BEHAVIORAL ECOLOGY, EPIDEMIOLOGY AND POPULATION GENETICS: THE UNDISCOVERED COUNTRY

MARC MANGEL

Section of Zoology and Center for Population Biology
University of California
Davis, CA 95616

BERNARD D. ROITBERG

Behavioural Ecology Research Group
Department of Biological Sciences
Simon Fraser University
Burnaby, BC V5A 1S6
Canada

INTRODUCTION

Behavioral ecology means different things to different people (or even to the same people at different times). Often it is defined as "the survival value of behavior". Alternatively, a focus on inclusive fitness often leads to the use of optimization methods. "Behavioural ecologists often preface their studies with statements such as 'individuals are expected to behave so as to maximize their reproductive success' " (Krebs and Davies 1991, pg 3). It is, in fact, extremely unfortunate that the early emphasis in behavioral ecology on optimization deflected discussion of more important concepts (Mangel and Ludwig 1992). In particular, the focus became one of "testing the optimization model" (in which case any variation of behavior disproves the theory) rather than considering fitness consequences of different behaviors (see Mangel and Clark 1988, Mangel and Ludwig 1992).

An alternative view is this: Behavioral ecology attempts to explain why Darwinian demons do not exist. A Darwinian demon (Law 1979), presumably modeled after Maxwell's demon, starts reproducing immediately after its own birth, produces large numbers of offspring, has extremely high survival rate, and is extremely effective at dispersal and at finding mates. Any reasonable person, of course, would assert that Darwinian demons do not exist because of trade-offs between reproduction and survival (both broadly defined) and it is our opinion that such trade-offs are the essence of behavioral ecology.

Defined in this way, behavioral ecology must focus on fitness (inclusive lifetime reproductive success) and behavior equally: working with proxies for fitness (such as the rate of acquisition of energy) is not sufficient. In order to relate behavior and reproductive success, it is usually necessary to consider the state of the organism. We must ask: how do behavior and ecology interact

to structure the fitness function of the organism being studied. In this way, we wish to predict both fitness and behavior (Mangel and Clark 1988) as related to the physiological states of the organism.

In this paper, we chart the road into the undiscovered country that joins behavioral ecology and other areas of population biology. Because of the focus on the ecological determinants of fitness, behavioral ecology can be linked "down" to quantitative genetics and in the process make the current formulations of quantitative genetics truly predictive. Because of the focus on behavior, behavioral ecology can be linked "up" to epidemiology and in this manner provide new kinds of population models in which physical mathematics (fully deterministic) is replaced by biological mathematics (which recognizes diversity).

QUANTITATIVE GENETICS: GOING BEYOND THE DATA

The link between behavioral ecology and quantitative genetics (QG) is a link "down", from individuals to genes. QG is generally not concerned with individuals, but with predicting the mean trait of a population (Bulmer 1985, Falconer 1981) and begins with the classical observation that if $\bar{z}$ is the mean value of the trait of the population in the current generation, then the change in this value in the next generation is

$$\Delta \bar{z} = h^2 [\ \bar{z}_w - \bar{z}\ ]$$

(1)

where h^2 is the heritability of the trait and $\bar{z}_w$ is the mean value of the trait after selection:

$$\bar{z}_w = \frac{\int z p(z) W(z) dz}{\int p(z) W(z) dz}$$

(2)

In this equation, $p(z)$ is the distribution of phenotypes in the current generation and $W(z)$ is the fitness (reproductive success) of an individual with phenotype z. If we define the denominator in (2) as $\bar{W}$, then (1) can be rewritten as

$$\Delta \bar{z} = h^2 \frac{\int \{z W(z) - z \bar{W}\} p(z) dz}{\bar{W}}$$

(3)

Over the last 15 years, R. Lande and his colleagues have extended this theory in a number of ways (Lande 1976, 1979, 1982, Lande and Arnold 1983, Via and Lande 1985). Some of the key insights

that have emerged include i) for a smooth, unimodal fitness function and a single trait, the phenotypic equilibrium corresponds to the value that maximizes the fitness function, ii) this result need not be true for multimodal fitness functions (if there is insufficient genetic variation) or for correlated characters and iii) it is possible to empirically estimate the "selection differential" without knowledge of the fitness function. Wade and Kalisz (1990) provide an alternate view.

Lande and Arnold (1983) write (1) as

$$\Delta \bar{z} = \mathbf{G}\beta \qquad (4)$$

where $\mathbf{G}$ is the heritable portion of the phenotypic variability and β is the selection differential defined as follows. We begin with N individuals, observe the phenotypic trait for each individual (z_i) and the relative fitness (w_i) of that individual. Then

$$\beta = \frac{\sum_{i=1}^{N}(z_i - \bar{z})(\frac{w_i}{\bar{W}} - 1)}{\sum_{i=1}^{N}(z_i - \bar{z})^2} \qquad (5)$$

One general assertion of workers in quantitative genetics is that one does not need to know fitness, but that it is sufficient to estimate the selection gradient β. We have two comments.

First, it is not a predictive theory. That is, in order to obtain the relative fitnesses $\{w_i\}$ one must wait and observe relative reproduction associated with the different phenotypes. In other words, (4,5) allows one to estimate what the selection gradient was, but does not allow one to predict what the selection gradient will be. In a sense, it is *curve-fitting* and this means that, in its current form, quantitative genetics cannot go beyond the data Even the most elaborate theories of quantitative genetics (Barton and Turelli 1991, Gomulkiewicz and Kirkpatrick 1992, Kirkpatrick and Heckman 1989, Kirkpatrick and Lofsvold 1992) are *what-if* stories (cf. Beecroft 1956, pgs 345-400). One assumes a fitness function and then asks if there is sufficient genetic variation to achieve the optimal fitness. Usually workers are coy about what they are doing, but sometimes not:

> "Since we lack any information regarding the actual form of selection acting on the growth trajectories of these mice, we created a hypothetical growth trajectory optimum. We imagine there is an optimal body size of 10 gms during lactation. Immediately following weaning, different selective forces act, for example the ability to forage independently and to avoid predators. We imagine that these factors favor a body size of 40 gms."
>
> (Kirkpatrick and Lofsvold, 1992 p 957).

Even the most rabid adaptationist, using the most absurd optimization methods, would not assert that the optimum growth trajectory involves an instantaneous four-fold increase in body size. The main point, however, is that the methods of behavioral ecology can provide realistic fitness functions to use with the machinery of quantitative genetics. As Wade and Kalisz (1990) note we want to understand "not only *how* selection is operating on the phenotypic distribution but *why* it operates in the observed manner...we view fitness as arising from the interaction of the phenotype and the environment" (pg. 1947).

Second, although Lande and Arnold derived their result from a regression model, (5) is also a discrete version of the fundamental equation (3). To see this, multiply numerator and denominator of (5) by $\bar{W}$, expand the resulting product in the numerator and simplify to obtain

$$\beta = \frac{\sum_{i=1}^{N} z_i w_i - z_i \bar{W}}{\bar{W} \sum_{i=1}^{N} (z_i - \bar{z})^2} \tag{6}$$

If we note that $\sum_{i=1}^{N}(z_i - \bar{z})^2$ is an estimate of the phenotypic variance σ^2 and use this in (4), we obtain

$$\Delta \bar{z} = \frac{G}{\sigma^2} \frac{\sum_{i=1}^{N} z_i w_i - z_i \bar{W}}{\bar{W}} \tag{7}$$

Now, $\dfrac{G}{\sigma^2}$ is h^2 and $\sum_{i=1}^{N} z_i w_i - z_i \bar{W}$ is the discrete form of the integral in (3).

Let us return to the first point. Because fitness is treated as an ad hoc function, the standard theory of quantitative genetics is not predictive. However, a fully empirical determination of fitness would require an enormous experimental design, since one would need to know fitness for each potential phenotype. Alternatively, in order to make quantitative genetics truly predictive, we need to construct hypotheses about how ecology and phenotype structure reproductive success. This is exactly what behavioral ecology can offer. By doing so, we are able to take quantitative genetics beyond the data, into the undiscovered country. In addition, when organisms exhibit phenotypic plasticity, fully empirical studies based on the approach of quantitative genetics will become

extremely (possibly hopelessly) complex; but the use of methods from behavioral ecology can considerably enhance the studies.

To illustrate how this can be done, we consider problems of clutch size for ovipositing insects (e.g. Mangel and Clark 1988, Chapter 4 and references there-in, Mangel 1989). We shall describe a sequence of three problems, each involving more complexity, and show how behavioral ecology and quantitative genetics can be linked, strengthening both fields.

In the simplest case, consider an insect that has many more eggs than reproductive opportunities, so that the physiological state of the insect can be ignored (cf. Mangel 1987, 1989). Assume that this insect attacks a single kind of host and has a constant mortality rate. Offspring survival within a host is determined by the number of eggs in the host:

Pr{individual egg reaches maturity, given c eggs in a host}

$$= 1 - \frac{c^{\gamma}}{c_m^{\gamma}} \tag{8}$$

where γ and c_m are two parameters describing host quality: c_m is the maximum number of eggs that a host can possibly support and γ is a "shape" parameter determining how rapidly survival decreases with additional eggs. The increment in lifetime reproduction accrued by an ovipositing female who lays a clutch of size c is then

$$f(c) = c(1 - \frac{c^{\gamma}}{c_m^{\gamma}}) \tag{9}$$

It is easy to see that f(c) has a "domed" shape, with an optimal clutch size c^*. In this simple case, consideration of the behavior that maximizes lifetime reproduction leads to the prediction that females will lay clutches of size c^*. The approach of quantiative genetics (Lande 1979) leads to the prediction that in a population of females, the mean phenotype (clutch size) $\bar{z} = c^*$, and that clutch sizes will be normally distributed with this mean and (unexplained) variance σ^2. Of course, this only holds when parameter values for (9) hold. The methods of behavioral ecology, however, allow us to predict how the mean $\bar{z}$ will change as the host parameters γ and c_m change. This can be an important question. For example, the apple maggot *Rhagoletis pomonella* evolved on hawthorn (*Crataegus*), for which $c_m \sim 4$; but then switched in the mid-1800s to apples, for which $c_m \sim 12$. Assuming that clutches on apples and clutches on hawthorn evolve independently (but see below), and assuming a value for the phenotypic variance, we are able to predict how the mean

clutch size will change after the introduction of apples. In this case, the phenotypic plasticity is expressed through the different clutch sizes in different hosts.

It is likely that clutches on apples and hawthorn do not evolve independently, but rather that they are correlated. We then must consider the evolution of correlated traits. In addition, we must consider how the fitness function is structured by the environment. That is, the rate of encounters with hosts of type i, λ_i, is now an important component of the behavioral ecology of the insect, and must also be so for the evolutionary genetics of the insect.

Suppose that $\bar{z}_1$ and $\bar{z}_2$ are the mean clutches on hawthorn and apple respectively. The analog of (1) is

$$\Delta\bar{z}_1 = h_{11}^2[\ \bar{z}_{w1} - \bar{z}_1\ ] + h_{12}^2[\ \bar{z}_{w2} - \bar{z}_2]$$

$$\Delta\bar{z}_2 = h_{21}^2[\ \bar{z}_{w1} - \bar{z}_1\ ] + h_{22}^2[\ \bar{z}_{w2} - \bar{z}_2]$$

(10)

where now

$$\bar{z}_{wi} = \frac{\int\int z_i p(z_1, z_2) W(z_1, z_2) dz_1 dz_2}{\int\int p(z_1, z_2) W(z_1, z_2) dz_1 dz_2},$$

(11)

$W(z_1, z_2)$ is the fitness associated with the clutch sizes $\{z_1, z_2\}$ and $p(z_1, z_2)$ is the phenotypic distribution. It is sometimes helpful to write h_{ij}^2 as g_{ij}, the heritable part of the genetic variance-covariance matrix. It is well known that if there is insufficient genetic variation, then the equilibria of (10) need not be $\bar{z}_i = c_i{}^*$. It appears less well known that equilibria need not exist at all. To see this, set the left hand side of (10) equal to 0, so that

$$h_{11}^2\,\bar{z}_1\ +\ h_{12}^2\,\bar{z}_2 = h_{11}^2\bar{z}_{w1}\ +\ h_{12}^2\,\bar{z}_{w2}$$
$$h_{21}^2\,\bar{z}_1\ +\ h_{22}^2\bar{z}_2\ =\ h_{21}^2\,\bar{z}_{w1} + h_{22}^2\,\bar{z}_{w2}$$

(12)

Viewed as a set of algebraic equations (12) might not have a solution so that an equilibrium might not exist. In that case, we would predict cycling of phenotypes (or possibly even chaotic behavior).

Because of the focus on the structure of the fitness function, we can predict norms of reaction (how the $\Delta\bar{z}_i$ will depend upon the current phenotypes $\bar{z}_i$ and properties of the environment such as host

quality (γ and c_m) and the host encounter rates λ_i), breeding values, and the genetic load, which is the fitness cost of genetic correlation:

Fitness cost of genetic correlation=

$$\frac{\lambda_1}{\lambda_1 + \lambda_2} f_1(c_1^*) + \frac{\lambda_2}{\lambda_1 + \lambda_2} f_2(c_2^*) - (\frac{\lambda_1}{\lambda_1 + \lambda_2} f_1(\bar{z}_1) + \frac{\lambda_2}{\lambda_1 + \lambda_2} f_2(\bar{z}_2)) \qquad (13)$$

We know from empirical work, however, that host choice behavior actually varies with the host encounter rates. Thus the mean phenotype should actually be viewed as functions $\bar{z}_i(\lambda_1, \lambda_2)$ and more elaborate theories (e.g. Kirkpatrick and Heckman 1989) are needed.
A similar elaboration is needed if the physiological state of the insect is included (Mangel 1987, 1989).

To be fair, we note the kinds of questions that would interest behavioral ecologists but might not interest quantitative geneticists. For example, it is often true that mortality depends upon clutch size, since a larger clutch requires more time on the host, during which period the insect is vulnerable to predation. This is an example of a "G by E" effect. Behavioral ecologists would be interested in understanding the interaction itself, whereas quantative geneticists might be content simply to view it as a form of constraint. On the other hand, the focus of the work in quantitative genetics is often the structure of the variance-covariance matrix for the phenotypes and the heritable portion of that matrix; this is usually not of interest to behavioral ecologists.

In summary, however, we believe that the focus on the ecological determinants of fitness can provide new links between behavioral ecology and quantitative genetics and in the process will make both fields stronger.

EPIDEMIOLOGY: ASSERTING VARIABILITY IN POPULATION DYNAMICS

The link between behavioral ecology and epidemiology is a link "up" from individuals to community processes in that disease-host interactions subsume at least two (three if a vector is involved) trophic levels. In fact, this kind of linkage leapfrogs the normal hierarchical linkage of individuals to populations to communities, but as we will show such a linkage is philosophically defensible and necessary. In this section we will concentrate on the epidemiology of the specific disease malaria. We believe that many of the concepts discussed here will hold true for other

diseases with insect vectors, but also note that malaria is a simple anthroponotic infection (relative to zoonotic infections e.g. leishmaniases). Thus, the kind of theory that we outline below may not accurately predict behavioural dynamis of the more complex diseases.

Malaria kills between 1 and 2 million people annually and is present in 102 different countries (see Oaks et al 1991 for further details). The causal agent of malaria is a protozoan *Plasmodium falciparum*. There are four species of the parasite, and the most dangerous one is increasing in frequency. The vector for malaria is the mosquito *Anopheles*. Malaria has killed more humans than have all the wars combined and has been intensively studied for decades by both medically oriented and ecologically oriented scientists.

One of the most important contributions by mathematical biologists to medical practitioners was the argument that disease is a problem of population biology first and of medicine second. For example, the classic Ross-Macdonald model for malaria considers the infected populations of humans and vectors. We let

$$
\begin{aligned}
&H_T = \text{total human population size} \\
&H = \text{population size of infected humans} \\
&M_T = \text{total vector population size} \\
&M = \text{population size of infected vectors} \\
&a = \text{biting rate} \\
&b = \text{probability that a bite leads to infection} \\
&c = \text{probability that a bite on an infected host leads to an infected vector} \\
&r = \text{recovery rate} \\
&\mu = \text{mortality of vectors}
\end{aligned}
\tag{14}
$$

In this case, the population dynamics are

$$
\frac{dH}{dt} = a\,b\,M\,(1 - \frac{H}{H_T}) - r\,H
$$

$$
\frac{dM}{dt} = a\,c\,H\,\frac{M_T}{H_T}(1 - \frac{M}{M_T}) - \mu\,M
\tag{15}
$$

If we convert these to the fractions of infected humans $x = H/H_T$ and vectors $y = M/M_T$, we obtain the more usual form of the equations (e.g. Anderson and May 1991 pg 394). These models have been used to determine control policies (e.g. vector control, immunization strategies, etc.).

The growth rate of the infection, R_o, is the number of new cases arising from one infection, and can be found directly (Anderson and May 1991, pg 395)

$$
R_o = \frac{M_T}{H_T}\ \frac{1}{r}\frac{1}{\mu}\,a^2\,b\,c
\tag{16}
$$

When $R_0 = 1$ the infective process is at equilibrium. Note that the biting rate appears as a square in the overall growth rate. This "double" effect of the biting rate can also be seen if we consider the conditons for persistence of the disease. To see this, we find the steady states of (15), which give a pair of equations relating M and H (Figure 1).

$$M = \frac{rH}{ab(1-\frac{H}{H_T})} \text{ and } M = \frac{acHM_T}{acH + \mu H_T} \tag{17}$$
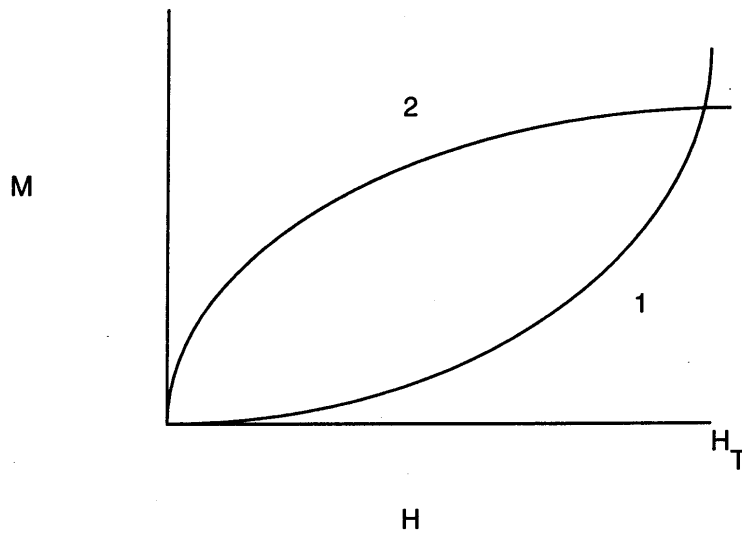

Figure 1. The steady-state curves of the epidemiological model (15) for the case in which the disease persists. The curve labelled 1 corresponds to the first equation in (17) and the curve labelled 2 to the second equation in (17). The disease persists if these curves intersect at a positive value of H, as well as at H=0. This occurs if the slope, as H --> 0, of curve 2 exceeds that of curve 1.

When H is small, the first equation in (17) reduces to $M \sim \frac{rH}{ab}$

and the second to $M \sim \frac{acM_T H}{\mu H_T}$. The condition for persistence of the disease (Figure 1) is then $\frac{r}{ab}$

$> \frac{acM_T}{\mu H_T}$ and we see once again that only the biting rate enters as a square. This expression is the

same as the condition for $R_0 > 1$.

In the model described above, the term for the biting rate is based on a mixing of mosquitoes and hosts. In other words, infected hosts are fed upon in direct proportion to their representation in the

host population. This assumption has received considerable scrutiny in recent years, at least from a perspective of population dynamics.

Kingsolver (1987) reworked the Ross-Macdonald model to include a biting preference that differed according to whether or not hosts were infected. Kingsolver found that the persistence and equilibrium values of infected individuals could vary dramatically when the biting rate was made a function of host availability and mosquito preference. Dobson (1988) modified the Ross-Macdonald model to include a term that accounts for the success of transmission when host or vector behavior are changed by infection. Dobson found that this behavioral modification affected the threshold values at which epidemics could occur.

The message from these two studies is clear: adding behavior to the basic epidemiological models can alter dramatically the insights that we gain from their use (also see Anderson's (1991) excellent analysis of behavior parameters and HIV epidemiology in humans). The question then becomes: "What kinds of behavior should we incorporate into epidemiological models". Kingsolver and Dobson offer some suggestions as to the sorts of behaviors we might study and even suggest plausible mechanisms (e.g. giving up times for vectors, etc.), but these suggestions are primarily of the "what if" sort in that the modification of the Macdonald-Ross models are done on an ad hoc basis. Given the wide range of ecological conditions under which mosquitoes search for hosts, however, a general theory of mosquito behavior from the perspective of behavioral ecology is necessary to make epidemiology a more predictive science.

There are really two issues that need be discussed with reference to the behavioral ecology of biting rates: (1) what happens to the dynamics of disease transmission when our models incorporate distributions rather than means (or constants) of biting behavior and (2) why do mosquitoes vary their attack behaviors under different ecological or physiological conditions? The first question is the one that is usually studied in mathematical biology, assuming the distributions are known. But where do those distributions come from? The second question leads to that answer and we now outline a procedure that can be used to do this. As noted in our discussion of quantitative genetics, behavioral ecology provides a means of elucidating the relevant population profiles within a general theoretical framework. Let us briefly examine how this might be so.

Mosquito Attack Thresholds

Dynamic theories of vector behavior are appropriate for predicting mosquito behavior because mosquitoes face somatic-gametic tradeoffs at two levels. First, two different external sources of energy, nectar and blood, are required to maintain somatic and gametic function, respectively. Given the limited amount of time available for search each day, allocation of time to seeking one

source necessarily deprives individuals of time to seek the other source. Second, due to limitations on abdominal capacity, size of blood meals (and thus reproductive output) is constrained by the volume of nectar found in the crop at the time of blood feeding. If selection acts on reproductive success, then mosquito behavior should be expressed in a manner that these trade-offs are addressed.

Imagine that individuals within a population of adult mosquitoes vary in (1) energy reserves accumulated from the larval stage and (2) renewable energy acquired as adults from feeding at nectar sources (e.g. Nasci 1991). Roitberg and Friend (1992) indexed individuals by their free energy state $\varepsilon(t)$ and crop energy state $c_{ij}(t)$, where i and j represent crop volume and concentration, respectively.

Roitberg and Friend (1992) used the approach of trade-offs in reproductive success to derive lifetime fitness (Mangel and Clark 1988):

$$F(\varepsilon, C_{ij}, t, T) = \text{maximum expected fitness from egg production between t and T}$$
$$\text{when free energy and crop nectar states at time t are } \varepsilon$$
$$\text{and } C_{i,j} \text{ respectively.} \tag{18}$$

The model based on (18) can be used to predict attack thresholds for varying exogenous (e.g. host availability) and endogenous (e.g. crop volume and concentration) state values. Thus, for any given population of mosquitoes that varies in physiological state as suggested above, the model can be used to produce an attack threshold probability distribution for both infected and healthy mosquitoes. How reasonable is such an assertion? To date, predictions from the theory of Roitberg and Friend have been corroborated by experiment. For example, Klowden (1988) describes how nutritional state interacts with host search propensity. Also, the theory of Roitberg and Friend predicts that host choice will only be exhibited under particular circumstances. This insight might explain the enigmatic patterns of host feeding in the field. By employing life history theory and dynamic optimization models we have retained generality but can deal with specific predictions.

Vector Persistence

Hosts vary in both the danger they present to their vectors as well as in their irritability. A mosquito may attempt to land and feed several or many times before achieving success or giving up and seeking other hosts. Behavioral ecology can predict the degree to which an individual mosquito will persist in its attack upon hosts. The work of Roitberg and Friend suggests that energy level will be an important variable in this regard though persistence was not employed as a behavioral response

in the original formulation of their theory. Recent work by Nasci (1991), however, supports the concept of an interaction between mosquito energy levels and attack persistence.

Host defense

No formal theory has been developed in an attempt to understand the response of hosts to blood sucking insects, but the basic problem does not seem insurmountable. Again, one can imagine that some tradeoff between intensity of defense against mosquitoes and the ability to hide from predators occurs such that behavior may be expressed that maximizes lifetime fitness, and that host defensive behavior will vary under different ecological and physiological settings. For example, work of Cully et al. (1991) shows that chipmunks that perceived the presence of predators were much less likely to display defensive behavior against mosquitoes than when predators were absent.

Host quality

Perspectives of behavioral ecology are valuable in that they often force scientists to focus their questions more clearly than they might otherwise. In the present case we must first ask "what is host quality?" before attempting to evaluate it for a given host. Given the objective function of reproductive maximization by mosquitoes, host quality can be directly related to egglaying rates as a function of host blood volume. This would take into account blood ingestibility, ATP levels, etc.

Though we have yet to complete our formal analysis of our behavior-based theory of malaria, one thing is clear: because the theory deals explicitly with variability among individual hosts (both humans and mosquitoes) we are almost certain to create dynamics which vary dramatically from traditional behavior-free models.

CONCLUSION

In this paper, we have argued that part of the undiscovered country for behavioral ecology involves links to other areas of population biology. The double-edged strength of behavioral ecology is a simultaneous focus on the ecological determinants of fitness and on behavior. The focus on fitness allows us to link individuals to genes; and the focus on behavior allows us to describe population dynamics not by physical mathematics but by mathematics that acknowledges and rejoices in the diversity of biology. We have at least two cases in which mixed marriages will work.

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