Host-Parasite Co-evolution and Optimal Mutation Rates for Semi-conservative Quasispecies

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In this paper, we extend a model of host-parasite co-evolution to incorporate the semi-conservative nature of DNA replication for both the host and the parasite. We find that the optimal mutation rate for the semi-conservative and conservative hosts converge for realistic genome lengths, thus maintaining the admirable agreement between theory and experiment found previously for the conservative model and justifying the conservative approximation in some cases. We demonstrate that, while the optimal mutation rate for a conservative and semi-conservative parasite interacting with a given immune system is similar to that of a conservative parasite, the properties away from this optimum differ significantly. We suspect that this difference, coupled with the requirement that a parasite optimize survival in a range of viable hosts, may help explain why semi-conservative viruses are known to have significantly lower mutation rates than their conservative counterparts.

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I. INTRODUCTION

Introduced over 30 years ago, the quasispecies model of evolution\cite{2,3,4} has provided an invaluable tool for the study of complex evolutionary behaviors. In the model, a fitness landscape is introduced, which accounts, often in a highly approximate manner, for the complex interplay between genotype, phenotype and environment by assigning a relative fitness for each genomic sequence (and thus associating phenotype with genotype, an approximation that must be treated with care). Through the consideration of numerous individually mutating copies of a genome, evolutionary systems can be studied analytically and numerically on these fitness landscapes, which has provided enormous insight into the process of evolution and the nature of mutation rates in real biological systems. In particular, it was found that a phase transition (known as the “error catastrophe”) occurs as the mutation rate increases, and a marked crossover can be observed from the existence of a quasispecies (wherein most individuals in the population contain genomes close to a fitness peak) to a near-random walk in genome space with no discernible quasispecies present\cite{1,2}.

The vast majority of the literature on the quasispecies model involve studies of asymptotic behavior on numerous stationary landscapes\cite{3,4,5,6}. This corresponds to a situation where static environmental conditions are considered to be the dominant evolutionary pressure on a species. However, this picture fails to describe the cornucopia of evolutionary pressures in nature. Many organisms, parasites, survive through the detrimental use of host biochemical processes. The parasite requires the host to live. The host survives better if it can avoid or destroy the parasite, providing an intriguing scenario: the host must evolve to defeat the parasite and the parasite must evolve to evade the host’s defenses. This creates a non-linear feedback cycle as both species scour a time-dependent fitness landscape that changes as the other species mutates.

Parasites are ubiquitous in nature, ranging from the microscopic (e.g. viruses, bacteria, protozoa) to fungi, helminths and arthropods. The interaction between parasites and hosts is very complex, with parasites exhibiting multistage life cycles, inert phases, and the use of multiple intermediate hosts, while hosts employ a wide variety of behavioral and immune defenses. This ongoing struggle has been well documented in mammals, birds, fish, bacteria and other organisms.

Recent work on time-dependent quasispecies landscapes\cite{6,7,8} has allowed for the study of a simple model of co-evolution by Kamp and Bornholdt\cite{9}, discussed in detail in Section III. They derived a parameter-independent expression for the optimal mutation rate for a host genome, which compared admirably with experimental results on B-cell mutation rates\cite{10}. An expression was also derived for optimal viral mutation rates\cite{10}, which, although dependent on the parameters of the model, explained numerous phenomena including the constancy of mutation rates within a viral class. However, this model considers the interaction only between a conservatively replicating parasite and host.

In its conservative formulation, the quasispecies model considers single stranded genomes that produce multiple copies of itself, each possessing a set of point mutations, while the original genome is conserved. While this model is obviously applicable to numerous RNA-based viruses, the vast majority of organisms, including many viruses and other parasites, store genetic information in double stranded DNA. DNA replicates semi-conservatively through a series of steps discussed in Section II. In a recent work, Tannenbaum et. al\cite{11} reformulated the quasispecies model to accurately represent semi-conservative systems, which were found to display fundamentally different behavior than conservative systems with respect to the error catastrophe in the infinite time limit on a static landscape. Thus, to properly model the co-evolution of a parasite and its host, the host system must replicate semi-conservatively, while the parasite can be modeled as...
either conservative, as, in the case of many riboviruses, or semi-conservative, as by many lysogenic double stranded DNA viruses or higher parasites. Retroviruses, such as HIV, likely display characteristics of both modes of replication, as do immune systems that undergo somatic hypermutation.

In this paper, we extend Kamp and Bornholdt’s model of co-evolution to the case of a semi-conservative host interacting with either a conservative or semi-conservative parasite. We consider the optimal behavior for both the host and parasite, and demonstrate the similarities and differences between the conservative and semi-conservative models.

The paper is organized as follows: in Section II we present the quasispecies model and its extension to semi-conservative replication. In Section III we discuss the model of host-parasite co-evolution for both conservative and semi-conservative organisms. Section IV presents the results and discussion and Section V presents our conclusions.

II. THE QUASISPECIES MODEL

In this section, we present some necessary background on the conservative and semi-conservative quasispecies models for the purpose of a self-contained discussion. Greater detail may be found in the original papers.

A. Conservative Replication

The quasispecies model studies the evolution of a population of organisms, each with a genome \( \phi = s_1s_2\cdots s_n \), where each \( s_i \) represents a “letter” chosen from an alphabet of size \( S \). Often, \( S \) is chosen to be two to model the pyrimidine and purine groups or four to model the nucleotides. Assuming first-order growth kinetics and associating phenotype with genotype (i.e. that the growth rate of an individual is directly determined by \( \phi \)), it can be shown that

\[
\frac{dx_\phi}{dt} = \sum_{\phi'} A(\phi') W(\phi, \phi') x_{\phi'} - f(t) x_\phi,
\]

where \( x_{\phi} \) denotes the fraction of the population with genome \( \phi \), \( A(\phi) \) represents the fitness, or growth rate, of sequence \( \phi \), \( W(\phi, \phi') \) is the likelihood of creating sequence \( \phi \) from \( \phi' \) by mutations, and \( f(t) = \sum_{\phi} A(\phi) x_{\phi} \) is the average fitness of the population, holding the population size constant and introducing competition. If only point mutations are allowed and a genome-independent mutation probability \( \epsilon \) is assumed, then \( W(\phi, \phi') \) can be written in terms of the genome length \( n \) and the number of bases at which \( \phi \) and \( \phi' \) differ, the Hamming distance \( HD(\phi, \phi') \), as

\[
W(\phi, \phi') = \left( \frac{\epsilon}{S-1} \right)^{HD(\phi, \phi')} (1-\epsilon)^{-HD(\phi, \phi')}.
\]

These equations can be greatly simplified in the case of a single fitness peak landscape, where a master sequence, \( \phi_0 \), has a fitness much greater than all other sequences. The rest of the genomes are assumed to be equally fit, which can be described by the growth rates

\[
A(\phi) = \begin{cases} \eta & \phi \neq \phi_0 \\ \sigma \eta & \phi = \phi_0 \end{cases}.
\]

The sequences can then be grouped into Hamming classes based on their distance from the master sequence by defining

\[
w_l = \sum_{\phi \in \{\phi | HD(\phi, \phi_0) = l\}} x_\phi
\]

and

\[
A(l) = A(\phi), \phi \in \{\phi | HD(\phi, \phi_0) = l\}.
\]

This reduces the problem from \( S^n \) dimensions to \( n+1 \) dimensions. If mutations that lead from higher to lower Hamming distances are ignored (an approximation that becomes exact as \( n \rightarrow \infty \)),

\[
\frac{dw_l}{dt} = \sum_{l'=0}^{l} \frac{(n-l')!}{(n-l)!} A(l') \left( \frac{\epsilon}{S-1} \right)^{l-l'} (1-\epsilon)^{n-(l-l')} w_{l'} - f(t) w_l,
\]

where \( f(t) = \sum_{l} A(l) w_l = \sigma w_0 + \eta (1-w_0) = (\sigma - \eta) w_0 + \eta \). Defining \( y_l = w_l \exp(\int_0^t f(s)ds) \) removes the non-linearity in these equations and the linear set of differential equations can be solved for any Hamming class. The solution for the master sequence is

\[
y_0(t) = y_0(0) e^{q^\sigma \epsilon t}
\]

and, for the first Hamming class,

\[
y_1(t) = y_0(0) n \left( \frac{(e^{q^\sigma \epsilon t} - e^{q^\sigma \eta t})(1-q)\sigma}{(S-1)(\sigma-\eta)q} \right),
\]

where \( q = 1-\epsilon \), a definition we shall use throughout the paper.

B. Semi-conservative Replication

In order to properly model a semi-conservative system, a double stranded molecule generated from an alphabet of size \( S \) must be considered, where each “letter” \( i \) uniquely pairs with \((i + S/2) \mod S\). DNA requires \( S = 4 \), where the letters can be assigned as \( A = 1, G = 2, T = 3, C = 4 \). A single DNA molecule of length \( n \) consists of a strand \( \phi = s_1s_2\cdots s_n \) and a complementary strand \( \overline{\phi} = \overline{s_1}\overline{s_2}\cdots \overline{s_n} \), where \( \overline{s} \) denotes the complement of \( s \). Hence, each DNA molecule may be represented by the pair \( \{\phi, \overline{\phi}\} \equiv \{\phi, \overline{\phi}\} \).
When a semi-conservative molecule replicates, it undergoes a three step process shown schematically in Fig. 1. First, each genome \{ϕ, ϕ\} unzips to form two single stranded genomes, ϕ and ϕ′. Each strand is then copied to produce two new pairs, \{ϕ, ϕ′\} and \{ϕ, ϕ′\}, where the primes denote the fact that the two fresh strands may contain replication errors. At this point, proofreading mechanisms can distinguish between the new and old strands and may fix all or some of the replication errors, which can be spotted by the fact that \(s_i' ≠ s_i\). All of these repair mechanisms are included in the base-independent error probability \(ε\). In the last step, the new and old strands become indistinguishable. Various maintenance enzymes repair the remaining mismatches, but cannot determine which of the strands ϕ and ϕ′ is the newly replicated strand. Hence, the repair is made in the new strand with 50% probability and in the old strand with 50% probability. The final result is that the original strand \{ϕ, ϕ\} is replicated to create two new strands, \{ϕ′′, ϕ′′\} and \{ϕ′′′, ϕ′′′\}.

The quasispecies equations for this system can be written as follows:

\[
\frac{dx_{\{\phi, \phi\}}}{dt} = \sum_{\{\phi', \phi'\}} A(\phi, \phi') x_{\{\phi', \phi'\}} (p(\phi', \phi, \phi) + p(\phi, \phi')) - A(\phi, \phi) + f(t)) x_{\{\phi, \phi\}}. \tag{9}
\]

where \(f(t) = \sum A(\phi, \phi) x_{\{\phi, \phi\}}\) and \(p(\phi', \phi, \phi)\) represents the probability that the 'unzipped strand' \(\phi'\) will produce the pair \(\{\phi, \phi\}\). To make these equations more useful, we can define \(A(\phi) = A(\phi, \phi)\) and \(x_{\phi} = \frac{1}{2} x_{\{\phi, \phi\}}\) if \(\phi ≠ \phi\) and \(x_{\phi} = x_{\{\phi, \phi\}}\) if \(\phi = \phi\). After some manipulation, we obtain

\[
\frac{dx_{\phi}}{dt} =
\]

\[
2 \sum_{\phi'} A(\phi') x_{\phi'} (\frac{\epsilon/2}{S-1}) H_D(\phi, \phi') (1 - \frac{\epsilon}{2})^{n-H_D(\phi, \phi')}

- (A(\phi) + f(t)) x_{\phi}, \tag{10}
\]

where \(f(t) = \sum A(\phi) x_{\phi}\).

We now turn our attention to semi-conservative replication on a single fitness peak landscape. This case is more complicated than for a conservative system, since viability genes often exist on both strands in nature. Hence, if there exists a sequence \(\phi_0\) with fitness \(σ\), it stands to reason that the sequence \(\phi_0\) should have fitness \(σ\) as well, effectively creating a double fitness peak landscape (this assumption is by no means fundamental to the work). However, noting that \(x_{\phi} = x_{\phi}\) for all times, both by definition and by conservation in Equation (10), this difficulty can be sidestepped. As long as \(n\) is not too small, the area around each fitness peak can be locally treated as a single fitness peak landscape as the two peaks are distant in sequence space. Hence, ignoring back mutations, the two master sequences obey the equations

\[
\frac{dw_i}{dt} = 2(1 - \epsilon/2)^n \sigma w_i - (\sigma + f(t)) w_i =
\]

\[
2(1 - \epsilon/2)^n \sigma w_i - (\sigma + f(t)) w_i \tag{11}
\]

\[
\frac{dw_0}{dt} = 2(1 - \epsilon/2)^n \sigma w_0 - \sum (\sigma + f(t)) w_0 =
\]

\[
2(1 - \epsilon/2)^n \sigma w_0 - \sum (\sigma + f(t)) w_0, \tag{12}
\]

where \(w_i\) represents the concentration of the \(i\)th Hamming class as before. Therefore, we can re-define the concentration of the master sequence to include both \(w_0\) and \(w_0\) and use equation (11) for the sum of the two. While this is not strictly necessary and has no effect on the results, it does reduce the bookkeeping, and the characteristics of the individual peaks can be obtained by simply dividing by two. A similar procedure yields

\[
\frac{dw_1}{dt} = 2(1 - \epsilon/2)^{n-1} (\frac{\epsilon/2}{S-1}) n \sigma w_0 +
\]

\[
2(1 - \epsilon/2)^n \eta w_1 - (\eta + f(t)) w_1, \tag{13}
\]
where we include sequences of Hamming distance one away from both master sequences. The definition \( y_i = w_i \exp(\int_0^t f(s)ds) \) once again removes the non-linearity. The solutions for the first two Hamming classes are

\[
y_0(t) = y_0(0)e^{\sigma(1-\epsilon/2)^n - \sigma} \tag{14}
\]

\[
y_1(t) = y_0(0)\left(\frac{\sigma(1-\epsilon/2)^{n-1}}{(S-1)(\sigma - \eta)(2(1-\epsilon/2)^{n-1})}\right) \times \left(e^{(2(1-\epsilon/2)^{n-1})t - \eta(2(1-\epsilon/2)^{n-1})t}\right) \tag{15}
\]

### III. HOST-PARASITE CO-EVOLUTION

Historically, the main focus of research on the quasispecies model has related to static and equilibrium properties of the system. A number of recent works, however, have explored the dynamics of the system under various conditions, which has allowed the study of the simple model of co-evolution described here. Following the work of Kamp and Bornholdt, we envision a population of host and parasite organisms, each described by a set of quasispecies equations. Ignoring the interspecies interaction, the immune and viral genomes, of length \( n_{is} \) and \( n_v \), respectively, evolve independently on a single fitness peak landscape, where the master sequences have fitness \( \sigma_{is} \gg \eta_{is} \) and \( \sigma_v \gg \eta_v \).

To model the deleterious effect of the immune system on the virus, the dominant immune genome imposes a large death rate \( \delta \) on the corresponding viral sequence. If this dominant immune genome matches the viral master sequence, the viral fitness peak will move to an arbitrary sequence of the first Hamming class. The viral quasispecies then adapts to this new fitness peak on a timescale \( \tau_v \), the time required for the population of the new master sequence to overtake that of the old. At this point, the immune system fitness peak adjusts to match the new viral peak, and adapts on a similarly defined timescale \( \tau_{is} \). Thus, through the iteration of these steps, the viral fitness peak scours sequence space in an attempt to avoid the immune system, which follows on its heels. Applying recent results on dynamic fitness landscapes, regions of stability can be defined for both the viral and immune quasispecies by determining a characteristic timescale for regrowth of a new master sequence. If the landscape moves slowly enough, the master sequence has time to regenerate to the master sequence concentrations reached before the peak shift and the species will survive for all time. If, however, the master sequence cannot regenerate rapidly enough, a second peak shift will occur before the new master sequence reaches the concentration held by the old master sequence before the first shift. The third master sequence cannot reach the levels of the second, and this continues until, eventually, there is no discernible master sequence in the population. For the conservative case, this can be stated rigorously by comparing the growth of a single member of the first Hamming class described by equation (8) with \( e^{\sigma\tau} \), the uninhibited growth of a random sequence far from the fitness peak (as mutations in and out of this sequence should cancel). Using equation (8) this ratio can be defined, for both the immune and viral quasispecies, as

\[
k \equiv \frac{w_1(\tau)}{w_1(0)} \equiv \frac{(e^{(q^\sigma-\eta)\tau} - e^{(q^\sigma-\eta)\tau})(1-q)\sigma}{(S-1)(\sigma-\eta)q}, \tag{16}
\]

where \( \tau \) is the lag time between peak shifts and the parameters \( \{q, \sigma, \cdots\} \) represent the parameters for either species. The quasispecies survives only when \( k \geq 1 \).

The last piece necessary to complete the co-evolution model, then, is the speed with which the landscape moves. By the definition of our model, \( \tau \) is the sum of the time required for the regeneration of the virus, \( \tau_v \), plus the time required for the regeneration of the immune system, \( \tau_{is} \). Hence, we must solve for \( \tau = \tau_{is} + \tau_v \) where

\[
e^{(q^v_{is} - \eta_v)\tau_v}w_{0,v}(\tau) = e^{(q^v_{0}\sigma_v\tau_v)w_{1,v}(\tau)/n} \tag{17}
\]

\[
e^{q^v_{is} \sigma_v \tau_is}w_{0,is}(\tau) = e^{(q^v_{0is} \sigma_{is} \tau_is)w_{1,is}(\tau)/n} \tag{18}
\]

This can be solved to obtain

\[
e^{(q^v_{is} - \eta_v)\tau_v}e^{q^v_0 \sigma_v \tau_v} = \frac{e^{q^v_0 \sigma_v \tau_v} - e^{q^v_{is} \sigma_v \tau_v}}{(S-1)(\sigma_v - \eta_v)q_v} \tag{19}
\]

\[
e^{q^v_{0is} \sigma_{is} \tau_{is}}e^{q^v_0 \sigma_v \tau_v} = \frac{e^{q^v_{0is} \sigma_{is} \tau_{is}} - e^{q^v_{0} \sigma_{is} \tau_{is}}(1-q_{is})\sigma_{is}}{(S-1)(\sigma_{is} - \eta_{is})q_{is}}, \tag{20}
\]

which yields, with the reasonable approximations that \( q \approx 1 \) and \( \sigma \gg \eta \) (the latter of which is used throughout the paper),

\[
\tau_v \approx -\frac{\ln(1-q_v)}{q_v(\sigma_v - \eta_v) + \delta} \tag{21}
\]

\[
\tau_{is} \approx -\frac{\ln(1-q_{is})}{q_{is}(\sigma_{is} - \eta_{is})} \tag{22}
\]

These equations can be applied to determine the optimal mutation rate for both the host and the parasite. The
host can minimize the region of viability for the parasite by evolving a mutation rate such that

\[
\frac{\partial \kappa_v}{\partial \epsilon_{is}} = 0,
\]

yielding

\[
\epsilon_{is} - 1 - n_v \epsilon_{is} \ln \left( \frac{\epsilon_{is}}{S - 1} \right) = 0.
\]

This equation has the nice quality of being independent of the parameters of the immune model, as well as the properties of the virus. The solution to this equation is shown in Fig. 2 and compared to the experimentally verified mutation rate for human B-cell receptors. This is discussed at length in section IV.

Optimizing the viral mutation rate requires solving for

\[
\frac{\partial \kappa_v}{\partial \epsilon_v} = 0
\]

of the form

\[
\ln \left( \frac{(1-\epsilon_v/2)^{n_v} - 1}{(1-\epsilon_v/2)^{n_v} - 1}(S-1) \right) = 0.
\]

FIG. 2: Optimal immune system mutation rate vs. \( n_{is} \).
The dashed lines represent experimental values for somatic hypermutation of B-cell complementary determining regions, adapted from[9].

We now proceed to find the optimal mutation rates for both organisms. Differentiating \( \kappa_v \) by \( \epsilon_{is} \) and setting the result to zero gives us a criterion for the optimal immune mutation rate,
This equation has all of the nice properties of Equation (24), defining an optimal mutation rate for any genome length, independent of the parameters of the system. The solution to this equation is plotted in Fig. 2, along with the conservative solution and the experimental range for observed rates per base pair per generation of somatic hypermutation in the complementary determining regions (CDR’s) found in B-cell antigen receptors.

To maximize the stability of the viral quasispecies we set \( \frac{\partial \kappa_v}{\partial \epsilon_v} = 0 \) as before. After a fair bit of work, we obtain an unwieldy expression omitted here in the interest of space. The expression simplifies immensely in the limit \( \delta \to \infty \), the limit of an ideally efficient immune system. In this limit,

\[
\frac{n_v \epsilon_v}{2(1 - 2(1 - \frac{\epsilon_v}{2}) n_v)^2} + \frac{n_v \sigma_v \epsilon_v (1 - \frac{\epsilon_v n_v}{2}) (\sigma_v - \eta_n) - 1}{1 - 2(1 - \frac{\epsilon_v}{2}) n_v} = 0.
\]  

(33)

The ideally efficient immune system is not an unreasonable approximation, as immune systems are highly efficient in destroying invaders once a suitable antibody is produced. The full expression as well as the above limiting form are dependent on both the parameters of the model and the properties of the immune system as in the conservative case. The solution of the full expression for a particular set of parameters is shown in Fig. 3.

### IV. RESULTS AND DISCUSSION

Given the fundamental differences between semi-conservative and conservative modes of replication, the most striking aspect of Fig. 2 and 3 is the similarity between the conservative and semi-conservative optimal mutation rates at high \( n \), particularly for the viral species. This is most easily understood by noting that, as \( (1 - \epsilon/2)^n \to 1 \) for any semi-conservatively replicating organism, the probability that a mutation will be found in the original strands after replication vanishes. Hence, in this limit, semi-conservative and conservative replication are expected to mimic each other. This parameter is shown in Fig. 4 for the optimal viral and immune mutation rates. Clearly, with the exception of small immune genomes, the conservative system can be used as a good approximation for semi-conservative replication. It is important to note, however, that this knowledge could not have been extracted from the data for the conservative system. A large value for \( (1 - \epsilon/2)^n \) in the conserva-

![FIG. 3: Optimal viral mutation rate vs. \( n_v \) for a conservative and semi-conservative virus interacting with a semi-conservative immune system. \( n_{is} = 100, \sigma_{is} = \sigma_v = 100, \eta_{is} = \eta_v = 1, \delta = 200, \epsilon_{is} = 0.001 \).](image)

![FIG. 4: \((1 - \epsilon/2)^n\) for the optimal mutation rate of a semi-conservative immune system and virus. This parameter can be used as a measure of the “conservativeness” of a semi-conservative system. \( \sigma_{is} = \sigma_v = 100, \eta_{is} = \eta_v = 1, \delta = 200, \epsilon_{is} = 0.001 \).](image)
A conservative calculation is required. To justify the use of a conservative model, and the full semi-conservative calculation is required.

Equation (24) remains dependent on the parameters of the model, but general trends are obvious when biologically reasonable parameters are employed. While the extremal behavior of Equation (27) and (30) differs little from Equation (16) for genome lengths that are not too small, the behavior away from the maxima differs greatly. Fig. 5 displays $\kappa_v$ vs. $\epsilon_v$ for a given set of parameters for both the conservative and semi-conservative models. It is immediately clear that, while the two models co-occur at small $\epsilon$ (with a slightly higher peak height for either species for some parameters), their behavior differs greatly otherwise, with the semi-conservative model displaying a more drastic dropoff in viability as $\epsilon$ increases, true for all biologically reasonable parameters studied. The parameters shown in Fig. 5 were chosen as a representative, rather than extreme, example of this behavior. The importance of this result is best understood in light of the evolutionary pressures one would expect a viral population to encounter. The independence of Equation (32) from the properties of the viral system suggests that there exists an optimal mutation rate for an immune receptor independent of the qualities of the parasite against which it is defending. Thus, it is reasonable to expect (within the limitations imposed by additional evolutionary pressures, such as the need to distinguish between self and foreign antigens) an immune receptor to evolve this mutation rate nearly exactly. However, in the viral case, the optimal mutation rate depends strongly on the nature of the immune system it is attacking. Thus, the virus must evolve the mutation rate that maximizes its overall viability against the range of immune systems it is likely to infect, including both inter- and intra-species viability. The mutation rate that optimizes defense against one host may be a poor choice for another, and the virus must find the mutation rate that affords the best protection against all hosts, even if this is not the best mutation rate for evading any particular immune system. Such a compromise clearly involves the behavior of $\kappa_v$ over a wide range of $\epsilon$, rather than just at the maximum. One would therefore expect the more drastic dropoff at higher $\epsilon$ to force the semi-conservative virus to develop a lower mutation rate so as to increase its viability against immune systems that lower the $\epsilon_v$ with the maximal value of $\partial \kappa_v / \partial \epsilon_v$. Quantifying this statement requires an intelligent estimate of the distribution of immune properties, a subject of future research. Qualitatively, this agrees well with the experimentally verified fact that semi-conservative viruses display significantly lower mutation rates than their conservative counterparts.

FIG. 5: $\kappa_v$ vs. $\epsilon_v$ for a conservative and semi-conservative virus interacting with a semi-conservative immune system. $n_{is} = n_v = 100, \sigma_{is} = \sigma_v = 100, \eta_{is} = \eta_v = 1, \delta = 200, \epsilon_{is} = 0.001$.

In this paper, we have extended Kamp and Bornholdt’s model of co-evolution to incorporate the semi-conservative nature of DNA replication for both species. A parameter-independent expression was derived for the optimal mutation rate of an immune receptor, which agrees well with experimental data. Convergence of the conservative and semi-conservative results was demonstrated for realistic genome sizes, justifying the use of a conservative model in this case.

Optimizing the stability of the immune species yielded a maximum that coincides with the conservative model for realistic genome sizes. A similar correspondence exists for the virus, albeit with a dependence on the parameters of the model. Away from the maximum, the conservative and semi-conservative models display different behaviors that provides a possible explanation for the high mutation rates found in conservative viruses. It is always dangerous to extrapolate from a simplified model of this kind to the complex systems found in nature. A true virus and immune system must contend with innumerable evolutionary pressures, biological, chemical and otherwise, such as the requirement that T-cells recognize and do not bind host proteins. The work represented in this paper describes a generalized model which we feel captures the robust qualitative features of host-parasite coevolution, providing insight into the complex workings of nature.

V. CONCLUSIONS

In this paper, we have extended Kamp and Bornholdt’s model of co-evolution to incorporate the semi-conservative nature of DNA replication for both species. A parameter-independent expression was derived for the optimal mutation rate of an immune receptor, which agrees well with experimental data. Convergence of the conservative and semi-conservative results was demonstrated for realistic genome sizes, justifying the use of a conservative model in this case.

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