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Self-organizing behavior in a lattice model for co-evolution of virus and immune systems

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We propose a lattice model for the co-evolution of a virus population and an adaptive immune system. We show that, under some natural assumptions, both probability distribution of the virus population and the distribution of activity of the immune system tend during the evolution to a self-organized critical state.

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I. INTRODUCTION

It is a routine practice since the seminal work by Eigen [1] to use kinetic equations on complex graphs for description of the dynamics of competing macromolecular organisms [2–4]. The quasispecies model introduced by Eigen and Schuster [5] describes the mutation within a given genome space visualized as a graph with sites representing different types of organisms and bonds connecting neighboring sites which are mutants with closest biological affinity. Usually, the rates of replication for each site are assumed to be constant in time, so the system evolves to the relatively stable quasispecies on a static fitness landscape [6].

Recently, some extensions to dynamic fitness landscape have been made [7,8]. The height of the fitness peak can change in time without changing its space location [7] or, vice versa, can move in the sequence space [8]. The dynamic fitness assumes an interaction of the evolving system with an adaptive environment. The closest example is the evolution of viruses in the presence of an adaptive immune system [9–11]. A virus activates the immune system which forces the virus to evolve and the further viral evolution strongly depends on the state of the relaxing immune system. Another example of competing behavior is known as the "Red Queen effect:" a species which does not change attracts parasites and predators. If it is itself a predator, its prey develops an efficient defense strategy. The way to avoid these drawbacks is to constantly change in changing circumstances [12,13].

Effects of the interaction between an evolving system and a changing environment have been considered in several works [14–17] where the evolving system has been taken as a simple random walk on a graph and the changing environment as a set of site variables depending on the presence of the walker at a given site. Usually, the site variable measures the degree to which a walker in the past has affected the site [16]. Leaving the site, the walker allows the site variable to relax with a characteristic time. Each new step the walker takes is to that site in its neighborhood which has the smallest value of the site variable.

To adapt these ideas to the viral evolution, we assume that at each discrete moment of time, the population of viruses has a single peaked probability distribution located at one of the sites of a graph. The evolution of the distribution is reduced in this approximation to jumps between neighboring sites of the graph. In the context of the quasispecies evolution model this implies that a fitness peak moves in the sequence space by jumps and the time interval between jumps is long enough for the virus population to reach a local stationary state.

In the absence of immune system, the trajectory of the peak of virus distribution is just a simple random walk on the graph provided that all sites of the graph outside of the peak of fitness are equivalent. The presence of immune system changes this picture drastically. The activity of the immune system is a function of coordinates of sites and time passed from the last visit of the given site by the peak of the virus distribution.

We assume that activity at a given site grows rapidly when the peak of the virus distribution comes into this site and relaxes slowly when the peak leaves this site. As a result, the immune system "remembers" all visits and its activity at each site is a monotonically decreasing function of time since the last visit of this site. These assumptions are enough to formulate the model.

Given a graph G whose vertices represent possible states of virus population, we associate the peak of virus distribution at given moment of discrete time with the position of the random walker at the given site. The activity of the immune system at the initial moment of time is described by a set of random numbers uniformly distributed on an interval. Starting a motion, the random walker located at a site chooses among its nearest neighbors the site where activity of the immune system is minimal and jumps there. During the initial period, the motion of the random walker is mostly random. The next period is characterized by the appearance of more sites visited before among nearest neighbors of each site. Using the rule of monotonic decrease of activity, the walker chooses the site visited at the earliest moment of time. During this period, the motion of the walker becomes more deterministic as the concentration of visited sites grows. At the last stage of evolution, when all sites of the

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graph are already visited at least once, the walk becomes purely deterministic.

We will show below, that the motion of the walker at the last stage converges asymptotically to a cycle which passes all sites of the graph and has a property of long-range correlations. Considering a specific graph (the Manhattan lattice), we will prove that the limiting cycle is a Hamiltonian walk, that is the closed path which passes all sites of the graph exactly once. The elements of the Hamiltonian walk are strongly correlated objects. The long-range correlations in the trajectory of the walk mean simultaneously the same correlations in the environment, namely, the correlation of activity of the immune system at two sites separated by the Euclidean distance r decays as a power law of r.

This paper is organized as follows. In Sec. II we give a formal definition of the model on an arbitrary graph. In Sec. III, we use the Manhattan lattice as the simplest graph where the scaling behavior of the model can be demonstrated explicitly. This section contains the proof of the theorem that the limiting cycle on the Manhattan lattice is the Hamiltonian walk. In Sec. IV we prove the equivalence of our model and the Eulerian walk model for the particular case of the Manhattan lattice. Asymptotic properties of the model on an infinite lattice are considered in Sec. V. The main results are summarized and discussed in Sec. VI.

II. MODEL

The model is defined for a general one-component graph G consisting of N sites $i=1,2,3,\ldots,N$ and bonds between some of them. The bond connecting sites i and j is denoted by (i,j) and we say that sites i and j are adjacent. The set of all sites adjacent to site i is denoted by $a(i)$ and the number of sites belonging to $a(i)$ is called the degree, $\deg(i)$, of the site i in the graph G.

The walk on the graph G is defined as a sequence $i_0,i_1,i_2,\ldots,i_P$ of sites visited at discrete moments of time $t=0,1,2,\ldots,P$ provided that i_k and i_{k+1} are adjacent sites for all $0\leqslant k<P$. The motion of the walker on a graph G corresponds to the evolution of the single-peaked distribution of a virus population.

The immune system is characterized by the set of numbers $\xi_i(t)$ where ξ_i is activity at the site i measured by positive numbers; the indices $1\leqslant i\leqslant N$ are sites of the graph and arguments $0\leqslant t\leqslant P$ are discrete moments of time. We assume for definiteness that the activities $\xi_i(0)$, $i=1,2,\ldots,N$ at the initial moment of time are independent random numbers uniformly distributed on the interval $[0, 1]$.

To describe the reaction of the immune system on the moving peak of distribution of the virus population, we should define a law which governs both the increase and decrease of activity when the walker comes in or leaves a given site. A natural form of the time dependence would be

$$\xi_i(t)=Ae^{-(t-t_n)/\tau},\quad t_n\leqslant t<t_{n+1},\quad n\geqslant 1 \tag{1}$$

and

$$\xi_i(t)=\xi_i(0),\quad 0\leqslant t<t_1 \tag{2}$$

where $t_1,t_2,\ldots$ are moments of successive visits of the site i by the walker. Equations (1) and (2) imply that the activity of the immune system grows rapidly up to a maximal level A when the walker hits the site i and relaxes with a characteristic time τ until the next visit. However, if we are interested only in relative activities at different sites, it is more convenient for computational purposes to use the function

$$\xi_i(t)=\xi_i(0)+t_{\max}, \tag{3}$$

where $t_{\max}\leqslant t$ is the maximal moment of time when the walker has visited site i before the moment t. One can verify easily that the ordering of sites by increasing activities given by Eqs. (1) and (2) coincides with that obtained by Eq. (3).

The walk interacting with the environment can be defined now as follows. Given the position of the walk i_k at time k, consider the set $a(i_k)$ of $\deg(i_k)$ sites. Let ξ_j^* be the minimal value of activity among the sites belonging to $a(i_k)$, $j\in a(i_k)$. Then, the next point visited by the walk will be $i_{k+1}=j$.

The rule of continuation of the walk mimics behavior of the virus population interacting with the adaptive immune system. Indeed, the peak of the virus distribution (i.e., the walker in our model) moves always in the direction of minimal activity of the immune system. At each moment of time, the walker sees the set $a(i_k)$ of target sites for the next step. If there are $n<\deg(i_k)$ sites which are not visited yet the minimal activity can be found among them with equal probability. If all sites in $a(i_k)$ are already visited at least once, Eq. (1) says that the walker will choose the site which is visited earlier than others and where the activity of immune system is maximally relaxed.

An intention of the walker to avoid the sites it visited before allows one to think about the model as a kind of the self-avoiding walk (SAW). However, the self-repulsion property relaxes with time passed since the last visit, so we can coin the model as the relaxing self-avoiding walk (RSAW).

As it was noted in the Introduction, the walk we defined is random (self-avoiding) at the initial stage of the process and deterministic at the stage when all sites are visited. Our basic aim below will be to describe the asymptotical properties of the walk in the large-time limit.

For any finite graph G the deterministic process enters into a limiting cycle. What are the properties of this cycle? To answer this question, one can write an elementary computer program and construct the limiting cycle for arbitrary initial conditions. A moment's reflection shows that a possible candidate for the limiting cycle is the Hamiltonian walk [18] if the graph G is the Hamiltonian one. Indeed, each step of the Hamiltonian walk from the site $i\in G$ obeys the rule that it is directed to a site which was visited earlier than others nearest neighbors of i.

However, if one continues the computer experiment, one will find that more complicated cycles are possible and a typical limiting cycle is a collection of self-avoiding loops densely packed on the graph and connected by "bridges" where the Hamiltonian property vanishes. Bearing in mind that our goal is a demonstration of the phenomenon of self-

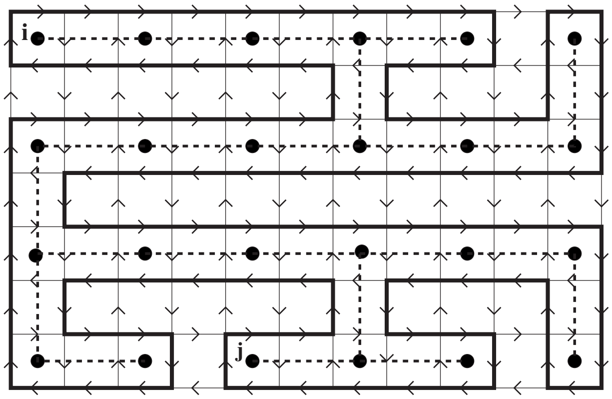

FIG. 1. The 8×12 Manhattan lattice $\mathcal{M}$ and the unoriented square lattice $\mathcal{L}$ (solid dots), the sites of which are the centers of clockwise plaquettes of $\mathcal{M}$. A clockwise Hamiltonian circuit on $\mathcal{M}$ (bold lines) encircles in a one-to-one correspondence a spanning tree on $\mathcal{L}$ (bold dashed lines).

organized behavior in an immune system, we must choose a graph where this phenomenon is most transparent and then use the principle of universality to extend our conclusions to other systems.

III. MANHATTAN LATTICE

Consider a simplest graph, the Manhattan lattice $\mathcal{M}$ (see Fig. 1), where the critical properties of the model can be demonstrated explicitly. The Manhattan lattice is a directed square lattice with a network of alternating "one-way streets" and "avenues" (similar to the Manhattan area of New York City), so that neighboring parallel bonds have opposite directions. We take here free boundary conditions, and the possibility of having the Hamiltonian circuit on the Manhattan lattice of $M\times N$ sites requires M and N to be even. For the even-even lattice, the Manhattan orientation must be properly chosen for closed Hamiltonian walks to be possible. The lattice external perimeter must form a closed oriented loop (Fig. 1).

The walker starts motion at arbitrary site i_0 and leaves it for the nearest neighbor site with lowest activity. The motion proceeds until after time T the walker returns to site i_0 for the first time, $i_T=i_0$. We must prove that the next period T' needed to return to i_0 will be $T'\geqslant T$, and eventually, the process converges to the Hamiltonian walk.

Theorem. The limiting cycle of the RSAW on the Manhattan lattice is the Hamiltonian walk.

Proof. Let us show first that no other site in the path $i_0, i_1, \ldots, i_T$ is visited twice except i_0. Assume the contrary and suppose that during the T steps the site i_j, reached from the point i_{j-1} is the first site which is visited twice. Let i_k be another neighboring site from which one can reach i_j. Due to the structure of the Manhattan lattice, there exists only one site i_m, besides i_j to which one can go from i_{j-1} and i_k (see Fig. 2). It is clear that the walker cannot visit site i_j from site i_{j-1} for the second time, since in that case the site i_{j-1} (but not i_j as supposed) become the first site which the walker visited twice. The only remaining possibility is to visit site i_j from site i_k. Site i_j can be reached from site i_{j-1} only if site i_m has been visited after the walker visited site i_j. Otherwise, the walker should visit site i_m instead of site i_j by the walking rules. But site i_m can be reached only from site i_{j-1} or site i_k, which is impossible, since in that case either i_{j-1} or i_k are the first sites that the walker visited twice. Thus, we have shown that to visit site i_j twice, one should first visit site i_{j-1} or i_k twice. This contradicts our assumption that site i_j was taken to be the first site visited twice. Thus all sites i_j, $j=0,1,2,\ldots,T-1$ are distinct.

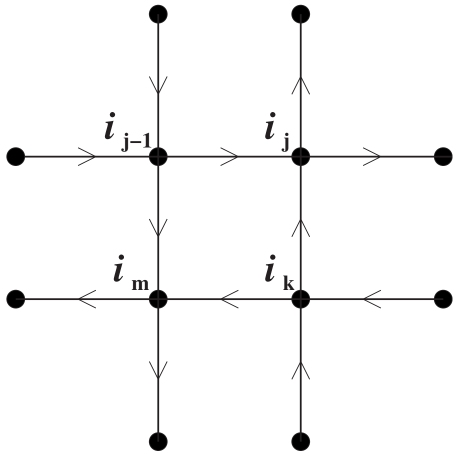

FIG. 2. To visit site i_j twice, a walker should first visit site i_{j-1} or i_k twice (see text).

If every site in $\mathcal{M}$ is visited, we have a Hamiltonian walk with $T=N$. If not, we will continue the walk. Using the rule of monotonic decrease of activity, the walker chooses a unvisited site or a site visited at the earliest moment of time. Let us consider the path $i_1 i_2 \cdots i_{T-1} i_T$. If $i_{T+1}=i_1$ we have another circuit of length T. We shift the beginning of the path until we reach a site x_t such that $i_{T+t}\neq i_t$. Such $t<T$ exists as long as there are points which have not been visited. Let T' be the first time when $i_{T'+t}=i_t$. Clearly $T'>T$. Iterating this process, we get self-avoiding loops of increasing lengths and finally we will get a Hamiltonian walk with the period $T=N$. This completes the proof. Thus, we have shown that the motion of the walker at the last stage converges asymptotically to a Hamiltonian walk which passes all sites of the graph.

The appearance of the Hamiltonian walk implies emergence of long-range correlations both in activity of the immune system and in the trajectory of the single-peaked distribution of the virus population. To see this, we introduce another square lattice $\mathcal{L}$ [19]. If we put a point in the center of each square oriented clockwise on lattice $\mathcal{M}$, and connect all pairs of nearest neighbors, we get a unoriented square lattice $\mathcal{L}$, whose cell is 2 times larger than that of $\mathcal{M}$ (Fig. 1). Following Kasteleyn [19], we can show that each clockwise (anticlockwise) Hamiltonian walk on $\mathcal{M}$ encircles a spanning tree on $\mathcal{L}$ giving two-to-one correspondence between Hamiltonian walks and trees (Fig. 1).

It is quite straightforward to calculate the correlation function in our model using the mapping onto the spanning trees. In particular, the correlation function $P_{1,1}(r)=\langle \deg(i)=1 \,|\, \deg(j)=1\rangle$, which is the probability that two sites i and j

of the spanning tree separated by distance r (see Fig. 1) both have $\deg(i)=\deg(j)=1$, can be written as

$$P_{1,1}(r) = P_1^2\left(1 - \frac{1}{2r^4} + \cdots\right), \tag{4}$$

where P_1 is the probability of site i, with $\deg(i)=1$.

The expression (4) is derived by Majumdar and Dhar [20] who showed that it coincides with the height-height correlation function in the Abelian sandpile model [21,22], namely

$$P_{1,1}(r) = \langle h_i = 1 | h_j = 1\rangle, \tag{5}$$

where h_i and h_j are the heights at sites i and j with minimal value 1. The Abelian sandpile model is the basic model of self-organized criticality [21,22]. The power-law decay of correlation functions signals about the critical behavior of the system.

It is instructive to compare the influence of immunity on self-organization in the RSAW and in the more traditional models of self-organized criticality [21,22]. One of these models is the Forest-Fire model introduced in [23]. An extended Forest-Fire model including the immunity, i.e., the probability that a tree is not ignited although one of its neighbors is burning, has been considered in [24]. It was shown that when a critical value of immunity is approached the fire cannot survive and a continuous phase transition takes place. The fire spreading at the phase transition represents a new type of percolation, so-called fluctuating site percolation. In the RSAW, a “fire” is concentrated at the single site associated with the walker and therefore the process of self-organization refers to the distribution of immunity on the lattice rather than to the distribution of fire. Nevertheless, the appearance of the long-range correlation is common for both cases.

The Kasteleyn’s solution [19] used above gives the exact number of Hamiltonian walks on any oriented lattice which is a covering graph of another oriented lattice. The enumeration is reduced then to counting all spanning trees of the underlying lattice, which is the solved problem due to the Kirchhoff theorem [18]. We have considered a particular case of covering lattice, i.e., the Manhattan oriented square lattice. The enumeration of Hamiltonian walks on an arbitrary lattice as well as the evaluation of correlation functions is a longstanding unsolved problem [25].

IV. EQUIVALENCE OF THE EULERIAN WALK AND RSAW ON THE MANHATTAN LATTICE

The property of self-organization of an environment due to activity of the walking particle has been considered in another model, the so-called Eulerian walker model [26]. This model describes a system of arrows pointing to the direction of continuation of the walk at each site. After each visit, the walk changes the direction of the arrow in the visited site to a next position in the clockwise direction. It was demonstrated in [26] that the motion of a diffusive particle converges asymptotically to the Eulerian circuit which passes each bond of the graph in both directions exactly once. On the other hand, the configuration of arrows, initially random, tends to a set of strongly correlated configurations corresponding to spanning trees on the given graph. The correlation functions of the spanning trees are well known [27] and decay with the distance by a power law. Moreover, the number of spanning trees exactly equals the number of recurrent configurations in the Abelian sandpile model [21] which is the basic model of self-organized criticality [22].

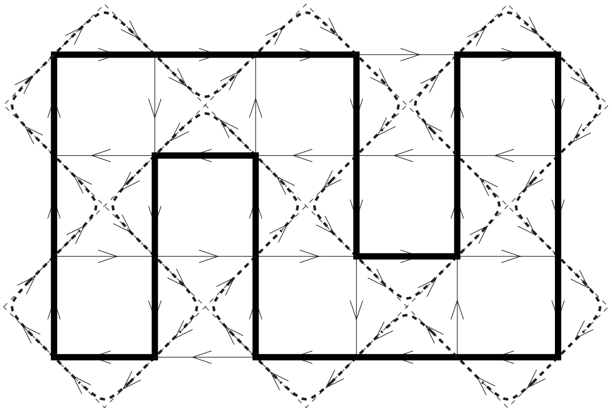

FIG. 3. The square oriented lattice $\mathcal{B}$ (diagonal dashed lines) and its covering graph, the square Manhattan oriented lattice. Any oriented Hamiltonian walk on $\mathcal{M}$ (bold lines) corresponds to an oriented Eulerian walk on $\mathcal{B}$ (bold dashed lines).

A direct attempt to map a model of viral evolution with dynamic fitness on the model of Eulerian walks fails as the state of the immune system is characterized by site variables rather than bond variables. However, we can use some observations by Kasteleyn [19] to prove an equivalence between the Eulerian walks defined on a specifically chosen lattice and RSAW on the Manhattan lattice. Consider the Manhattan lattice $\mathcal{M}$ as the covering graph of a directed underlying square lattice $\mathcal{B}$ which is oriented in diagonal position with respect to $\mathcal{M}$ as shown in Fig. 3. The edges of $\mathcal{M}$ can be obtained by joining the medium points of the edges of $\mathcal{B}$ and directing them according to the orientation of $\mathcal{B}$. Kasteleyn noticed [19] that there is one-to-one correspondence between the Hamiltonian walk on $\mathcal{M}$ and the oriented Eulerian cycle on $\mathcal{B}$.

Let us recall the Eulerian walk model on the oriented lattice $\mathcal{B}$. Each site i of $\mathcal{B}$ has two outgoing and two incoming bonds. The outgoing bonds at i are labelled by integers 1 and 2. We associate with each site an arrow which can point along one of the outgoing bonds. Then, $n_i \in \{1,2\}$ denote the current direction of the arrow at i and the set $\{n_i\}$ specifies the arrow direction at all sites of $\mathcal{B}$. At each time step, the Eulerian walker makes two operations: (1) after arriving at site j, it changes the arrow direction from n_j to $n_j+1 (\mathrm{mod}\, 2)$; (2) the walker moves one step from j along the new arrow direction at j.

It is proven in [26] that the Eulerian walk tends to the Eulerian circuit where each bond is passed once in each allowed direction. In the case of oriented lattice, each bond has only one allowed direction, therefore the limiting cycle is the Eulerian cycle where each bond is visited exactly once. Figure 3 shows one-to-one correspondence between the Eulerian cycle on $\mathcal{B}$ and the Hamiltonian walk on $\mathcal{M}$. Now, we must

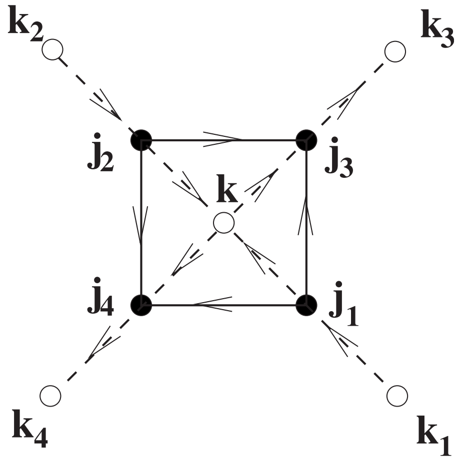

FIG. 4. The cell of lattice $\mathcal{M}$ (solid dots and solid lines) containing the vertex of lattice $\mathcal{B}$ (open dots and dashed lines).

prove the correspondence between the RSAW rules and changing the arrow directions in the Eulerian walk. Consider a cell of the lattices $\mathcal{M}$ containing a vertex of $\mathcal{B}$ (Fig. 4). Let us put one-to-one correspondence between steps on the lattice $\mathcal{M}$ and $\mathcal{B}$. Connecting the medium points of steps on $\mathcal{B}$, we see that if the Eulerian walker reaches sites k_3 (or k_4) on the lattice $\mathcal{B}$ from sites k_1 (or k_2), the corresponding sites j_3 (or j_4) on the lattice $\mathcal{M}$ should be visited by the RSAW from sites j_1 (or j_2), respectively. Suppose the Eulerian walker arrives at site k for the first time from site k_1 or k_2 and then moves one step from k to k_3. Then, the corresponding walker on the Manhattan lattice should visit site j_3 for the first time from site j_1 or j_2, respectively. If the Eulerian walker reaches the site k for the second time, it moves one step from k along the new arrow direction at k to site k_4. The corresponding walker on the Manhattan lattice will visit sites j_1 or j_2 for the second time and then move to the site j_4 because the sites j_3 or j_4 can be reached only from the sites j_1 or j_2 and the site j_3 was visited later than j_4. Thus, the Eulerian and RSAW rules are in accordance one with another at each step where the choice is essential (the random choice in the RSAW corresponds to a random one in the Eulerian walk).

V. RSAW ON INFINITE LATTICES

Up to now, we considered the RSAW on finite lattices where a limiting cycle does exist. At the same time, many characteristics of walks with specific rules of motion, such as SAW, True SAW (TSAW) [28], etc., are exhibited on infinite lattices. The most important characteristic of a unrestricted walk is the average distance from origin R reached by the walker at time t. An analogy between the RSAW on the Manhattan lattice and the Eulerian walk calls up an anomalous diffusion law $R \sim t^{1/3}$ which is true for the Eulerian walk on the square two-dimensional lattice [26]. Below, we examine the long-time behavior of the RSAW on different two-dimensional lattices.

The dynamics of the RSAW on the infinite square lattice coincides with that for the Red Queen's walk on the infinite lattice with random initial conditions [16]. Extensive simulations reported in [16] show that there is only a weak deviation from the diffusion law $R \sim t^{1/2}(\ln t)^{\beta}$ where $\beta \simeq 0.2$.

The behavior of the RSAW on the Manhattan lattice is quite different. Simulations of walks of 3×10^6 steps each averaged over 10^3 runs give $R \sim t^{\nu}$ with $\nu \simeq 0.566$. This enables to conjecture [29] that $\nu = \frac{4}{7}$ exactly which coincides with the exponent for θ-polymers [30].

The deviation from the diffusion law is typical for many active walkers having a long memory on the previously visited sites. The motion of the RSAW can be separated into two regimes. The first one is when the walker sees sites among its nearest neighbors which were not visited yet. Choosing one of the unvisited sites randomly, the walker moves like a self-avoiding walk. The second regime corresponds to the motion through an area visited before. The RSAW rules say that the walker has a tendency to repeat the trajectory passed before inside this area until it finds a site which is not visited yet. Then, the walker returns to the first regime and so on. This complicated behavior leads to different exponents in the law $R \sim t^{\nu}$ for different lattices.

The described scenario shows that the exponent ν can be sensitive not only to dynamics of the walker but also to the length of characteristic time interval where this exponent is determined. In order to demonstrate different types of behavior of an active walker at different time scales, one can complicate the Eulerian walker rules in the following way. Visiting some lattice site i the walker reflects the arrow at i, and moves in the opposite direction. Visiting this site the next time, it reflects the arrow again and keeps moving in this direction. After the third return to this site it flips the arrow by 90° and repeats the motion it performed being at this site the first and second times. Denoting by N,E,S,W four possible directions of arrows, we can write the sequential orientations of arrows at site i after a series of visits as $\ldots N,S,N,S,E,W,E,W,N,S,N,S,\ldots$ The resulting pattern at each site is the cross drawn by the arrow 2 times.

It is worth noting that the suggested "double cross" dynamics in a certain sense is intermediate between the clockwise Eulerian walk on a square lattice and the Eulerian walk model on the oriented lattice $\mathcal{B}$ considered in Sec. IV. Indeed, each site allows all possible walk directions and in this respect it is similar to the clockwise Eulerian model on a square lattice. On the other hand the "double cross" model has common features with the Eulerian walk on the oriented lattice $\mathcal{B}$, since at local time intervals the motion is reflective.

This modification of the Eulerian walk dynamics leads to crossover phenomena at the different time scales (Fig. 5). At the initial stage (up to 10^5 steps) the scaling behavior is consistent with $\nu \simeq \frac{1}{2}$, specific to the RSAW model. Then it passes through the intermediate regime and finally achieves the scaling law $\nu \simeq \frac{1}{3}$ at a large number of steps ($t = 150 \times 10^6$). The last exponent corresponds to the Eulerian walk on a square lattice.

VI. CONCLUSIONS

We have considered a model of the virus population with a single-peaked distribution which evolves in the presence of an adaptive immune system. The model called the relaxing

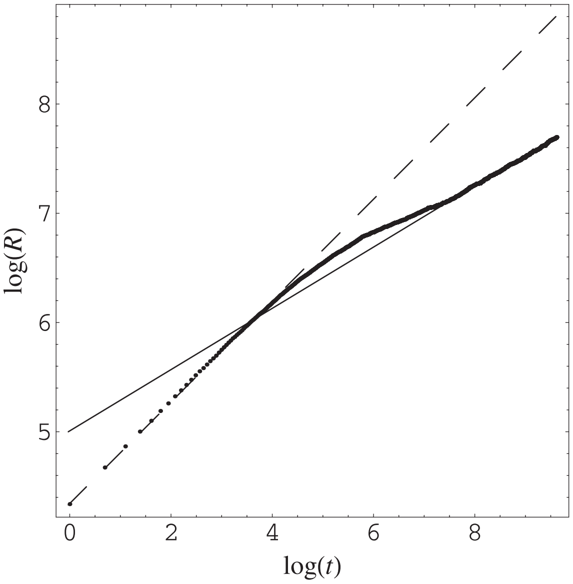

FIG. 5. Log-log plot of the diffusion law for the "double cross" dynamics. Simulations of 150×10^6 steps averaged over 2×10^4 runs (bold curve). The thin line corresponds to the fit with incline $\nu\simeq\frac{1}{3}$ and the dashed line with $\nu\simeq\frac{1}{2}$, respectively.

self-avoiding walk, although being simplified, still retains the basic features of the general system. Two of them are crucial: (a) the long memory of the immune system about the presence of a given kind of virus; (b) the selective principle of evolution when the moving peak of virus population is looking for mutants corresponding to the minimum of activity of the immune system.

The main simplification of our consideration is the planar character of the graph representing the states of virus population. In this respect, we follow a tradition of the statistical mechanics which starts investigations of critical phenomena with low-dimensional systems. In many cases, a system revealing a critical behavior in two dimensions, retains it in higher dimensions, usually with different critical exponents.

Our choice of the Manhattan lattice allowed us to avoid approximate estimations of correlation functions and to prove appearance of the long-range correlations rigorously. By the universality principle, one can expect the similar behavior for any two-dimensional lattice.

The main result of this paper is the explanation of possible mechanisms of the long-range correlations emerging due to co-evolution of virus and immune systems. The RSAW model we used in our approach, has a much broader experimental basis in nature. The selective principle works everywhere that a migrating biological system looks for areas of best survival conditions. On the other hand, a typical environment has a long memory for all "visits" of biological organisms as its resources used by visitors are renewed slowly.

The RSAW itself as a model of statistical mechanics has its own interesting problems. For a general d-dimensional lattice ($d\geqslant2$), the Hamiltonian walk is no longer a unique possibility for limiting cycles. However, computer experiments show that the limiting cycles remain strongly correlated on the hypercubic lattice. Additional computational and analytical efforts are needed to describe the properties of the limiting cycles of RSAW in a general case.

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