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HOST-PARASITE RELATIONS AND RANDOM ZERO-SUM GAMES: THE STABILIZING EFFECT OF STRATEGY DIVERSIFICATION

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In many host-parasite relations, the parasitic species has numerous variants, antigenic strains, or types. The host species also has many types of reactions and defenses, such as specific antibodies, cellular defense mechanisms, and genetically determined resistances or susceptibilities. We propose here a simple phenomenological model, based on a game with random payoffs, to explain how the evolution by natural selection of antagonistic hosts and parasites may lead to large and roughly comparable numbers of strategies of parasitic attack and host defense.

Diversification in strategies of parasitic attack and host defense may lead to, be accompanied by, or be a consequence of speciation. Examples of parasite-mediated speciation were reviewed by Price et al. (1986, pp. 498–499). Because the model we propose relates to interspecific diversity as well as to intraspecific diversity, the model provides a theoretical basis for Eichler's rule. Eichler's rule asserts that "when a large taxonomic group, for example, family, of hosts consisting of many species is compared with an equivalent taxonomic group consisting of few representatives, the large group has the greater diversity of parasitic fauna" (Noble and Noble 1982, p. 461). In support of Eichler's rule, Price reviewed "many examples . . . of a significant relationship between number of species in each host category and number of [species of] parasites that exploit members of that category" (1980, pp. 27–29).

After we describe the game-theoretical model and analyze its properties mathematically, we interpret it in greater detail. We describe what the model achieves and what the model omits or ignores. We consider other explanations of the diversity of host and parasitic adaptations and review some other uses of game theory to describe host-parasite relations.

Kinds of Models of Host-Parasite Coevolution

Models of host-parasite coevolution fall into three broad classes (Holmes 1983, pp. 176–177). In mutual-aggression models, selection acting on the parasite diametrically opposes selection acting on the host. The parasite is selected to

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exploit the host as much as possible, and the host is selected to exclude or limit the damage done by the parasite. Among the mutual-aggression models are the gene-for-gene model and Van Valen's Red Queen models (for references, see Holmes 1983). In prudent-parasite models, the parasite is selected to limit the damage that it does to its host, allowing both the host and its resident parasites to live longer. According to Holmes, "This is the traditional view, envisaging a de-escalating aggressive system that evolves from a relatively pathogenic to a relatively benign one" (1983, p. 177). In incipient-mutualism models, both host and parasite cooperatively evolve to promote the continued presence of the other.

The random-game model we describe here is a model of mutual aggression. It shows that even directly opposed interests can be stabilized by sufficient diversification of strategies on both sides. The model is thus relevant, for example, to the interaction between virulent phage and their bacterial hosts but not to the potentially mutualistic interaction between temperate phage and their bacterial hosts (Levin and Lenski 1983).

May and Anderson commented about many of the coevolutionary models they reviewed: "Too often, the real situation and the theoretical model bear a disquietingly metaphorical relation to each other" (1983, p. 206). That comment applies to the model presented here. The model stands in the same relation to a realistic model, like the malarial model of Dietz et al. (Molineaux and Gramiccia 1980), as the highly abstracted ecological model of May (1972; for generalizations, see Cohen and Newman 1984) stands in relation to the concrete realities of Coughenour et al. (1985). The analogy extends one step further: the model of May (1972) was introduced to investigate the relation between the complexity of ecosystems (as measured by the number of interacting species and their connectivity) and the stability of ecosystems. Our model is intended to shed light on the relation between the complexity of host-parasite interactions (as measured by the numbers of strategies of attack and defense) and the stability of the host-parasite system. The meaning of stability in our game-theoretical model differs from the meaning of stability in May's: here the host-parasite system is stable if the value of a random game, defined below, tends to zero.

Diversity in the Malarial Parasite

We begin with a concrete example of the phenomena that inspire our simplified model. Malaria is one of many host-parasite systems in which diversity is a striking feature (Cox 1982). We briefly sketch the diversity of hosts and parasites in malaria, starting with the parasites (Walliker 1983).

Roughly 80 species of malaria (genus *Plasmodium*) are recognized. Four species of rodent malaria are differentiated by their enzymes and are reproductively isolated. An individual rodent in the wild may be infected with as many as three different species. The parasites of a single species in one rodent generally display genetic variation in enzymes and antigens and mate randomly within the species. Subspecies of a malarial species, differentiated by their enzymes, are found in different parts of Africa, but these subspecies are not reproductively isolated in the laboratory. Laboratory experiments to select for drug resistance demonstrate that new stable genes can arise by mutation.

At least one experiment with monkey malaria suggests that when a single malarial organism infects a single monkey host, the clone of malaria that develops in the monkey host can display immunologically detectable antigenic variation over time. The high rate at which this antigenic variation occurs suggests that it results from the sequential expression of different genes present initially rather than from the emergence of new genes by mutation. Field observations indicate that the diversity experimentally demonstrated for rodent and monkey malarias also exists for the human malarias.

Thus, many levels of variation exist among malarial parasites. Within a single host individual, as well as within host populations with geographically extensive ranges, like the rodent and human hosts of malaria, there may be antigenic variation within a single clone of malarial parasite, genetically diverse clones within a single subspecies of malarial parasite, more than one subspecies within a single species of malarial parasite, and different species of malaria.

Diversity in Host Susceptibility and Response to Malaria

Genetically determined intraspecific variation in susceptibility and resistance to infection by malarial parasites has been demonstrated for several mosquito species that transmit avian malarias. "The factors which determine the success or failure of malarial infections in mosquitoes are not understood and the processes controlled by the genes concerned are unknown" (Wakelin 1978, p. 224).

In the human host, many factors affect susceptibility to infection and the effectiveness of immune responses (Wyler 1983; Molineaux and Gramiccia 1980). Experimental and epidemiological evidence suggest that blood-group substances, including those that specify the Duffy blood-group phenotype and other less common blood-type variants, affect the ability of malarial merozoites to attach to or invade red blood cells. In red cells with hemoglobin SS or SA, the infection and growth of *Plasmodium falciparum* parasites are lowered, when compared with cells with AA hemoglobin, under conditions of reduced oxygen tension. Fetal hemoglobin also retards the intracellular growth of *P. falciparum*.

Immune responses to intra-erythrocytic malarial infections in mice involve both T-cells and IgG antibodies as well as the spleen. Host antibodies that are effective against one stage of the malarial life cycle do not appear to be effective against another.

Thus, hosts' responses to malarial parasites vary at many levels. Within a given vertebrate host, a diversity of antibodies and cell-mediated immune responses may be directed at each stage of the parasite's life cycle. Within a population of human hosts, a diversity of blood-group substances, hemoglobin types, and possibly other genetic factors affect the ability of malarial parasites to attach to, invade, and grow in red cells and to complete other stages of the life cycle. All of these factors may vary among species of rodent hosts of a given species of rodent malaria. In addition, mosquitoes exposed to malaria vary intraspecifically in susceptibility or resistance to infection.

It is plausible that these differential responses have effects in evolutionary time. The taxonomic diversity of malarial parasites seems to be related to the taxonomic diversity of various groups of mammalian hosts (Garnham 1973). For example,

malaria may be partly responsible for the speciation of macaque monkeys (Wheatley 1980).

A Game-Theoretical Model to Account for Diversity

The model we describe bears a metaphorical relation to the detailed complexities of malaria. Our model is intended to explain the diversity of parasite and host, and the coordination of host-parasite diversity, as a general feature of antagonistic host-parasite relations.

The model is based on a two-player (host and parasite), zero-sum game, in which the payoffs represent changes (from some base level) in each player's net rate of reproduction (NRR). All game-theoretical terminology used in this paragraph is standard (e.g., Dresher 1981) and is explained and interpreted below. To focus attention on the number of strategies of each player rather than on the details of the payoffs, the model assumes that elements of the payoff matrix are random. The model implies the unremarkable fact that it is to each player's advantage to diversify his strategies. Analysis of the model gives bounds to how quickly each player must diversify, relative to his opponent, to avoid any change in average NRR. Within these bounds, the probability of a substantial change in average NRR for either player tends to zero as both players diversify. The model suggests that antagonistic host-parasite relations frequently lead to the evolution of large numbers of parasite and host strategies, when the change in NRR for different strategies is generated by a random mechanism which, on the average, does not favor either player.

Game theory has long been in vogue in discussions of the theory of evolution, coevolution, and host-parasite interactions. Rapoport (1956) investigated a two-player, non-zero-sum game with a continuum of pure strategies for each player. He showed how one player could evolve into a parasite of the other as each player tries to maximize his own payoff by trial and error without knowing the full payoff function. Foster and Rapoport (1956) extended the analysis to three-person games. Another early use of game theory in evolution is Lewontin's (1961). Auslander et al. (1978) modeled the interaction of a moth and a wasp that parasitizes the moth. Their game-theoretical model assumes that the moth and wasp each have two strategies.

Applications of game theory in ecology (Riechert and Hammerstein 1983) and in evolution (Van Valen 1980) have been reviewed. Slatkin (1983, pp. 30–32) presented a concise and penetrating summary of the virtues and limits of game-theoretical models of coevolution, with some specific mention of host-parasite coevolution. Other recent authors who used game theory for modeling evolution and host-parasite relations include Zeeman (1980), Bremermann and Pickering (1983), Losert and Akin (1983), Jayakar (1984), and Brown and Vincent (1987).

To the best of our knowledge, the model we now describe and analyze is novel in that it emphasizes the numbers of strategies employed by the host and parasite.

A RANDOM GAME WITH ARBITRARILY MANY POSSIBLE PURE STRATEGIES

In this initial description of the model, when we speak of a host and a parasite, we do not specify whether we are speaking of individuals, clones, genetically

diverse demes, or species of hosts and parasites. Thus, the model is subject to several interpretations (see the section "*Level at Which Selection Acts*," below).

Suppose a host and parasite interact in direct opposition. Any reproduction or survival of the parasite is at the direct expense of the reproduction or survival of the host. For concreteness, we suppose that the host and parasite contend over changes in the parasite's net rate of reproduction (NRR). The analysis that follows applies equally to any other quantity that the parasite might want to maximize and the host to minimize, such as the probability of survival over a long time. If natural selection acting on the parasite favors an increase in the NRR of the parasite, then we suppose that natural selection acting on the host favors a decrease in the NRR of the parasite.

In the language of game theory, consider two players (a host and a parasite) playing a zero-sum game in which the payoff to the maximizer (the parasite) is measured by changes in its NRR. The payoff to the minimizer (the host) is assumed to equal the negative of the changes in the parasite's NRR but could just as well be directly proportional to the negative of these changes.

Suppose that the parasite has a finite set of variants (e.g., strains, surface-coat antigenic variants, or pneumococcal types), enumerated by $i = 1, \ldots, m$, where $m > 1$). Suppose that the host has a finite set of types of defense (e.g., variable regions of immunoglobulin molecules in man) or of genetic factors affecting the response to infection, enumerated by $j = 1, \ldots, n$, where $n > 1$. When parasites of variant i infect a host of type j or are faced with a host defense purely of type j, let the change in the NRR of the parasite be a_{ij}. We refer to the variants of the parasite and the types of the host collectively as the strategies of the players. Thus, a_{ij} measures the change from a strategy-independent baseline level of NRR.

Suppose that each parasitic variant i encounters each host type j with a relative frequency $x_i y_j$, where $x_i \geq 0$, $\Sigma_{i=1}^{m} x_i = 1$, $y_j \geq 0$, $\Sigma_{j=1}^{n} y_j = 1$. We may interpret x_i as the effective relative frequency, or simply the abundance, of parasitic variant i, and y_j as the abundance of host type j. Denote by $\mathbf{x} = (x_1, \ldots, x_m)^{\mathrm{T}}$ the (column) vector of abundances of parasitic variants and by $\mathbf{y} = (y_1, \ldots, y_n)^{\mathrm{T}}$ the (column) vector of abundances of host types. (The superscript T denotes transpose; since $(x_1, \ldots, x_m)$ is a row vector, the transpose $(x_1, \ldots, x_m)^{\mathrm{T}}$ is a column vector.) We call a single parasitic variant or a single host type, as well as a vector $\mathbf{x}$ or $\mathbf{y}$ with only one positive element, a pure strategy. When at least two elements of $\mathbf{x}$ (or $\mathbf{y}$) are positive, we call $\mathbf{x}$ (or $\mathbf{y}$) a mixed strategy. The mean change in NRR of parasitic variant i, when confronted with the vector $\mathbf{y}$ of abundances of host types, is

$$\sum_{j=1}^{n} a_{ij} y_j = (\mathbf{A}\mathbf{y})_i .$$

The mean overall change in NRR of the parasite, given the parasite's vector $\mathbf{x}$ of abundances of variants, is

$$\sum_i x_i \sum_j a_{ij} y_j = \mathbf{x}^{\mathrm{T}} \mathbf{A} \mathbf{y} .$$

The preceding two formulas make two implicit assumptions. First, they assume that it is possible to aggregate over strategies whatever is measured (here, change

in NRR) by the elements a_{ij} of the payoff matrix **A**. Second, they assume that a simple averaging is the right way to do the aggregation. The reasonableness of both assumptions depends on the biological situation being modeled but cannot be taken for granted (Cohen 1985).

We now suppose that natural selection of the parasite favors a distribution **x** of abundances of variants that maximizes the mean change in NRR $\mathbf{x}^T\mathbf{A}\mathbf{y}$ of the parasite, given the distribution **y** of host types, while natural selection of the host favors a distribution **y** of abundances of host-defense types that minimizes $\mathbf{x}^T\mathbf{A}\mathbf{y}$, given a distribution **x** of parasitic variants.

We call

$$v_{mn} = \min_{\mathbf{y}} \max_{\mathbf{x}} \mathbf{x}^T\mathbf{A}\mathbf{y}$$

the value of the host-parasite interaction in this model. The subscripts m, n of v_{mn} emphasize that the parasite has m strategies and the host has n. In game theory (e.g., Dresher 1981), v_{mn} is the value of a two-person, zero-sum game with $m \times n$ payoff matrix **A**.

The value is the mean change in NRR of the parasite after the parasitic variants have found a distribution of abundances that maximizes their mean change in NRR, for any given distribution **y** of abundances of host types, and then the host types have found, on a slower time scale, a distribution of abundances **y** that minimizes the best mean change in NRR that the parasite can achieve.

The optimal strategies **x** and **y** are not necessarily unique. When the payoff matrix **A** admits more than one possible optimal strategy, the actual optimal strategy attained might depend on history, for example, the initial strategies of host and parasite.

The assumed optimization of **x** and **y** by the parasite and host, respectively, may occur on behavioral, ecological, or evolutionary time scales. These time scales are all assumed to be fast compared to the time scale on which new strategies are introduced. This last evolutionary time scale is our main interest here.

Assuming that **A** is a fixed matrix, von Neumann (1928) proved that

$$v_{mn} = \max_{\mathbf{x}} \min_{\mathbf{y}} \mathbf{x}^T\mathbf{A}\mathbf{y}\,.$$

That is, the same overall mean change in NRR of the parasite results if, for any given distribution **x** of abundances of parasite variants, the host first finds a distribution **y** of abundances that minimizes the parasite's change in NRR, and then the parasitic variants find, on a slower time scale, a distribution **x** of abundances that maximizes the parasite's mean change in NRR.

The best mean change in NRR that the parasite can achieve is the same whether the parasite optimizes its abundances **x** more quickly or more slowly than the host optimizes its abundances **y**. In this phenomenological model, we do not discuss further the relative time scales on which **x** and **y** are changed.

Now suppose that the parasite invents (by genetic or somatic mutation or by ecological or behavioral innovation) a new variant, labeled $m + 1$. Suppose that the invention of this new variant has no effect on the payoffs to the previously existing variants. Thus, assume that whatever cost is associated with the genetic, developmental, physiological, or behavioral mechanism of the new variant is

reflected in the payoffs of that variant (or possibly subsequent variants) only, and not in the payoffs of the previously existing variants.

Let $v_{m+1,n}$ be the value of the game with an $(m + 1) \times n$ payoff matrix in which the first m rows are identical to **A** and the elements of row $m + 1$ are arbitrary. If the parasite ignores the possibilities created by the new variant by setting $x_{m+1} = 0$, the parasite's change in NRR can be no worse than before. Taking advantage of the new strategy might possibly improve the parasite's change in NRR. Thus,

$$v_{m+1,n} \geq v_{mn}.$$

Similarly, suppose the host invents (by some mechanism) a new type of defense or reaction, labeled $n + 1$. Once again, suppose that the invention of this new variant does not affect the payoffs to the previously existing variants. Let $v_{m,n+1}$ be the value of the game with an $m \times (n + 1)$ payoff matrix in which the first n columns are identical to **A** and the elements of column $n + 1$ are arbitrary. The host's new strategy only enlarges its possibilities for combating the parasite but does not eliminate any of the host's old possibilities. Hence,

$$v_{m,n+1} \leq v_{mn}.$$

These two elementary inequalities indicate the potential reproductive advantage of increasing the diversity of strategies for parasites and hosts. These inequalities presuppose that no old strategy bears any costs that are incurred by creating new strategies.

The remaining analytical results of this paper investigate how many types of defense a host needs to keep its average payoff approximately even when challenged by a growing diversity of parasitic variants, and vice versa. To carry out this investigation, we construct a qualitative model that ignores the details of individual host-parasite systems. We assume that the change in the parasite's NRR for each combination of parasitic variant i and host of type j is a random variable A_{ij}. The game-theoretical value of an $m \times n$ random matrix **A** of these random elements A_{ij} becomes a random variable instead of a fixed number. We denote the value by V_{mn} instead of v_{mn}. Once chosen, each element A_{ij} is fixed in time, and therefore so are the matrix **A** and the value V_{mn}. To investigate the evolutionary consequences of numbers of parasitic variants and host types, we now describe how V_{mn}, the mean change in NRR of the parasite, depends on m and n.

Most of our mathematical results are derived under the rather strong assumption that the A_{ij}'s are independent and identically distributed random variables from a single probability distribution, with cumulative distribution F. However, as indicated in the discussion following the proof of theorem 1 (in the Appendix) our main conclusions are fairly robust and remain valid under various weakenings both of the assumption of independence and of the assumption of a single common distribution. Even these weakenings, we recognize, leave us with an abstract and simplified model. The model is more useful for qualitative insight into parasite-host diversification generally than for quantitative predictions about particular host-parasite systems.

ANALYTICAL RESULTS

Previously Known Results

An $m \times n$ matrix of independent and identically distributed (i.i.d.) elements with a common continuous distribution function F has a saddle point with probability $P_S(m, n) = m!n!/(m + n - 1)!$, independent of F (Goldman 1957). (A saddle point is an element of a payoff matrix that equals the minimum of its row and the maximum of its column. If a finite payoff matrix has a saddle point, then the value of the game equals the value of that element. An optimal strategy for each player is to play the saddle point.) The larger either m or n becomes, the smaller the probability $P_S(m,n)$ of a saddle point. Hence, when either a host or a parasite has a substantial number of pure strategies, it is rare for the payoff matrix to have saddle points. One can expect most optimal strategies to be mixed strategies when m or n or both are large.

Given that a payoff matrix of i.i.d. elements with a common continuous distribution function F does have a saddle point, we denote the value of the game by W_{mn}. This random variable has the distribution of the nth largest of $m + n - 1$ i.i.d. random variables that have the common distribution function F (Thrall and Falk 1965; Thomas and David 1967, p. 243). If m is greater than n, then W_{mn} is distributed as the nth largest of at least $2n$ variables with distribution F. If F is symmetric with respect to zero, then the mean of W_{mn} is positive. Thus, if the game has a saddle point and F is symmetric, whichever player can arrange a larger number of pure strategies can also arrange a favorable mean value for the game. If $n/(m + n - 1) \to 1 - \alpha$ as $n \to \infty$, then W_{mn} tends to the (100α)th percentile of the distribution F. Consequently, when the mean of F is zero, W_{mn} approaches zero for large n only when m/n approaches one, that is, only when the two players have approximately the same numbers of strategies.

We henceforth assume that the mean of F is zero. If the mean is not zero, F can be centered by subtracting the nonzero mean, and the value of the payoff matrix will be shifted by the same amount. Equivalently, we can think of the elements A_{ij} as the difference between the net rate of reproduction (NRR) of an i,j encounter and the overall mean parasitic NRR. In particular, a host-parasite game having a mean value of zero can be made consistent with a stationary parasitic population having a mean NRR of one simply by adding one to every matrix element.

When the elements of $\mathbf{A}$ are independent with mean zero and F is symmetric and continuous, the probability $P(m,n)$ that the value of the game exceeds zero, $P(m,n) = P(V_{mn} > 0)$, is (Cover 1966)

$$P(m,n) = \tfrac{1}{2}^{m+n-1} \sum_{k=0}^{m-1} \binom{m + n - 1}{k}.$$

Let int[t] be the integer part of a nonnegative number t. Then, for any $\epsilon > 0$,

$$\lim_{m\to\infty} P(m, \text{int}[(1 + \epsilon)m]) = 0,$$

$$P(m,m) = \tfrac{1}{2} \quad \text{for all } m,$$

$$\lim_{m\to\infty} P(m, \text{int}[(1 - \epsilon)m]) = 1.$$

Cover stated that "large rectangular games tend to be strongly biased in favor of the player having the greater number of alternatives" (1966, p. 1796). This is true in the sense implied by the preceding limits, namely, that the sign of the value of the game favors the player with more alternatives, with probability approaching one as m increases. However, our analysis below shows that, in the limit considered by Cover (with reasonable restrictions on F), the value of the game converges to zero (in probability or almost surely). Cover's and our results may be reconciled by saying, for example, that if the host has $1 - \epsilon$ times as many strategies as the parasite ($\epsilon > 0$), then the value is positive with a probability approaching one, but it is positive by an amount that approaches zero (in probability or almost surely).

New Analytical Results

We now describe informally some new facts about random games with arbitrarily large numbers of pure strategies. The theorems, proofs, and discussions of the proofs appear in the Appendix.

Let A_{ij} $(i,j = 1, 2, \ldots)$ be a doubly infinite sequence of i.i.d. random variables. A_{ij} is the change in NRR of parasitic variant i interacting with a host type j. Define V_{mn} as the (random) value of a game with $m \times n$ payoff matrix $\mathbf{A}$ whose ijth entry is A_{ij}:

$$V_{mn} = \min_{\mathbf{y}} \max_{\mathbf{x}} \sum_{i=1}^{m} \sum_{j=1}^{n} x_i A_{ij} y_j = \max_{\mathbf{x}} \min_{\mathbf{y}} \sum_{i=1}^{m} \sum_{j=1}^{n} x_i A_{ij} y_j , \tag{1}$$

where the minimum and maximum are taken over all $\mathbf{y}$ and $\mathbf{x}$ with nonnegative elements summing to one. For ease of presentation, we consider two nondecreasing sequences $\{m_k, n_k \mid k = 1, 2, \ldots\}$ of values of m and n, with the proviso that $m_{k+1} > m_k$ or $n_{k+1} > n_k$ or both. We define $V_k = V_{m_k n_k}$.

The first theorem gives a number of weak assumptions about the relative rates of increase of m_k and n_k that imply the convergence of V_k to zero (in probability or almost surely). By definition, V_k approaches zero in probability if and only if, for all $\epsilon > 0$,

$$\lim_{k \to \infty} \mathrm{P}(|V_k| \geq \epsilon) = 0 . \tag{2}$$

To illustrate, suppose that the distribution of every element A_{ij} has a moment-generating function (e.g., suppose the A_{ij}'s are bounded random variables or they are normally distributed) and that the host is diversifying its types of defense by increasing n_k. Then the parasite keeps its mean change in NRR (the value of the game) above any fixed negative value by increasing the number m_k of its variants at any rate faster than the logarithm of n_k (so that $m_k/\log n_k \to \infty$), and the host keeps the parasite's mean change in NRR below any fixed positive value so long as m_k increases at any rate less than the exponential of n_k (so that $(\log m_k)/n_k \to 0$).

Prékopa (1972) and Kabe (1983), in obtaining results related to those of theorem 1, always assumed that the ratio m_k/n_k is bounded away from zero and infinity. Under certain assumptions about the existence of moments or moment-generating functions, our result allows for the possibility that m_k/n_k may behave differently, for example, that m_k may increase as slowly as $(n_k)^{1/2}$ or even as $(\log n_k)^2$, and as

rapidly as n_k^2 or even as $\exp[(n_k)^{1/2}]$. The biological point of this mathematical extension of previous results is that, for example, the parasite in our simplified model need not diversify its pure strategies in strict proportion to the diversification of the host's defenses in order to keep the asymptotic value of the game converging to zero.

Theorem 3 shows that, at least when the distribution of A_{ij} has a moment-generating function, the restrictions on the behavior of m_k/n_k given in theorem 1 are essentially optimal. In particular, if $m_k/\log n_k$ tends to a sufficiently small constant, then the asymptotic value of the game is strictly negative. Similarly, if $n_k/\log m_k$ tends to a sufficiently small constant, then the asymptotic value is strictly positive.

Theorem 1 describes neither the rate at which V_k converges to zero nor the number of nonzero components in the optimal-strategy vectors of either the host or the parasite. Motivated by our results, Faris and Maier (1987) found numerically that with $m_k = n_k = k$ and with F either normally or uniformly distributed and standardized to mean 0 and variance 1, V_k behaves proportionally to $1/k$ and the fraction of components that are nonzero tends to ½.

BIOLOGICAL INTERPRETATION OF THE MODEL

Level at Which Selection Acts

A model of natural selection assumes some level at which natural selection operates (Slatkin 1983): individual, kinship groups, demes, species, or ecosystems. Depending on the mechanism by which parasites generate variants, the model we propose here could be interpreted as acting at the level of individual parasites; parasitic clones; parasitic demes that reproduce within a single host individual or a deme of hosts; or parasitic species (for a discussion of species selection, see, e.g., Eldredge 1985, pp. 152–179). Similarly, depending on the mechanisms by which hosts generate types of defenses, our model could be interpreted as acting at the level of individual hosts or host demes or species of hosts.

In malaria, selection would act at the level of individuals if the novel strategies available to the parasite were limited to those arising from mutations of a clone and if the novel strategies available to the host were limited to those arising from a particular person's immune system and genome. At the other extreme, selection would act at the level of the subgenus of human malarial parasites and at the level of the human species if the parasite's strategies included all the options open in multispecies malarial infections (e.g., Molineaux et al. 1980) and if the host were defined as the whole human species with all its genetic diversity and possibilities for chemotherapeutic interventions.

Price (1980, pp. 39–43) reviewed the evidence, mechanisms, and theories of rapid sympatric speciation of parasites on different species of host plants and animals, remarking: "For such small, short-lived, precisely adapted organisms as parasites, evolution will operate in miniature—in short times, in small spaces, but with impressive results" (p. 43).

Extending the Interpretation of the Model

In presenting the model, we interpreted **x** as the vector of abundances of different parasitic variants and **y** as the vector of abundances of different host types. For certain parasites and hosts, **x** and **y** can be interpreted as the vectors of abundances of different environmental conditions affecting the parasite and host. The abundances in **x** and **y** are controlled by the behavior of the parasite and host, respectively. For example, the miracidial stage of the schistosome parasite can emerge from its snail intermediate host at different times of day in waters running at different velocities. The density of emergent miracidia in water is remarkably matched to the times and conditions when human hosts are likely to be in contact with the water. Similarly for hosts (Smith 1979): the Neotropical colonial birds *Zarhynchus wagleri* (chestnut-headed oropendola) and *Cacicus cela* (yellow-rumped cacique) establish colonies in umbrella-like trees in which colonies of stinging or biting wasps and bees either are or are not present. When the wasps or bees are present, they discourage *Scaphidura oryzivora* (the giant cowbird) from acting as a brood parasite, that is, from inserting its young in the nest of the host species for the host to feed and raise. However, because the wasps or bees do not establish nests at the same time that breeding normally begins, a host that insists on the presence of wasps or bees must delay building its nest and breeding by about 2 months. The relative frequency with which hosts nest in trees with or without wasps or bees appears to be determined by the hosts' behavior.

In our initial interpretation of the model, we assumed all hosts to be infected, or we considered only the infected portion of the host population. The model can represent the portion of the host population without parasites—that is, the uninfected fraction—by adding one more type, "uninfected." The model leaves unspecified the dynamics that determine the abundance of uninfected hosts. In the column of the payoff matrix corresponding to uninfected hosts, the elements describe the change in the net reproductive rate (NRR) of each parasitic variant outside of a host. Assuming that the game is zero-sum means assuming that the more a parasitic variant's NRR suffers from not finding a host, the more a host type's NRR benefits from the absence of the parasite. This assumption appears to be testable experimentally.

Achievements of the Model

The model shows that additional strategies of attack can only help a parasite, and additional strategies of defense can only help a host, provided that the cost of additional strategies can be neglected or is absorbed only in the payoffs of the additional strategies. This elementary conclusion does not depend on any assumptions about the specific sizes of payoffs or the numbers of strategies that the host and parasite currently use. (This conclusion leaves open an interesting question: If the cost of additional strategies is distributed over the payoffs of previously existing strategies, what cost would be worth paying?) The ecological value of a diversity of strategies of attack and defense has been emphasized before (Bremermann 1980).

The model shows that interactions between a single species of host and a single species of parasite are enough to favor a diversity of strategies on the part of both host and parasite. May and Anderson suggested another explanation of diversity. Because hosts have to deal with a variety of co-occurring parasite species, "immune systems in vertebrates or chemical defenses in many plants represent generalized defenses against an array of possible parasites" (1983, p. 205). Similarly, the diversity of variants in a parasite might be adaptations to diverse hosts. The model proposed here shows that it is not necessary to invoke multiple species of parasites and multiple species of hosts to explain diversity in hosts and parasites. The explanation offered by our model in no way excludes the alternative that May and Anderson proposed.

Our model suggests that as the numbers of strategies of both parasite and host increase, within the bounds of the theorems in the Appendix, the change in the NRR of either player tends to zero.

When different strategies are recognizable or interpretable as species differences, these implications of the model provide a theoretical basis for Eichler's rule, which asserts that comparable taxons with more species of hosts have more species of parasites. Price (1980, p. 27) tabulated six linear regressions of the number of parasitic species as a function of the number of host species available. For our purposes, what is significant is neither the slopes of these regressions nor the proportions of variance accounted for by the linear regression (ranging from 0.34 to 0.99) but the choice of a linear relation as a first approximation to the data. Our model predicts that in stable host-parasite systems, the regression should be less than exponential and more than logarithmic. This broad range of possibilities obviously includes linear regressions.

Using protein-electrophoretic data, Hafner and Nadler (1988) showed a high concordance between the phylogenetic tree of pocket gophers and the independently assessed phylogenetic tree of their ectoparasitic chewing lice. In addition to demonstrating the similarity between the topologies of the two phylogenetic trees, Hafner and Nadler demonstrated a similarity, in most cases, between the genetic distances of hosts and parasites. This direct evidence of agreement between hosts and parasites in the pattern and timing of speciation is consistent with the pattern of diversification modeled here.

Our model further suggests that if the parasite's diversity does not sufficiently keep up with the host's diversity, or vice versa, the more diverse player will gain an advantage in mean NRR. If the parasite gains the advantage and can disperse without encountering density-dependent defenses of the host, then one might expect to see nearly all hosts infected. If the host gains the advantage, however, the reproduction of the host could outrun the reproduction of the parasite. If the prevalence of infection with the parasite approaches zero, the host-parasite system is eliminated. According to the model, in host-parasite systems that have existed long enough for both the host and the parasite to evolve many strategies, either the diversity of host and parasite strategies should match within the bounds given by our theorems or, if not, the infection should be universal or nearly absent.

Omissions of the Model

The model ignores the possibility of limits on the ability of parasite and host to generate new variants. In experiments on virulent phage and their bacterial host *Escherichia coli* (Lenski and Levin 1985), a genetically unchanging bacterial population eventually becomes established and persists for the duration of the experiments, even though, as assumed in our model, the interaction between phage and bacteria is plausibly purely antagonistic. This finding would appear to contradict our assumption that host and parasite will always generate new variants. However, as they observed, the experiments of Lenski and Levin cannot exclude the possibility that host and parasite can produce mutants on time scales much longer than that of the experiments. Moreover, Lenski (pers. comm.) has suggested that recombination among independently evolved phage lineages, which was not possible in these experiments, could generate a greater diversity of phage variants in nature than in the experiments.

The model makes no explicit reference to the spatial structure of the host and parasite populations. However, in those hosts and parasites that can choose or influence their own spatial location, location can be made part of the specification of a strategy (e.g., chemotherapy applied in a malarious area).

The model omits changes that may occur over time even in a constant physical environment in the payoff to the interaction between parasitic variant i and host type j. Thus, it omits "escalation," a term Vermeij used to describe "the process in which the capacities of enemies as well as the competitive and defensive performances of potential victims increase through time in a given environment" (1987, p. 418). Prime examples of escalation are evolutionary increases in the thickness of molluscan defensive armor and in predators' offensive abilities to drill through shells. Vermeij distinguished such escalation from the diversification of chemical and immunological defenses characteristic of hosts and parasites (p. 424).

The model omits the physiological, immunological, behavioral, ecological, and genetic mechanisms in the host and in the parasite through which the optimization of $\mathbf{x}$ and $\mathbf{y}$ and the evolution of m and n occur. These mechanisms are the subjects of extensive speculation concerning, for example, molecular mimicry and the function of the major histocompatibility complex (for a good review, see Holmes 1983). In a sense, our model distills the formal structure of some of that speculation without making a commitment to any specific physical or biological mechanism. May and Anderson remarked that the coevolutionary models they reviewed "all tend to oversimplify either the genetics or the epidemiology" (1983, p. 206). Our model omits both.

The model does not mention the possible influence of other parasites that may occur in the same host. The model could be extended to allow for this possible influence by considering all the parasitic species as one extended parasite pool and subsets of the parasite pool as strategies of the pool.

The model omits the effect on the parasite, in the individual host or host population under consideration, of the presence, abundance, and evolution of

other host species and populations. For example, Hairston (1962) showed that the chief mammalian reservoir of *Schistosoma japonicum* parasites in the Philippines is the local rodent population and that man is only incidentally infected. An analysis that focused on the human-schistosome interaction could be misleading because natural selection was acting chiefly elsewhere.

Finally, the model specifies no details of virulence, pathogenicity, or transmissibility but summarizes all the effects of the host on the parasite by one number, here interpreted as the change in NRR. When the fine structure of the change in NRR is important, this model is unable to help.

SUMMARY

In many host-parasite relations, the parasite has numerous variants, antigenic strains, or types. The host also has many types of reactions and defenses. A simple phenomenological model proposed here shows how evolution by natural selection could explain this diversity, and why the diversity of a host roughly corresponds to the diversity of a parasite. At the level of species diversity of hosts and parasites, the model provides a theoretical basis for Eichler's rule.

The model is based on a two-player (host and parasite), zero-sum game. To focus attention on the number of strategies of each player rather than on the details of payoffs, the model assumes that the elements of the payoff matrix are chosen at random, once and for all. For concreteness, the model supposes that the host and parasite contend over changes in the parasite's net rate of reproduction.

The model implies that it is to each player's advantage to diversify its strategies if the cost of additional strategies can be neglected. This elementary and unremarkable conclusion does not depend on any assumptions about the details of payoffs or the numbers of strategies that the host and parasite currently use. Analysis of the model gives bounds on how quickly each player must diversify, relative to its opponent, to avoid any change in average net rate of reproduction (NRR). Within these bounds, the probability of a substantial change in average NRR for either player tends to zero as both players diversify. The model suggests that, when the change in NRR for different strategies is generated by a random mechanism, which on the average does not favor either player, an antagonistic host-parasite relation will either evolve large numbers of parasite and host strategies or else become evolutionarily unstable.

The model shows that it is not necessary to invoke selective effects of multiple species of parasites and multiple species of hosts to explain this diversity of strategies. It shows that even directly opposed interests can be stabilized by sufficient diversification of strategies on both sides.

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APPENDIX

Theorem 1.—Suppose that the A_{ij}'s ($i, j = 1, 2, \ldots$) share the distribution of a fixed random variable X of mean 0. If for some $H > 0$, $E(e^{tX}) < \infty$ for $|t| < H$, then $V_k \to 0$ almost surely (and in probability), provided that $m_k = O(e^{cn_k})$ and $n_k = O(e^{cm_k})$ for every $c > 0$ (i.e., $(\log m_k)/n_k \to 0$ and $m_k/\log n_k \to \infty$). If for some $r \geq 2$, $E(|X|^r) < \infty$, then $V_k \to 0$ in probability, provided that $m_k = O(n_k^{r-1})$ and $n_k = O(m_k^{r-1})$. If for some $r > 3$, $E(|X|^r) < \infty$, then $V_k \to 0$ almost surely, provided that $\Sigma_k\, n_k^{-r+1} m_k < \infty$ and $\Sigma_k\, m_k^{-r+1} n_k < \infty$.

The proof of theorem 1 is based on the following simple proposition (which is not restricted to independent and identically distributed (i.i.d.) A_{ij}'s) and on known results about convergence rates in the law of large numbers.

Proposition 2.—For any random $m \times n$ real matrix $\mathbf{A}$ and any real v, $V(\mathbf{A})$, defined as the V_{mn} of equation (1), satisfies

$$P[V(\mathbf{A}) \geq v] \leq \sum_{i=1}^{m} P\left(n^{-1} \sum_{j=1}^{n} A_{ij} \geq v\right), \tag{A1a}$$

$$P[V(\mathbf{A}) \leq v] \leq \sum_{j=1}^{n} P\left(m^{-1} \sum_{i=1}^{m} A_{ij} \leq v\right). \tag{A1b}$$

Proof of proposition 2.—By choosing $y_j = 1/n$ for all j, it follows from equation (1) that

$$V(\mathbf{A}) \leq \max_{\mathbf{x}} \sum_{i=1}^{m} x_i \left(n^{-1} \sum_{j=1}^{n} A_{ij}\right) = \max_i \left(n^{-1} \sum_{j=1}^{n} A_{ij}\right). \tag{A2}$$

Thus,

$$P[V(\mathbf{A}) \geq v] \leq P\left(n^{-1} \sum_{j=1}^{n} A_{ij} \geq v \quad \text{for some } i = 1, \ldots, m\right), \tag{A3}$$

which immediately yields inequality (A1a). The inequality (A1b) follows by an analogous argument or as a consequence of (A1a) and of $V(-\mathbf{A}^T) = -V(\mathbf{A})$.

Proof of theorem 1.—Defining S_k as $X_1 + \ldots + X_k$, where the X_i's are i.i.d. and equidistributed with X, we have from inequalities (A1) that

$$P(|V_{mn}| \geq \epsilon) \leq m P(n^{-1} S_n \geq \epsilon) + n P(m^{-1} S_m \leq -\epsilon). \tag{A4}$$

If for some $r > 1$, $E(|X|^r) < \infty$, it follows (see, e.g., Petrov 1975, p. 286, theorem 28) that

$$P(j^{-1}|S_j| \geq \epsilon) = o(j^{-r+1}). \tag{A5}$$

Petrov (1975, p. 324) gave credit for a stronger result (his theorem 27) to Baum and Katz (1965).

If $E(e^{tX}) < \infty$ for $|t| < H$, it is a standard large-deviation result, a simple consequence of a more sophisticated result of Petrov (1975, p. 54, theorem 16 and lemma 5), that for $\epsilon > 0$,

$$P(j^{-1}|S_j| > \epsilon) = O(e^{-Cj}) \tag{A6}$$

for some $C = C(\epsilon) > 0$. The convergence in probability results follows easily from expressions (A4)–(A6), and almost sure convergence then follows from the Borel-Cantelli lemma when $\Sigma_k\, P(|V_k| \geq \epsilon) < \infty$.

Theorem 1 can be extended to A_{ij}'s that are independent (but not necessarily identically distributed) in j for fixed i and in i for fixed j by estimating the right sides of inequalities (A1) using known results about sums of independent random variables. For example, the

estimate (A6) can be replaced by one given by Petrov (1975, p. 288, a result credited to Baum et al. 1962).

Each assumption of the form $E(|X|^r) < \infty$ can be weakened to $P(|X| > x) = o(x^{-r})$ by using Petrov's theorem 27 in the proof rather than his theorem 28.

The estimates (A5) and (A6) are essentially refinements of Chebyshev's inequality (see Petrov 1975). In the case of nonindependent variables, one may try to use some variant of Chebyshev's inequality to estimate the right-hand side of inequalities (A1). For example, let

$$G_k(t) = \max_{i \le m_k} \left\{ n_k^{-1} \log \mathrm{E}\left[\exp\left(t \sum_{j=1}^{n_k} A_{ij} \right) \right] \right\}$$

$$G(t) = \limsup_{k \to \infty} G_k(t) .$$

Now the right side of inequality (A1a) is bounded by

$$\sum_{i=1}^{m_k} \exp(-n_k v t) \, \mathrm{E}\left[\exp\left(t \sum_{j=1}^{n_k} A_{ij} \right) \right] \le m_k \exp\{ n_k [G_k(t) - vt] \} .$$

Suppose that $G(t)$ is finite for t in some interval $[0, t_0)$ and $G(t)/t \to 0$ as $t \to 0+$. Then, for any $\epsilon > 0$, we may first choose t so small that $G(t)/t < \epsilon/2$ and then choose k so large that $G_k(t) \le G(t) + \epsilon t/4$. With these choices, we have

$$P[V_k(A) \ge \epsilon] \le m_k \exp[n_k(-\epsilon t/4)] .$$

Thus, $\limsup V_k(A) \le 0$ almost surely if $m_k = O(e^{cn_k})$ for every $c > 0$. Similar results can be stated for $P[V_k(A) \le -\epsilon]$. Such large-deviation arguments for sums of dependent variables originate in the statistical-mechanics literature (e.g., Lanford 1973; Newman 1979) and have been formulated in a general probabilistic context by Ellis (1984, 1985).

The basic ideas of theorem 1 and proposition 2 are contained in the papers of Prékopa (1972, theorems 1, 2) and Kabe (1983, eqs. 52, 55). However, since we assume i.i.d. matrix elements with a distribution independent of m and n, rather than merely independent entries with a distribution that may depend on m and n, we are able to show that when m and n grow proportionally, then the value converges in probability to zero, assuming only that the matrix elements have finite second moments rather than finite and uniformly bounded fourth moments. We are able to prove that the value converges almost surely assuming only finite moments of order $3 + \epsilon$ for any $\epsilon > 0$, rather than finite moments of order 8.

Theorem 3.—Suppose that the A_{ij}'s ($i, j = 1, 2, \ldots$) share the distribution of a fixed random variable X. If, for some $\epsilon > 0$, $c_+ = P(X > \epsilon) > 0$ and

$$\limsup_{k \to \infty} (n_k / \log m_k) < 1/|\log c_+| , \tag{A7}$$

then almost surely (and in probability) $\liminf_{k \to \infty} V_k \ge \epsilon$. If, for some $\epsilon > 0$, $c_- = P(X \le -\epsilon) > 0$ and

$$\limsup_{k \to \infty} (m_k / \log n_k) < 1/|\log c_-| , \tag{A8}$$

then almost surely (and in probability) $\limsup_{k \to \infty} V_k \le -\epsilon$.

The proof of theorem 3 is based on the following proposition, which is restricted to independent A_{ij}'s.

Proposition 4.—For a random $m \times n$ real matrix $\mathbf{A}$ with independent entries and any real c, $V(\mathbf{A})$, defined as the V_{mn} of equation (1), satisfies

$$P[V(\mathbf{A}) \ge c] \ge 1 - \exp\left[-\sum_{i=1}^{m} \prod_{j=1}^{n} P(A_{ij} \ge c) \right] , \tag{A9a}$$

$$P[V(\mathbf{A}) \le c] \ge 1 - \exp\left[-\sum_{j=1}^{n} \prod_{i=1}^{m} P(A_{ij} \le c) \right] . \tag{A9b}$$

Proof of proposition 4.—By using the middle expression of equation (1) and minimizing only over vectors $\mathbf{x}$ with a single nonzero component, it follows that

$$V(\mathbf{A}) \geq \min_{\mathbf{y}} \max_i \sum_{j=1}^{n} A_{ij} y_j \geq \min_{\mathbf{y}} \max_i \min_j A_{ij} = \max_i \min_j A_{ij}. \tag{A10}$$

The inequality (A9a) is then obtained as follows:

$$\begin{aligned} \mathrm{P}[V(\mathbf{A}) \geq c] &\geq \mathrm{P}(\max_i \min_j A_{ij} \geq c) = 1 - \mathrm{P}(\max_i \min_j A_{ij} < c) \\ &= 1 - \prod_i \mathrm{P}(\min_j A_{ij} < c) = 1 - \prod_i [1 - \mathrm{P}(\min_j A_{ij} \geq c)] \\ &\geq 1 - \exp\Big[-\sum_i \mathrm{P}(\min_j A_{ij} \geq c)\Big] \\ &= 1 - \exp\Big[-\sum_i \prod_j \mathrm{P}(A_{ij} \geq c)\Big], \end{aligned}$$

where the second inequality is a consequence of the elementary estimate $1 - \alpha < e^{-\alpha}$ for $\alpha > 0$. The inequality (A9b) follows by an analogous argument or as a consequence of (A9a) and of $V(-\mathbf{A}^{\mathrm{T}}) = -V(\mathbf{A})$.

Proof of theorem 3.—Since the A_{ij}'s are equidistributed with X, we have (from A9a) that

$$\mathrm{P}(V_k < \epsilon) \leq \exp\{-m_k[\mathrm{P}(X \geq \epsilon)]^{n_k}\}. \tag{A11}$$

The assumption (A7) implies that, for some $\delta > 0$,

$$\mathrm{P}(V_k < \epsilon) \leq \exp[-\exp(\delta \log m_k)] \leq \exp(-m_k^{\delta}). \tag{A12}$$

Assumption (A7) and the fact that $\max(m_{k+1} - m_k, n_{k+1} - n_k) > 1$ imply that $k = \mathrm{O}(m_k)$; thus, we have from inequalities (A12) that $\Sigma_k \mathrm{P}(V_k < \epsilon) < \infty$. By the Borel-Cantelli lemma, almost surely $\liminf_{k\to\infty} V_k \geq \epsilon$. The proof that inequality (A8) implies $\limsup_{k\to\infty} V_k \leq -\epsilon$ almost surely is obtained analogously or by using the already obtained result and $V(-\mathbf{A}^{\mathrm{T}}) = -V(\mathbf{A})$. This proves the theorem.

Suppose that X has a continuous symmetric distribution. Then, as the ϵ of theorem 3 approaches zero, the c_+ approaches ½. It follows that if m_k grows like $(2 + \delta)^{n_k}$ for some $\delta > 0$, in the sense that

$$\lim_{k\to\infty} (\log m_k)/n_k > \log 2, \tag{A13}$$

then for some $\epsilon' > 0$, almost surely $\liminf V_k \geq \epsilon'$. If X in addition has a finite moment-generating function, as in theorem 1, then it can be proved that the $C(\epsilon)$ of equation (A6) may be made arbitrarily large by taking ϵ arbitrarily large. This can be demonstrated by using the formula for $\Gamma(\epsilon)$ (which replaces $C(\epsilon)$) given below, which shows, under the assumptions of this paragraph, that $C(\epsilon)$ is even, positive, and convex and $C(\epsilon)$ approaches infinity as ϵ approaches infinity. It follows by the arguments used to prove theorem 1 that if

$$\lim_{k\to\infty} (\log m_k)/n_k < \infty, \tag{A14}$$

then for some sufficiently large $b < \infty$, $\limsup V_k \leq b$ almost surely. It thus seems that if inequalities (A13) and (A14) are both valid, then V_k should have some limiting distribution on the positive half line (actually supported on $[\epsilon, b]$). It is not clear whether this distribution should be nondegenerate. Our arguments do not guarantee that any limit actually exists, but since the probability is restricted asymptotically to a finite interval, various subsequences do have limits.

Suppose X has zero mean and a finite moment-generating function as in theorem 1. Suppose further that $\lim_{k\to\infty} m_k/n_k$ exists and is neither zero nor infinity. A more precise

version of equation (A6), which is a standard large-deviation result, is a pair of equations (see, e.g., Ellis 1985, theorem II.4.1):

$$P(j^{-1}S_j \geq \epsilon) \leq \exp[-j\Gamma(\epsilon)],$$

$$P(j^{-1}S_j \leq -\epsilon) \leq \exp[-j\Gamma(-\epsilon)],$$

where

$$\Gamma(\epsilon) = -\inf_{-\infty<t<\infty} [\log E(e^{tX}) - \epsilon t].$$

This $\Gamma(\epsilon)$ may be expanded about $\epsilon = 0$:

$$\Gamma(\epsilon) = (2\sigma^2)^{-1}\epsilon^2 + O(\epsilon^3)$$

as $\epsilon \to 0$, where σ^2 is the variance of X. Combining these results with inequality (A4) shows that there is some constant $K < \infty$ such that if

$$\epsilon_k \geq K[(\log k)/k]^{1/2}$$

then almost surely $V_k \leq \epsilon_k$ for sufficiently large k. In other words, under all the above assumptions, almost surely

$$\lim \sup_{k\to\infty} (k/\log k)^{1/2} V_k < \infty.$$

An interesting related open problem is to find some ϵ_k so that V_k/ϵ_k has a limit in distribution that is neither zero nor infinite and to determine the nature of the limiting distribution. Numerical results of Faris and Maier (1987) suggest that $\epsilon_k = 1/k$.

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