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Community-level analysis of risk of vector-borne disease

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Summary Ecological community structure is particularly important in vector-borne zoonotic diseases with complex life cycles. Qualitative community model analysis may provide a meaningful alternative to standard population-based models of vector-borne disease. We built on recent mathematical developments in qualitative community modeling coupled with conventional biomathematical models of vector-borne disease transmission, to provide a procedure to analyze risk. Using this procedure, we can hypothesize changes in risk of vector-borne disease from disturbances, such as control measures, habitat alteration, or global warming. We demonstrate the application of this procedure to an oak forest community to predict the risk of Lyme disease. Our predictions of Lyme disease risk in an oak forest community confirm reports of positive associations between deer abundance and risk of disease and are consistent with published observations.

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1. Introduction

Ecological community structure is a key factor in understanding the public health risk of communicable disease emergence, mode of transmission, and control options (Forget and Lebel, 2001). Community structure is particularly important in vector-borne parasitic diseases, where a minimum of three species, namely, host, vector, and pathogen, is involved. In the case of human dis-

eases such as malaria and dengue fever, zoonotic components can be irrelevant or negligible. In the case of zoonotic diseases, systems often involve numerous and complex vector and zoonotic components in their transmission, and perhaps more than one host. The number of parameters and variables needed to characterize such vector-borne disease dynamics is greater than that typically used in public health models.

Deterministic and stochastic population models are important in characterizing our understanding of the relationship of vector-borne disease with ecological communities (Dobson and Hudson, 1994). These models stem from the landmark concept of basic reproduction rate developed by Ross

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(1908, 1910) and Lotka (1923), and later popularized by Macdonald (1952). Bailey (1982) provides a useful and more formal presentation of these concepts. The models were used to demonstrate regulatory roles that parasites have on animal populations (Dye, 1992; Dobson and Hudson, 1994; Hudson et al., 1998; May, 1993; Tompkins and Begon, 1999).

Understanding the role that disease and parasitism plays in population regulation, as well as in community dynamics, is integral to the development of wildlife conservation strategies (Dobson and May, 1986; Hess, 1996). However, because current disease models focus on population dynamics, they subsume within their parameters direct consideration of community-level interactions. This limitation is due in no small part to insufficient quantitative information available to model community interactions as well as to the lack of appropriate models.

Qualitative community models can provide a practical and rigorous alternative to modeling transmission of vector-borne disease. One form of qualitative modeling, loop analysis, involves both signed digraphs and matrix analysis (Puccia and Levins, 1985, 1991). From the signed digraph model, a community matrix can be developed and used to assess stability conditions, and to make qualitative predictions of population response to press perturbations (hereafter referred to as 'press') in community structure. A press is a permanent change in a growth parameter such as a birth or death rate. These models are particularly useful in predicting responses to anthropogenic disturbances. Recent mathematical developments have provided degrees of flexibility and reliability that were previously lacking in the approach (Dambacher et al., 2002a, 2003a, 2003b). Loop analysis has been used to characterize predator–prey systems (Dambacher et al., 1999) and changes in abundance (Dambacher et al., 2002a), to predict the impact of species introductions (Castillo et al., 2000; Li et al., 1999), and to explain complex transitions in community composition over time (Bodini, 1998; Ortiz and Wolff, 2002). Experimental comparison of various community modeling approaches suggests that loop analysis is the theoretical approach best suited for predicting the behaviour of complex community structures following a press (Hulot et al., 2000).

We have developed a qualitative (loop analysis) model of community-level impacts to predict risk of transmission of vector-borne diseases. Insights from the qualitative models can lead to novel and more flexible management of vector-borne diseases.

2. Models and methods

Here we summarize models used in public health and community ecology that we considered in developing a procedure for predicting community-level response to stress (equivalent to a press) and vector-borne disease risk. We apply this procedure using Lyme disease as an example of a vector-borne disease where the disease ecology is well known.

2.1. Basic reproduction rate

Ross (1908, 1910) first developed a biomathematical model characterizing the disease status between host and vector populations, later formalized by Lotka (1923). The Ross model, as popularized for malaria by Macdonald (1952), provides a basic model of disease transmission that can apply to vector-borne diseases. The model, often called the Ross–Macdonald model, focuses on the basic reproduction rate (R_0), which is the number of secondary infections that can arise from a single primary case. A counter-intuitive conclusion of Ross's analysis (1908, 1910) is that survival of the vector outweighs relative density. Mosquito longevity is a greater determinant of risk than abundance. The model also indicates that there are non-zero thresholds, as of vector density and life expectancy, below which transmission will not be maintained.

During its worldwide campaign of malaria eradication, the World Health Organization adopted a model of malaria control based on vectorial capacity (VC), defined as the maximal average daily number of infective contacts possible between a vector population and its host (Bailey, 1982; Garrett-Jones, 1964). Vectorial capacity is an index directly proportional to basic reproduction rate. A major practical advantage is that VC is determined solely from the entomological parameters of the Ross–Macdonald formulation of basic reproduction rate. Another benefit of the VC equation is that the impact of an infected vector population on the epidemiology of a disease can be evaluated even in the absence of the parasite (Bailey, 1982). Thus, there are fewer parameters to consider and evaluate than in the Ross–Macdonald equation for R_0 .

The parameters of VC (Bailey, 1982) are: (i) the daily biting rate (ma), where m is the relative number of vectors with respect to host and a denotes the biting habit of the vector; (ii) the probability of vectors surviving to become infective (p^n), where p is the probability of daily survival and n is the duration of the extrinsic incubation period (a constant under most conditions); and (iii) the life expectancy of the vector ($1/(-\log_e[p])$). Parameter, a ,

is the product of the host preference (proportion of competent to non-competent hosts fed upon) to frequency of feeding, which is equal to the inverse of the oogenic cycle in the case of mosquitoes. The biting habit (a) is factored into the equation twice, once to account for the initial bite, then a second time to account for bites that infect a host. The derivation is as follows: A relative number (m) of vectors bite an infected host at a specific rate (a); a proportion (p) of which survive each day of the extrinsic incubation period (n). Once infective, vectors live for a period $(1/-\log_e[p]^{-1})$ and bite at a rate (a). Therefore:

$$VC = ma^2 p^n / -\log_e(p)$$

In both the basic and daily reproduction rate models, a key variable is survival of the vector, which is the parameter p in $(-p^n/\log_e[p])$. In the basic reproduction rate model, this term, being exponential, can be the most important parameter in malaria transmission, rather than the intuitive, but linear, relative density (m), when considering control options of vector-borne diseases. Garrett-Jones's (1964) concept of VC reinforced this counterintuitive finding. Once the relative abundance, or any other parameter, of vectors falls below a certain threshold, disease will decline to extinction.

2.2. Qualitative community models

We demonstrate that direction of change following input in the form of a press perturbation in the important parameters of the generalized Ross-Macdonald model, namely, relative density (m), frequency of contact, or the biting habit (a), and vector survival (p) can be evaluated from community models. These determinations are presented in the Results section.

Density-dependent interactions, within and between biological variables of a community, form the structure of the community matrix (\mathbf{A}) (Levins, 1968, 1975). The negative of the inverse of the community matrix, $(-\mathbf{A}^{-1})$, predicts direction of change in abundance of a population within a community following a press (Bender et al., 1984). The negative of the inverse is equal to the classical 'adjoint' of the matrix divided by its determinant. Based on the adjoint, Dambacher et al. (2002a) derived a 'weighted-predictions matrix' that assesses the theoretical indeterminacy of qualitative predictions.

While a press may only affect one variable of a community directly, other variables may be affected as a result of the web of interconnections within the community (Puccia and Levins,

1985). A press may affect the abundance of organisms in a population and impact other population demographics, such as age structure, that lead to turnover of the population (Puccia and Levins, 1985). Turnover, the reciprocal of life expectancy of a population (Puccia and Levins, 1985), is determined from the adjoint, or inverse, of the community matrix. Dambacher et al. (unpublished data) developed an algorithm (see <http://www.jambrosi.com>), based on Puccia and Levins (1985), for predicting change in life expectancy following a press.

A computer drawing interface that generates Maple compatible community matrices is available (<http://www.jambrosi.com>). A recently updated Maple program generates mathematical analyses of these systems (Dambacher et al., 2002d) and mathematical foundations of the analyses are available (Dambacher et al., 2002b,c).

2.3. Lyme disease

Lyme disease is found in temperate, forested landscapes and in North America is the result of long-term ecological disturbance related to the presence of deer. It is caused by a spirochete bacterium, *Borrelia burgdorferi*, that infects ticks, wildlife, and humans (Schauber and Ostfeld, 2002; Sigal and Curran, 1991). Although Lyme disease has likely always been present in North America, it reached public and scientific attention in the 1970s following the discovery of a cluster of childhood arthritis cases in Lyme, Connecticut (Ostfeld, 1997). The disease is carried by a tick vector, *Ixodes scapularis* (*I. dammini*) found in northeast and midwestern USA and *I. pacificus* in western USA. In humans, the disease is first exhibited as a skin rash; neurological problems and arthritis in the knee, hip or other joints can follow in chronic cases (Cooke and Dattwyler, 1992). Transmission and propagation of the disease in the human population involves an interrelationship between the tick vector and three principal hosts: small mammals such as the deer mouse (*Peromyscus leucopus*), white-tailed deer (*Odocoileus virginianus*), and humans. Deer mice serve as the main reservoir for the bacterium. As tick larvae hatch, they become infected when they feed on infected deer mice (Ostfeld, 1997). The infected larvae molt into nymphs, considered the principal agent for disease transmission because they are more difficult to detect than adult ticks. Nymphs can infest deer mice, deer, and humans. Deer are important hosts in the tick life cycle because adult ticks prefer large mammals; deer seem to play little role in maintaining the pathogen.

3. Results

To evaluate vector-borne disease risk within the context of a community model, we integrate the parameters of the Ross–Macdonald model, and specifically of VC, with loop analysis involving the community matrix. Changes in key parameters for VC: relative abundance, frequency of contact (host preference), and life expectancy are evaluated from mathematical manipulations of the community matrix.

To illustrate our procedure, we constructed a model of a Lyme disease vector–host community (Figure 1) based on Ostfeld et al. (1996). The community and adjoint (predictor of changes in population density) matrices are shown along with their interpretation in Figure 2; the ‘life expectancy’ matrix (predictor of population turnover) is presented in Figure 3. Ostfeld et al. (1996) suggest that a press from increased oak mast (i.e. increased acorn production) would favour deer, mice, and other mammals, and result in an increase in ticks that potentially carry Lyme disease, thus increasing disease risk (Ostfeld, 1997). Qualitative predictions developed from loop analysis lend support to Ostfeld’s observations. Increases in population density of mice and ticks follow a press from acorn production (Figure 2). Similarly, a positive press on gypsy moths (increasing gypsy moth abundance) would result in decreased acorn production, presumably because gypsy moths feed on oak leaves.

Predicting changes in population abundance, however, does not constitute a complete assessment of risk. Community structure itself also affects risk. Referring to the loop model (Figure 1)

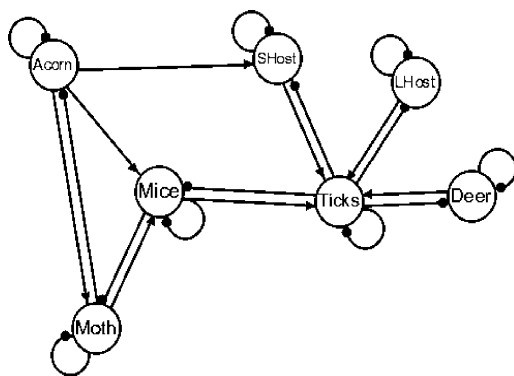


Figure 1 Signed digraph of a Lyme disease vector–host community, modified from Ostfeld et al. (1996). Circles represent variables, lines (or links) represent interactions (with arrows indicating positive effects; small, dark circles indicating negative effects). Curved lines with small, dark circles are self-regulating effects.

based on the Ostfeld et al. (1996) model of an oak forest community, we developed a qualitative prediction of risk from the community matrix, which serves as the basis for determining changes in the parameters of VC (Figure 4). Responses depicted in the adjoint and life expectancy matrices serve as an index for the parameters in the VC equation. Thus, a change in relative abundance (m) is determined by a change in the ratio of vector to competent (capable of disease transmission) host following a press perturbation to a variable such as deer (Figure 4). The adjoint of the community matrix is also used to determine host preference (a). Assuming a constant contact frequency, change in host preference (a) is estimated from the ratio of the abundance of the competent host (mice) to that of a non-competent host (small hosts) within the community (Figure 1). Finally, change in the vector survival, p in $(p^n / -\log_e p)$, is determined from the response of the vector in the life expectancy matrix (Figures 3 and 4).

Any change in one of these three parameters of VC might result in a predicted increased or decreased risk. For example, our model predicts that a positive press to deer would increase tick and gypsy moth abundance, thus decreasing the abundance of acorns, mice and other small hosts, but not affect tick life expectancy (Figure 4). As a result, risk for Lyme disease would increase due to the increased ratio of tick abundance to mice. This prediction is supported by field observations on Nantucket and Great Islands, off the coast of Massachusetts, where Lyme disease was endemic (Lane et al., 1991; Wilson et al., 1984). Deer were drastically reduced on Great Island resulting in a significant reduction of tick populations infesting rodents. Tick populations on Nantucket Island, where there was no deer intervention, remained stable. Thus, by altering the community structure, risk was reduced.

In another example, Ostfeld (1997) documented that mice and tick populations increased after an increased oak mast, increasing the infection rate of nymphal ticks, thus increasing the risk of Lyme disease. While our procedure supports Ostfeld’s observations of changes in tick and mice abundance (Figure 4), the epidemiologic implications are less clear. We can predict that a positive press on acorns increases the abundance of mice and ticks. However, taking the ratio of these responses from the VC equation, the parameter (m) is not clearly changed. A positive press to acorns also increases the abundance of small, non-competent hosts and mice, thus the ratio for (a) is again not clearly changed. This positive press to acorns has no impact on tick life expectancy (Figure 4) suggesting no clear impact on disease risk. To increase risk unambiguously, there

Predicted Life Expectancy Matrix

	Ticks	Deer	Acorn	Gypsy Moths	Mice	Small NC Host	Large NC Host
Ticks	+/-	-	-	?	-	-	-
Deer	0	0/-	0	0	0	0	0
Acorn	0	0	0/-	0	0	0	0
Gypsy Moths	+	+	-	+/-	-	+	+
Mice	0	0	-	0	0/-	0	0
Small NC Host	+	+	-	+	-	+/-	+
Large NC Host	0	0	0	0	0	0	0/-

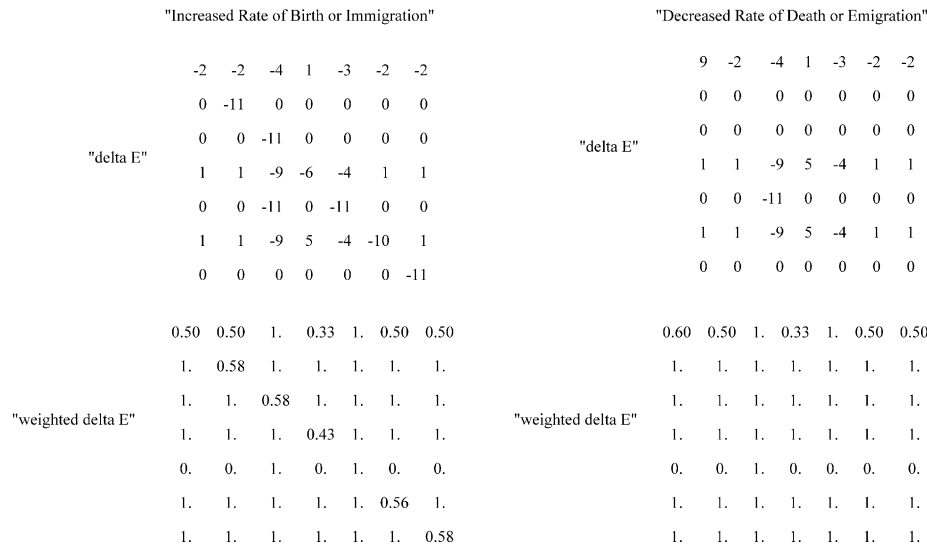


Figure 3 Changes in life expectancy of each community variable, including vector ticks, following a positive press within a Lyme disease host–vector community (Figure 1). The elements reflect the results of a positive press perturbation death or birth rates. Life expectancy responses, increased (+), decreased (–), or ambiguous (?), are determined by comparing the sign of the response from the $\Delta E d$ (death) and $\Delta E b$ (birth) matrices for a variable with the weighted value ($weighted_delta E d$ and $weighted_delta E b$) for that variable (Puccia and Levins, 1985; Dambacher et al., unpublished data). Diagonal elements have dual responses, representing input from decreased death or increased birth, respectively. Weights <0.5 are deemed unreliable.

community analysis may provide useful predictions of the impacts of anthropogenic change, such as habitat availability on population density of vectors and hosts within the community or climate change.

Our approach differs from vector-borne disease models that are age-structured (Anderson and May, 1979; Hudson et al., 1998; Randolph et al., 2001) or simulation models used to estimate spread of disease (LoGuidice et al., 2003; Nicholson and Mather, 1996). These types of models address impacts of disease arising from interactions between vector

and competent host species, but do not address specifically the whole ecological community. Our modeling approach allows us to address the impact of community perturbations on parameters of vectorial capacity, which includes vector age structure, without the high degree of quantitative input required in other approaches. Thus, we can predict changes in risk of Lyme disease following input to deer (Figure 4), and that this modified risk will arise from changes in relative tick abundance rather than tick life expectancy. The minimal

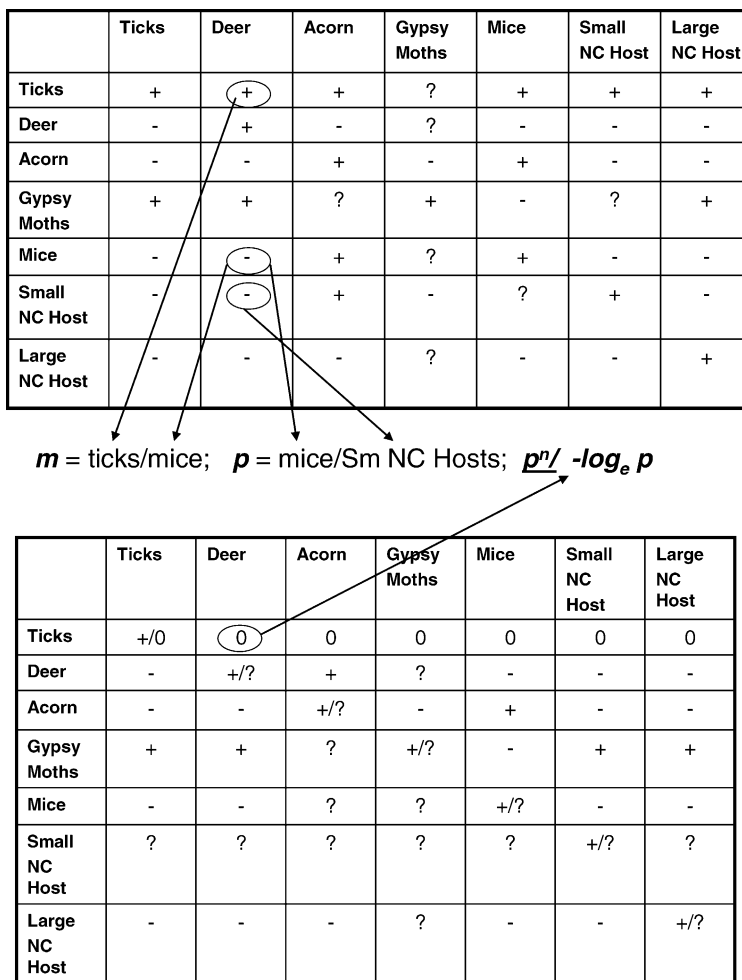


Figure 4 Assessment of change in vectorial capacity from community parameters. In the top matrix, changes in population abundance determine changes in vector/host ratio (m) and in competent/non-competent hosts ratio, corresponding to m and a parameters of vectorial capacity, respectively (see text); similarly for changes in life expectancy (p) of the vector (bottom matrix). Following a positive press to deer, risk is determined from the ratio of responses for different variables. A press to acorn (third column) is discussed in the text. Parameter m is determined from the ratio of ticks to mice. Parameter a is the ratio of the response in mice to that of small non-competent hosts.

quantitative aspect of the prediction is compensated for by a greater insight in community components of the disease, giving an important intervention target.

For Lyme disease specifically, the basic reproduction rate (of which vectorial capacity is a linear proportion) was found to be an important determinant of spread. Stage structure of the vector population emerges, as expected, as an important parameter in its calculation (Caraco et al., 2002). The life expectancy matrix can provide ecologists and epidemiologists with a qualitative solution to this problem under many circumstances. As suggested by Puccia and Levins (1985), there are numerous instances where quantification of community parameters will add little to a conclusion and even more situations where quantification is not possible or

practical. A precise quantitative validation of the Ostfeld model discussed above thus is likely not possible, and we argue that such quantification generally is not necessary. Simulations demonstrate that community structure alone is a significant predictor of system behaviour (Dambacher et al., 2003a).

Another recent Lyme disease model examines the problem of host diversity and its dilution impact on transmission (Schauber and Ostfeld, 2002). This phenomenon, so-called zooprophylaxis, arises from community complexity and presents serious challenges in the epidemiology of zoonotic disease. The original models of malaria had a minimal consideration of non-competent hosts, reasonably so given that human malaria is a parasite only of human beings. Zoonoses, by definition, are nested in complex natural communities. Schauber and

Ostfeld (2002) predict that diversity will impact risk. We can generate testable hypotheses on the effect of a press to one of these community variables not only on the abundance of other community variables but on the age structure of the variables, a crucial consideration for vectors. Predicted changes in ratio of competent/non-competent hosts, in vector/host abundance and in vector life expectancy allow us to link community modeling to conventional vector-borne modeling. Epidemiological indicators of zoonotic disease can be derived from the formalized and rigorous perspective of community ecology.

The advantage to our modeling approach is that qualitative analysis is rapid and better suited to address poorly specified (quantitatively speaking) complex systems. We have contributed consideration on life expectancy of vectors and thus tied it directly to vectorial capacity. For vector-borne zoonoses, our procedure can effectively predict an ecological community's response to a perturbation, which in turn can generate focused hypotheses to guide experimental design, data collection and control management strategies.

Conflicts of interest statement

The authors have no conflicts of interest concerning the work reported in this paper.

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