both functional and causal analyses in an attempt to understand the bases of mosquito behavior.

The stimulus-response approach can be particularly detrimental to our understanding of mosquito attractants. The reason is that the causal connection between the stimulus and the response appears to involve internal factors that have previously been ignored. A simple example shows just how serious this problem can be. Imagine that some airborne compound X is released into a cage containing mature female mosquitoes. If most or all of the mosquitoes fly upwind toward the source of the compound we

would say that compound X is highly attractive (i.e., a strong stimulus). If, however, we were to rerun that same experiment but in so doing replace the original mosquitoes with another batch that had been recently bloodfed we would likely find far fewer mosquitoes responding. How would we interpret such a result given that our previous conclusion was that compound X is a strong attractant? The answer is that we would be forced to couch our conclusions within a narrow set of conditional statements.

The example described above is only one of many wherein changes in either the exogenous or endogenous state of the mosquito affect responses to host-location cues. For example, *Culex nigripalpus* Theobald females must be at a certain nutritional level to produce enough juvenile hormone to become responsive to blood-host odors; females from nutritionally deprived larvae have to sugar feed before they reach this point (Hancock and Foster 1993).

It is likely that we have only touched the surface in terms of describing factors that mediate odor responses by mosquitoes. If this is true then it is also true that previous statements issued for the many "compound Xs" must be couched in conditional terms with regard to their attractiveness. An additional problem concerns the generality of the conditionals. For example, there are at least 2 mechanisms that reduce or inhibit host-seeking behavior following a blood meal. Meals above a critical volume cause inhibition until eggs are laid in *Aedes aegypti* (Linn.); initially, this is due to abdominal distention, mediated by stretch receptors (Klowden and Lea 1978); later a humoral factor is released that reduces the sensitivity of the antennal lactic acid receptors used in host-seeking behavior (Davis 1984). If we are to deduce the general validity of such conclusions, we need some theoretical framework within which to categorize the various compounds and concomitant responses, across a range of conditions.

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In summary, it is important, and maybe crucial, that we develop a general theory explaining how mosquito response to odiferous compounds will change as a function of mosquito state. Only then will we understand why mosquitoes might display different responses to the same compound under different conditions.

There are 2 solutions to the above problem: 1) We can continue to gather empirical evidence on the relationships between the various parameters and their effects in the hopes that some sort of theory will emerge. This kind of science-by-induction may not be effective because one can not decide, *a priori*, what kinds of data should be gathered, and over what ranges of conditions (Gale 1979). 2) We can develop a theory from first principles that specifically addresses those factors that mediate mosquito response to chemical compounds, and in so doing critical questions and experimental designs should emerge. Here, we concentrate on the 2nd approach, while freely admitting that few of us ever practice either approach (1) or (2) in their strictest sense.

The first step in the development of a mosquito response theory requires some attempt to clarify the form of the biological phenomenon we wish to understand. We maintain that focusing on the term attractant has been detrimental to development of a mosquito response theory for reasons stated above (i.e., any given compound can cause a variety of responses that may be interpreted as attraction. Thus, it may be more useful to think in terms of mosquito response thresholds (Mangel and Roitberg 1993). These thresholds will be generated by the interaction between mosquito physiology and environmental conditions. For example, a recently fed mosquito in a particular ecological situation will generally have a high response threshold whereas a starved individual will have a low one. As a result, encounters by both types with the same compound will frequently lead to contrasting expressions of response.

Miller and Strickler (1984) used similar terminology to describe the relationship between insect herbivores and stimuli that signal food plant quality. In their discussion they related an individual's response to the position of a see-saw that sits on a moving fulcrum. Providing a downward force on one side of the fulcrum are external excitatory inputs, while external inhibitory inputs act on the other side of the see-saw. The position of the fulcrum is determined by internal inhibitory and excitatory inputs. Thus, the position of the see-saw (i.e., the likelihood of host acceptance) is determined by both the strengths of the external stimuli and the position of the fulcrum. The theory we wish to develop is in the spirit of the Miller/Strickler model but as such

we hope to define an internal theory for the fulcrum (e.g., why the fulcrum shifts a particular distance when guts are filled a particular amount).

All of the above means that our theory views individual mosquitoes as having response profiles (i.e., a particular set of responses to a given stimulus under various conditions). In addition, the theory considers such profiles from an evolutionary perspective; it may, for example, explain how and why such profiles evolve in nature and thus help us avoid the dangers of employing a too narrow perspective (e.g., exclusively functional or causal) (Roitberg 1992).

### FIRST PRINCIPLES

We begin development of our mosquito response theory by asking the following question: "How would mosquito host-cue response profiles evolve in habitats that differ in terms of resource structure and availability?" In order for response profiles to evolve the following conditions must be met (see Endler 1986):

- 1) Phenotypic variation (i.e., response profiles varying among individuals) must be present within mosquito populations.
- 2) This phenotypic variation must have a heritable basis.
- 3) There must be consistent covariance between phenotypic expression and fitness (i.e., contribution to gene pools).
- 4) Genetic correlations must not constrain evolution (e.g., selection for expression of one behavior must not select against expression of another).
- 5) For habitat-specific responses to evolve there must be limited gene-pool exchange between populations inhabiting the various environments.

For the remainder of the paper we will concentrate on condition (3) although acknowledging the importance of the other conditions. In fact, studies on each of the above conditions could constitute a lifetime's work. Our reason for specifically addressing condition (3) stems from our reading of the literature; apparently this is the one area where little effort has been devoted even though it is crucial to understanding extant mosquito behavior.

Condition (3) specifies that different variants will contribute differentially to the gene pool and as such only then can their representation in the population change over time. In order to quantify such contributions we will use a surrogate of fitness: lifetime reproductive success. There has been much discussion on how fitness should be calculated (e.g., Yoshimura and Clark 1992, Koslowski 1993). Needless to say, lifetime re-

productive success is a reasonable surrogate for the formulation of our theory. Given that this is so, our theory must be designed to express the outcomes of different response profiles in terms of differential reproductive success rates.

In addition to the above we incorporate several other biological features/assumptions, some of which are specific to the mosquito system:

- 1) The world is not deterministic. Thus, certain biological events only occur with some probability. When such events are mutually exclusive, the sum of those probabilities equals one (Mangel and Clark 1988).
- 2) Mosquitoes require energy to support both somatic and gametic function and the sources of those energies differ. The primary source of energy for somatic function comes in plant nectar whereas for gametic function it is from animal blood.
- 3) Mosquitoes face a time-allocation tradeoff. Because there is a limited amount of time available each day that can be devoted to host search and because the sources of energy come from 2 different sources, time devoted to exploiting one source cannot be employed for exploiting the other.
- 4) Mosquitoes face an abdominal space tradeoff. Because both the crop (nectar storage organ) and the midgut (blood storage organ) reside in the abdomen, space devoted to one organ necessarily detracts from the other. We have found in the laboratory, female *Culiseta inornata* (Williston) can be induced to take maximal meals of either sucrose or blood, which go to the crop and midgut, respectively, where maximal represents complete filling of the available abdominal space (J. J. B. Smith, unpublished data). Thus, a "full" meal of sugar necessarily precludes bloodfeeding. For the purposes of the present model, we assume that the maximal size of a blood meal is maximal meal size minus the present crop volume.
- 5) Host exploitation events unfold in a sequential fashion (see below).

### THE MODEL

Taken together, the various assumptions, conditions, and constraints provide a framework for development of a theory for mosquito response profiles. To build the framework, we chose the methodology of Stochastic Dynamic Programming (SDP) or State Variable Approach. This methodology, as originally described by Bellman (1957) and later explained in an ecological context by Mangel and Clark (1988), is highly appropriate because it provides for calculation of

lifetime fitness as a function of response under various forms of constraint (see Mangel and Clark [1988] for an excellent discussion of the topic). Using SDP one calculates the fitness payoff from responses to particular events, each of which are weighted by their probability of occurrence. However, the payoffs for different responses can be constrained by various physiological and ecological parameters. For example, a mosquito with a full crop will be unable to feed on any nectar regardless of that nectar's quality. In our theory, the primary constraints are: 1) crop volume, 2) midgut volume, 3) crop emptying rates, 4) crop filling rates, 5) midgut filling rates, and 6) somatic energy (Roitberg and Friend 1992). Further, we assume the presence of some critical somatic energy threshold; any mosquito whose somatic energy falls below that threshold dies (i.e., starves).

The theory says that each mosquito goes through life experiencing and responding to various encounters and events. Thus, crop volume, crop nectar concentration, and somatic energy levels (the "state variables") can rise and fall as a result of nectar-based decisions. In addition, egg production will be directly influenced by decisions concerning the blood host.

For the problem of host response profiles we considered several mutually exclusive events that could occur during any one moment of time during the mosquitoes active search period (i.e., scotophase).

- 1) The mosquito is not in a searching mode (i.e., resting). Under such conditions it cannot encounter a host odor. On the other hand, its energy consumption and probability of mortality are also much lower than would be the case for a flying mosquito. The mosquito can respond to its current situation in 2 ways: a) remain stationary, or b) initiate airborne search.
- 2) The searching mosquito does not receive any odor signal (with a probability that is based upon the ecological conditions and the randomness of the environment). In this case the mosquito can respond to its current situation in one of 2 ways: a) by continuing to search, or b) by initiating rest.
- 3) The searching mosquito receives an odor signal from a nectar source. If the mosquito chooses to ignore the signal then it can either continue to search or initiate rest. If, however, the mosquito chooses to search for the odor source then the following 2 possibilities can occur: a) the mosquito searches unsuccessfully (with probability  $[1 - \omega]$ ) for some period of time before abandoning the search, or b) the mosquito locates the host with probability  $\omega$  and samples the nectar. The nectar

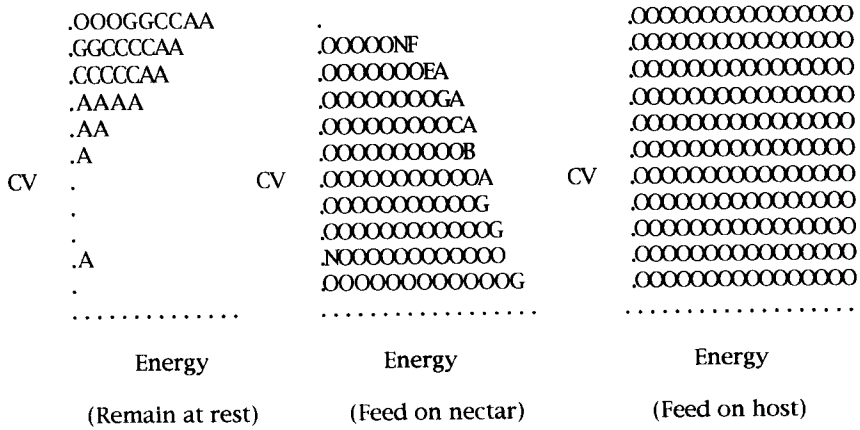


Fig. 1. Sample decision matrices for mosquito feeding behavior at a time about 1/3 through the simulated lifetime. The 3 graphs show the values for internal energy level (Energy), crop volume (CV), and crop sugar concentration for which the choice would be to remain at rest, to feed on nectar, or to feed on a blood host. Letters indicate the sugar concentration in the crop, where the letter value (A = 1, B = 2, etc.) is the sum of the relevant 4 concentrations used in the model, coded as C1 = 1, C2 = 2, C3 = 4, C4 = 8. Thus, the letter A indicates a choice only at the lowest crop sugar concentration, and the letter O (1 + 2 + 4 + 8 = 15) represents all possible concentrations. The matrices indicate, for the particular conditions of this run, that mosquitoes should choose to remain at rest with full crops over most sugar concentrations, should choose to feed on nectar unless their energy levels and crop volumes are high, and should bloodfeed under all circumstances.

can vary in concentration over a 10-fold range. If the mosquito chooses to initiate feeding it will ingest an optimal amount of nectar that maximizes lifetime egg production. If it chooses not to feed then the state variables change depending on the amount of time required for these processes.

- 4) The mosquito receives an odor signal from a blood host. If the mosquito chooses to ignore the signal then it can either continue to search or initiate rest. If however the mosquito chooses to search for the blood host then the following 2 possibilities can occur: a) the mosquito searches unsuccessfully (with probability  $[1 - v]$ ) for some period of time before abandoning search, or b) the mosquito locates the host with probability  $v$ . The mosquito may be prevented from landing (with probability  $[1 - \tau]$ ); otherwise, the mosquito lands on the host and initiates feeding. It may be interrupted during the first minute with probability  $(1 - \tau')$ , or it may feed to repletion, with the actual amount ingested depending upon the volume of nectar in the crop. The number of eggs produced depends on the volume of blood ingested, and the next cycle begins after some time has passed.

A formal version of the theory is presented in Roitberg and Friend (1992). By solving the complex equations backwards in time one can solve for the optimal response for a mosquito as a function of various internal (e.g., crop volume)

and external (e.g., nectar availability) states. Figure 1 shows a sample set of optimal responses (a "decision matrix") for a given set of parameter values.

Several important points should be considered. First, even though we might only be interested in responses by mosquitoes to compounds that mimic odors from a blood host, we must also consider potential responses to nectar odors. By doing so, we consider responses to blood-host odors relative to lifetime reproductive success, which clearly will be a function of ability to 1) maintain somatic function, and 2) exploit blood hosts. Second, the theory arises from a blend of functional and causal perspectives wherein the goal or function of response to odors is to maximize reproductive success whereas the physiological constraints that are explicitly built into the theory defines how (i.e., the mechanism) such a goal can be achieved. Third, by considering odors to be sources of information, one can now estimate the value of such information and, for instance, rank compounds according to their evolutionary value. For example, the value of "compound X" will be a function of the quality of the host from which it emanates, and that quality can be calculated by that host's potential contribution to the receiver's lifetime reproductive success (i.e., it will be a function of blood quality, host defensive abilities, etc.). The value of a common odor will be based upon the summation of values for each of the potential hosts from which such a compound could arise weight-

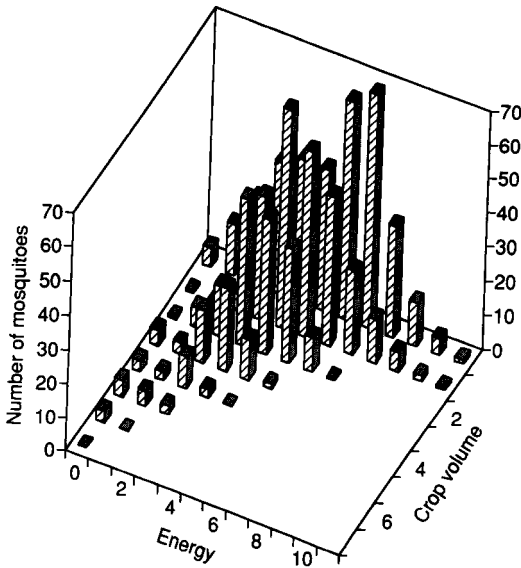


Fig. 2. Representative data from population simulation using decision matrices. Columns show the number of mosquitoes for each combination of crop volume (units represent  $1/10$  maximum volume) and internal energy level (units represent  $1/15$  or maximal energy level). The model tracks 1,000 insects over their lifetime, allowing each to encounter hosts, be preyed upon, etc. according to some probability values used in the decision model. Behavioral choices are made according to the precomputed relevant decision matrix. Data are smoothed somewhat by summing values from 5 consecutive time periods.

ed by those hosts' relative availability in the habitat. Fourth, differences in lifetime payoff between optimal and nonoptimal responses can vary from exceedingly small to very large. When such differences are taken into account they can help explain patterns in variation of response profiles within and among populations (see Roitberg 1990).

Finally, while elucidating the response profiles of mosquitoes in general is of interest, one may also ask how such profiles could be used to evaluate attraction potential for various compounds in nature. After all, a vast majority of individuals within a given population of mosquitoes may exist under a very narrow range of physiological states (e.g., low somative energy and low crop energy values). If this were the case then much of the profile that is deduced is unlikely to be expressed, and our categorization of some compound as highly attractive would be suspect. For this reason, data collection is as important as it would be were we to attempt to develop a theory by induction. The difference, however, is that the theory can be used to guide us as to which data we should collect. For example, were the theory

to show that response profiles are relatively insensitive to differences in flight energetics, then we might collect ballpark estimates for that parameter and concentrate our efforts on those parameters to which the theory is particularly sensitive. Smith et al. (unpublished data) also show how one can use theory-driven computer simulation models to identify critical experiments that need to be undertaken, and to predict population-level patterns of feeding rates and energy states, both of which will have an impact on response profiles (Fig. 2). Clearly, variation in response, at the population level, is a feature that is both predicted by our theory and observed in nature.

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