Metabolic network dynamics in open chaotic flow

György Károlyi
Program in Applied Mathematics, University of Arizona, 617 North Santa Rita, 85716 Tucson, Arizona 85721, and Department of Structural Mechanics, Budapest University of Technology and Economics, Műegyetem rkp. 3, H-1521 Budapest, Hungary

István Scheuring and Tamás Czárán
Department of Plant Taxonomy and Ecology, Research Group of Ecology and Theoretical Biology, Eötvös University, Pázmány Péter sétány 1/c, H-1117 Budapest, Hungary

(Received 31 October 2001; accepted 8 January 2002)

We have analyzed the dynamics of metabolically coupled replicators in open chaotic flows. Replicators contribute to a common metabolism producing energy-rich monomers necessary for replication. The flow and the biological processes take place on a rectangular grid. There can be at most one molecule on each grid cells, and replication can occur only at localities where all the necessary replicators (metabolic enzymes) are present within a certain neighborhood distance. Due to this finite metabolic neighborhood size and imperfect mixing along the fractal filaments produced by the flow, replicators can coexist in this fluid system, even though coexistence is impossible in the mean-field approximation of the model. We have shown numerically that coexistence mainly depends on the metabolic neighborhood size, the kinetic parameters, and the number of replicators coupled through metabolism. Selfish parasite replicators cannot destroy the system of coexisting metabolic replicators, but they frequently remain persistent in the system. © *2002 American Institute of Physics.* [DOI: 10.1063/1.1457468]

One of the main theoretical challenges related to the origin of life is to sketch a plausible scenario explaining how early replicators might have coexisted and even cooperated without being encapsulated into independently selected units, i.e., without any kind of a proto-cell structure. Nowadays the generally preferred scenario assumes that early replicators must have existed and reacted with each other bound to the surface of positively charged mineral surfaces like that of pyrite. It has been shown previously that metabolically coupled replicators can coexist on such a surface,[1] and this system is usually resistant to selfish parasitic replicators as well. We also investigate the dynamics of replicators dynamically coupled through the common metabolism they drive, but our model assumes that the replicators are advected and interact in an open chaotic flow. We show that coexistence and resistance against selfish replicators is possible in this fluid system as well.

I. INTRODUCTION

The origin of life is a research subject with many unsolved problems ranging from the prebiotic synthesis of biologically important molecules (like ribose and purin bases) to the emergence of the first proto-cells.[2] Now it seems certain that there was a phase along the evolutionary route to proto-cells characterized by the development of self-replicating macro-molecules.[2] Recent RNA molecules are capable of replication (with some catalytic help), and they are also shown to have catalytic activity themselves,[3] so the assumption that this intermediate stage of prebiotic evolution might have been dominated by self-replicating, RNA-like nucleic acid oligomers seems to be a plausible one.[4,5] If this is indeed the case, these oligomers must have been able to replicate without the aid of specific peptide enzymes, and they must have competed for a few limiting resources such as mononucleotids and energy rich compounds.

Replication is never perfect, that is, due to mononucleotide pairing mismatches, the copy is never identical to the original macro-molecule. Replication is even less accurate without specific replicase and proofreading enzymes, which were indeed not present in the RNA world. In his keystone paper Manfred Eigen[6] described mathematically the mutation-selection process of these ancient replicating macro-molecules. The most important result of his study was that the maximum amount of selectively maintained information, i.e., the maximum length of the fittest replicator molecule, is limited by copying fidelity. More precisely, $N < \ln(s)/(1-q)$, where N is the number of nucleic acid monomers in the replicator molecule, s is the selective superiority of the fittest replicator (i.e., the replication rate of the fastest replicator divided by that of the average of all the rest) and q stands for the per nucleotide per replication copying fidelity. If the fittest macro-molecule is longer than this limit, its concentration will be very low, and it can easily disappear from the system by stochastic drift.[7] Estimating the selective superiority of the best replicator and the copying accuracy per nucleotide without replicase enzymes (enzymes helping self-replication of macro-molecules), it is concluded that the maximum length of persistent molecules ranges from 10 to 100 nucleotides.[6,8,9] This means that the winner of the mutation-selection process is the fittest macro-molecule consisting of some dozens of nucleotides, and the system also maintains a distribution of the closest mutants of the winner

type.[6,10] However, even the simplest RNA viruses contain 4000–5000 monomers. How can we surmount the size gap between these primitive replicators and the simplest recent evolving entities? Specific replicase enzymes are needed to increase copying fidelity, and thus the length of the persistent replicators, but these replicators are too short for coding specific enzymes. This is the ''Catch 22'' of prebiotic evolution:[11] no genome without enzymes, and no enzyme without genomes. One way of resolving this problem is through maintaining the *coexistence* of several different replicator molecules, so that the information necessary for coding a replicase enzyme can be stored and transmitted by a ''community'' of smaller information carriers. We note here that there is an alternative resolution to the ''Catch 22'' which assumes that the template- and the enzymatic functions had co-evolved, thus the length of the replicators and their replicase activity had increased in parallel.[9,12,13]

Recent developments in the field of hydrodynamics encouraged the revision of population dynamics of purely competing species in *open aquatic systems*.[14] In fluid systems of large extension, on the time scales characteristic to the life cycle of replicators, hydrodynamical flows are locally open, i.e., there is a net current, transporting both competitors and nutrients, flowing through the typical observation region. It is even more obvious that the flow is open around deep sea hot springs where the cradle of life probably swung.[15] It has been shown that the coexistence of passively advected competing species is typical in *open chaotic flows*.[14]

In this article we focus on the dynamics of metabolically coupled replicators in open chaotic flows. In particular, we are interested in the possibility of coexistence in a metabolic system, and its resistance against parasitic mutants in a chaotically mixing aquatic medium. We show that the fractal patterns arising in open flows lead to an efficient, but imperfect, mixing of replicators. This enhances the biological activity, and this leads to the coexistence of replicators necessary for information integration in early evolution of life.

II. COEXISTENCE OF REPLICATORS, THE GRID MODEL OF METABOLISM

The coexistence of different replicators can be attained if there is some kind of obligate cooperation among them. The earliest hypothesis considered replicating molecules as molecular mutualists, assuming that every molecule type catalyzes both its own replication and that of another member of the system, hetero-catalytic connections forming a cycle in the topological sense. This system of replicating molecules is called the *hypercycle* (Fig. 1), in which the coexistence of replicators is typical.[10] However, the hypercycle is not really realistic in chemical terms, and it is not stable against parasitic mutants (i.e., replicators accepting the catalytic help of another member of the system, but not helping any other). Such mutants can spread and destroy the hypercycle.[7]

The hypercycle model (just like many others) is based on the idealization that replicating molecules are pointlike objects in a perfectly mixed medium. This assumption is offset in more recent investigations in which molecules are viewed as discrete entities moving on a surface by diffusion.[1,16] Boerlijst and Hogeweg[16] studied the hypercycle

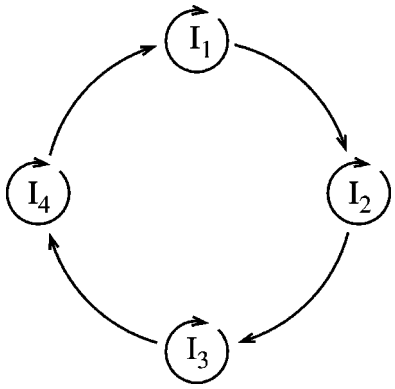

FIG. 1. Replicators $(I_1,\ldots,I_4)$ cooperate in a hypercycle. Circular arrows denote self-replication, and solid arrows indicate catalytic help for the replication.

in a spatially extended model, whereas Czárán and Szathmáry[1] analyzed the dynamics of *metabolically coupled* replicators on a surface. It has been shown that the hypercycle is resistant against parasites in a spatial setting, provided the number of different types of replicator exceeds four.[16] Resistance is critically dependent on the emergence of a specific spiral-wave structure in the hypercycle model, but spiral wave structures generally are not robust against spatial noise and inhomogeneity.[17,18] Thus the hypercycle remains an evolutionarily unstable model even in the case of spatial extension. In the chemically more realistic metabolic system replicators help catalytically the common metabolism which in turn supplies energy-rich monomers for replication (Fig. 2). It is assumed that all the replicators are necessary to drive the metabolic machinery, which means that the replicators act as obligate mutualists in ecological terms. Since metabolism provides an aspecific help to replication, the fastest replicator excludes all the others, and the metabolic system collapses in the ODE version of this model, but coexistence and resistance against parasites is possible in the spatial version.[1] That is, reaction and diffusion on a surface (according to the so-called ''prebiotic pizza'' scenario[19]) ensure coexistence and evolutionary stability of mutualistic replicators in the metabolic system.

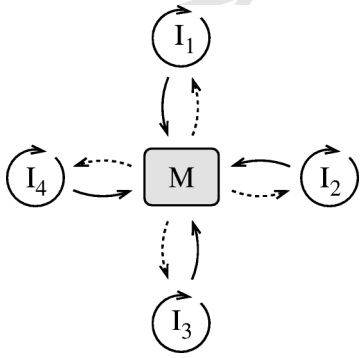

FIG. 2. Replicators $(I_1,\ldots,I_4)$ cooperate in a metabolic system (M). Circular arrows denote self-replication, dashed arrows denote the metabolically produced monomers and solid arrows indicate the catalytic help for monomer production through metabolism.

The dynamics of the nonspatial version of a metabolic system in a well-mixed environment can be described by

$$\frac{dx_i}{dt} = x_i[k_i m(\mathbf{x}) - \Phi(\mathbf{x})], \tag{1}$$

where x_i is the concentration of the ith replicator, $\mathbf{x}$ is a vector of these concentrations, and k_i is the replication constant of the ith competitor. The term $m(\mathbf{x})$ is a multiplicative function of all concentrations, and Φ represents an ''outflow:'' a constant total concentration is enforced. As Eigen and Schuster[10] observed, the fact that replication of any species is impossible without the presence of *all* other competitors does not prohibit competitive exclusion: the multiplicative function $m(\mathbf{x})$ of all concentrations is the same in all equations, hence the system essentially behaves as a collection of Malthusian competitors whose dynamics are influenced by a common concentration-dependent factor. It is easy to see that the only stable fixed point of (1) is $\mathbf{x}=\mathbf{0}$, that is, all metabolic replicators go extinct in this well-mixed system.

We assume that the replicators have two functionalities: they catalyze their own replication (auto-catalysis), and act as *ribozymes* (RNAs able to act as enzymes) contributing to the metabolism by producing monomers. We consider a two-dimensional square lattice of binding sites as the scene of the replication process. As the replicators have finite size, their number is limited to one in each grid cell, or, equivalently, the size of the grid cells is chosen to be the size of the replicators.

The replicators are placed into an aquatic environment, hence there is a hydrodynamical flow transporting the replicators in our region of observation. The flow we have chosen is probably the simplest model of *open* flows, discussed in more detail in the following section. The openness of the flow means that there is an *in-flow* into the region of observation bringing resources necessary for replication, and there is also an *out-flow* advecting out a certain portion of the competitors from the region of observation.

The model of replication-advection starts with some replicators of equal abundance in the region of observation. Time is considered discrete: in each time step advection, decay, and replication take place. In the advection phase, the replicators are transported into new grid cells according to the hydrodynamics of the system. Some of the replicators will be advected out of the observation region as the flow is open; these are ''lost'' forever for the model. Then a certain portion of the competitors dies out due to natural ''death;'' the portion is specific to competitor type. In other words, a competitor of type i dies out with a small probability δ_i in each time step. The next phase is replication, according to the rules of metabolic coupling between the competitors.

The effect of monomer-producing metabolism is implicit in the model: it acts directly on the replication process through a *local metabolic function* $M(f_s)$. The arguments of this function are copy numbers $f_s(i)$ giving the number of competitors of type i in a *metabolic neighborhood* of site s. The metabolic neighborhood is a square of grid cells around site s, having linear size $2\sigma+1$ (see Fig. 3). The size of the metabolic neighborhood models the diffusion of the intermediate metabolites and the monomers. As the presence of all replicators is necessary for metabolism to produce monomers for replication, the metabolic function must contain all $f_s(i)$ multiplicatively. The simplest choice is the geometric mean of the copy numbers $f_s(i)$ within a metabolic neighborhood of site s:

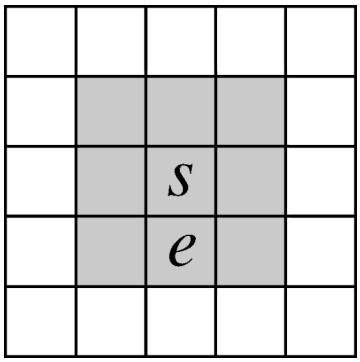

FIG. 3. Metabolic neighborhood of site s beside an empty grid-cell e. Gray sites indicate a 3×3 ($\sigma=1$), gray and white sites together indicate a 5×5 ($\sigma=2$) neighborhood.

$$M(f_s) = \left[\prod_{i=1}^{n} f_s(i)\right]^{1/n}, \tag{2}$$

where n is the number of replicator types, i.e., the *community size*. This choice of the metabolic function $M(f_s)$ warrants zero value if any of the replicator types is missing from the metabolic neighborhood of site s. It also accounts for larger values, that is, a more efficient metabolism, when the copy numbers $f_s(i)$ of the replicators in the metabolic neighborhood are larger and more uniform. Note that in the case of omitting spatial heterogeneity, i.e., when the metabolic function is the same for all sites, M becomes independent of s, and depends uniquely on the overall replicator abundance vector $\mathbf{x}$. This means that in the simplest mean-field approximation $M(f_s)$ turns into $m(\mathbf{x})$ of Eq. (1), and there is no coexistence in the mean-field limit.

Given an empty grid cell e as in Fig. 4, the replicators in its *replication neighborhood* might have a chance to put offsprings into site e. The replication neighborhood of an empty cell consists of the eight closest neighboring sites (see Fig.

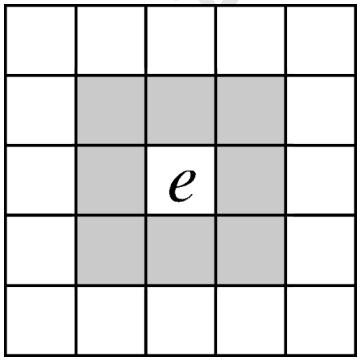

FIG. 4. Replication neighborhood of an empty site e. Replicators in the gray area of size 3×3 sites (not including e) might have chance to replicate into e, according to the value of their metabolic function $M(f_s)$.

4). Each of the replicators in the replication neighborhood has a *potential* to place a replica of itself into the empty site. This potential depends on its value of local metabolic function $M(f_s)$ and on its type-specific replication constant k_i:

$$C(s)=k_s M(f_s). \tag{3}$$

However, the empty cell also has a potential C_e to remain empty, thus the chance P_s that competitor in site s replicates into the empty space becomes

$$P_s=\frac{C(s)}{C_e+\Sigma_{\ell} C(\ell)}, \tag{4}$$

where ℓ enumerates all macro-molecules in the replication neighborhood. Accordingly, the probability that e remains empty is

$$P_e=\frac{C_e}{C_e+\Sigma_{\ell} C(\ell)}. \tag{5}$$

Thus the ''biological phase'' of each discrete time step consists of spontaneous decay of each competitor with probability δ_i for replicator type i, followed by the updating of the whole lattice synchronously according to the metabolic replication process described above. Prior to these, however, each time step includes the phase of the advection of replicators by the underlying hydrodynamical flow, which updates the contents of each site of the lattice, again, synchronously.

III. THE FLOW MODEL

The passive advection of particles in hydrodynamical flows is one of the most appealing applications of chaos theory. Assuming that inertial effects are negligible, the equation of motion for a particle expresses the coincidence of the tracer's velocity $\dot{\mathbf{r}}$ with the velocity field $\mathbf{v}(\mathbf{r},t)$ of the flow that is assumed to be known: $\dot{\mathbf{r}}(t)=\mathbf{v}(\mathbf{r}(t),t)$. This is a simple set of ordinary differential equations for the unknown tracer motion $\mathbf{r}(t)$ with a given, typically nonlinear right-hand side. The solution of such an equation can be chaotic. In the last decade, a comprehensive knowledge has accumulated in this field both for flows in *closed* containers[20–29] and for *open* flows with asymptotic simplicity.[30–44] *Piece-wise steady* flows have long been playing an important role in understanding chaotic advection. They are maintained by keeping the flow steady for a time interval (often half of the full period), and then jumping suddenly to another flow kept steady for another time interval. Then a jump follows back to the original flow, and the whole process is repeated periodically. The corresponding particle motion is then a kind of kicked dynamics due to the sudden jumps in the flow field. A pioneering example of this kind is Aref's blinking vortex system.[20] Another famous model for stirring in closed regions is related to the journal bearing flow[21,22] whose experimental realization was also possible.[22,23] A piece-wise steady model for open flows with Hamiltonian particle dynamics is based on a periodic repetition of a vortex action and of a homogeneous flow.[38]

To investigate the effects of chaotic mixing in open flows on the metabolic system, we use the *blinking vortex-sink system* invented by Aref *et al.*[31] and studied in detail by Károlyi and Tél.[43] It models the *out-flow* from a large bath tub with two sinks that are opened in an alternating manner. In the course of this process, a chaotic mixing might take place.

During each half time period, a sinking vortex, that is, a super-position of an ideal point vortex and of a point sink, governs the behavior of the transported particles. Hence the particles follow logarithmic spirals around the sinking vortex,[31,43] that is, if one starts at a dimensionless distance r_0 from the sinking vortex at an angle φ_0 in polar coordinates, then after dimensionless time t its position will be

$$r(t)=(r_0^2-2\eta t)^{1/2}, \quad \varphi(t)=\varphi_0-\xi \ln\frac{r(t)}{r_0}. \tag{6}$$

Here ξ is the ratio of the vortex strength to sink strength, and η is the dimensionless sink strength. These are the only essential parameters of the advection of particles in this flow. Because the motion is undefined after reaching the sink center, the time in this expression has to be limited from above:

$$t\leqslant\frac{r_0^2}{2\eta}. \tag{7}$$

The blinking vortex-sink system[31,43] is obtained by having two such sinking vortex points some distance apart from each other, both being active alternately for a duration of $T/2=\frac{1}{2}$. In this system the velocity field is periodic with $T=1$, but in a special way: it is stationary for half a period and stationary again but of another type for the next half period $T/2=\frac{1}{2}$. The velocity field corresponds to a sinking vortex flow centered at $(x,y)=(-1,0)$ and at $(x,y)=(1,0)$ in the time intervals $(0,\frac{1}{2}]$ and $(\frac{1}{2},1]$, respectively. The entire flow is no longer stationary; there are jumps in the velocity field at each half period.

For a detailed investigation we choose the parameter values $\eta=0.5$ and $\xi=10$. At these parameter values the advection of particles is *chaotic*.[43] Two initially close particle trajectories are shown in Fig. 5. In the course of time, the two particle paths diverge rapidly from each other, indicating a sensitive dependence on the initial conditions, which is a unique sign of chaos. A generic feature of chaotic advection in open flows is that an ensemble of particles traces out a *fractal set* as time goes by. This is shown in Fig. 6 for the blinking vortex-sink system: particles originally injected into the flow in a rectangular area trace out a fractal pattern after already six time periods of the flow. This pattern changes with time, but is time periodic according to the time periodicity of the flow.[43]

Note that the appearance of such fractal patterns is not unique to this particular flow model; it is generic for open flows.[30–44] The appearance of these patterns is often found in natural flows, like, e.g., in the wake of islands[45] where plankton populations trace out nontrivial filamental structures. An example for such a filamental fractallike structure is shown in Fig. 7, where the distribution of sea-ice is shown on a satellite image close to Kamchatka.

The effect of this fractal structure for chemically or biologically active particles was studied in detail,[46,47] and it was

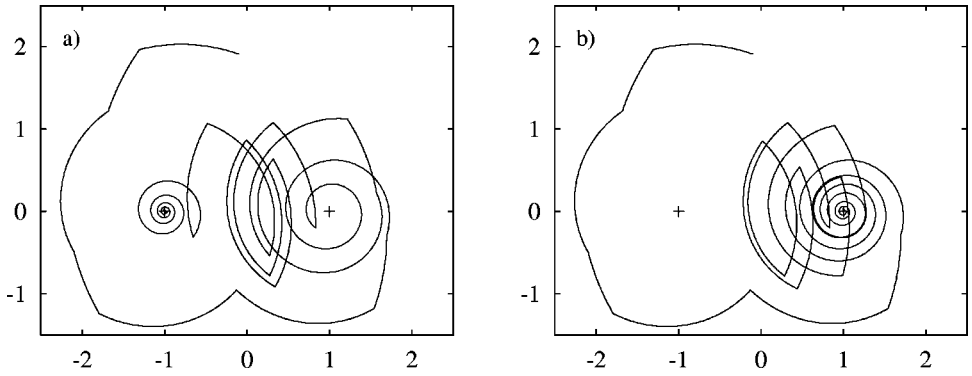

FIG. 5. Two initially close trajectories are shown for $\eta=0.5$, $\xi=10$. The initial positions of the trajectories were $x_0=-0.1$ and (a) $y_0=1.9103$, and (b) $y_0=1.9104$. Note that the trajectories, consisting of segments of logarithmic spirals around either of the sinking vortices (crosses) diverge rapidly from each other; they even leave the system through different sinks.

shown that the chaos and fractality parameters appear in the equations describing the dynamics of chemical reactants or biological populations. In fact, it was possible to obtain a possible solution for the coexistence of the purely competing auto-catalytic replicators in terms of these modified equations containing the fractality of the distribution of the active particles.[14]

Here we are interested in whether the coexistence can also be maintained by chaotic mixing in open flows in the case of the metabolic system described in the previous section. To check this, we apply the blinking vortex-sink system for the lattice where the model of metabolism was defined. We discretize the flow both in space and time. We choose the time step of the metabolic activity to be $\Delta t=T/10=\frac{1}{10}$ of the time period of the flow. That is, the competitors have chance to replicate ten times during one time period of the flow. Increasing the replication frequency could increase the chance of coexistence, due to the fact that there will be less competitors leaving the region of observation between two replication phases.

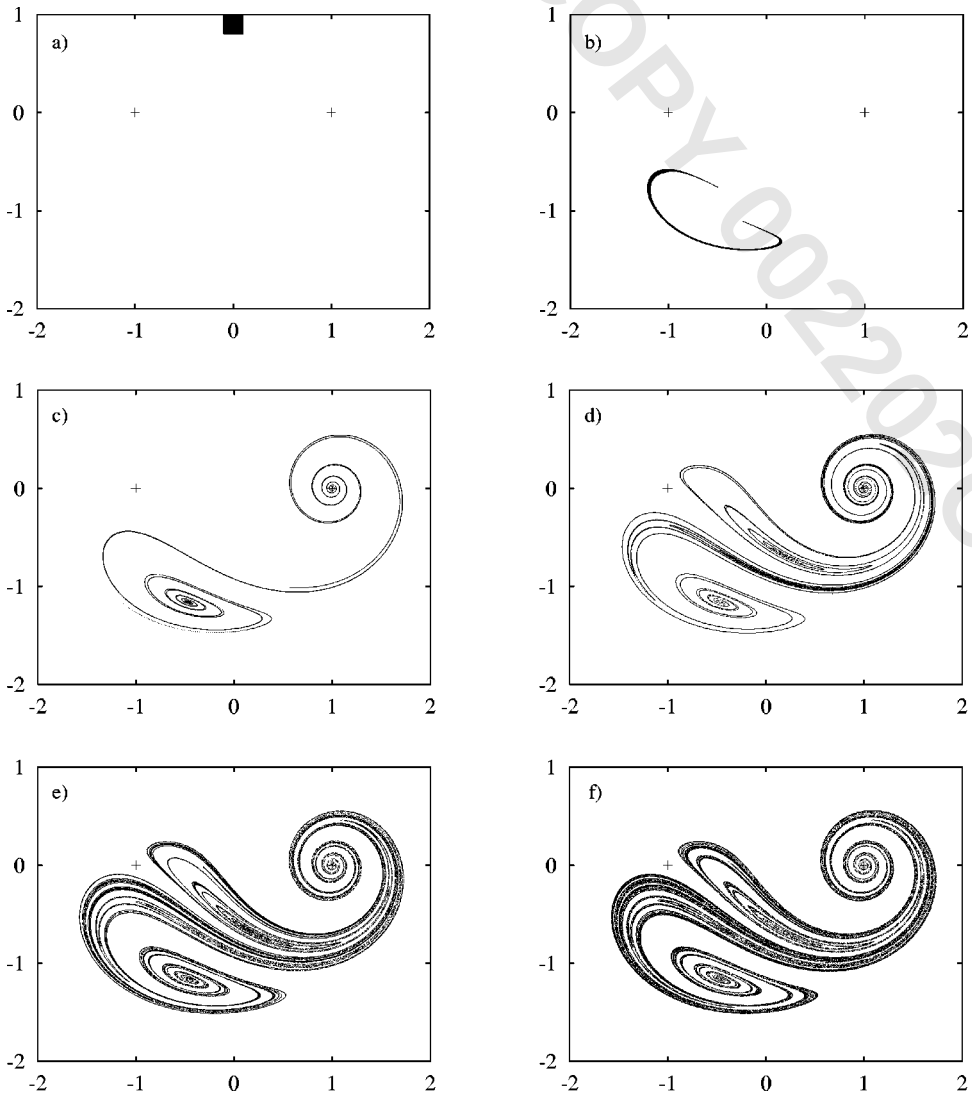

FIG. 6. Snapshots of an ensemble of particles advected by the flow. The 1000×1000 particles originally were uniformly distributed in the rectangular area $x\in[-0.1,0.1]$, $y\in[0.8,1.0]$. In the course of time, they trace out a fractal object. The snapshots are taken at (a) $t=0$, (b) $t=2$, (c) $t=3$, (d) $t=4$, (e) $t=5$, and (f) $t=6$, at the instance when the right sinking vortex (cross) was closed and the left one (cross) is about to open. The flow parameters were $\eta=0.5$, $\xi=10$.

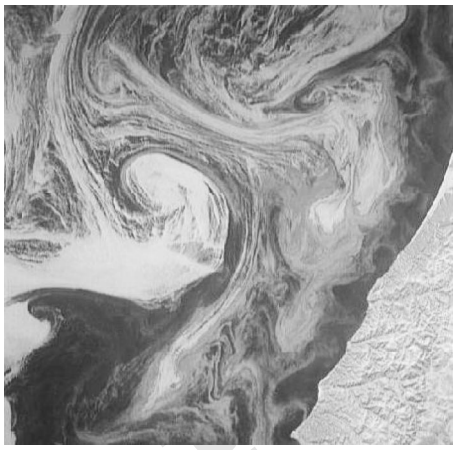

FIG. 7. Satellite image of the distribution of sea-ice close to Kamchatka. Observe the filamental structure traced out by sea-ice (white). From the NASA archive (http://images.jsc.nasa.gov/iams/images/earth/STS045/html/10068879.htm).

Having a replicator in a grid cell, the advection will move it into another grid cell according to the hydrodynamical model. We say that the *center* of the site is occupied by the replicator, and then it is advected by the flow $\mathbf{v}(\mathbf{r},t)$ according to $\dot{\mathbf{r}}=\mathbf{v}(\mathbf{r}(t),t)$ for the duration of the time step Δt. In other words, we imagine that the *center of the site* moves along a logarithmic spiral towards the sinking vortex currently active. If the replicator starting from the center of the grid cell does not leave through the active sink during time interval Δt, it will be situated in another grid cell. Then we say that the replicator has moved into that grid cell, and we replace it into the center of this new site. Then this replicator is ready for the decay-replication phase of the time step, according to the rules described in the previous section. So, it is assumed that the speed of molecular diffusion is small compared to the speed of advection, which is evidently true in the case of biological macro-molecules.

IV. RESULTS

There are two possible outcomes from the model of metabolism superimposed on chaotic advection in open flows: either the process ends up in total extinction, or it leads to the coexistence of the competing species. One of the most important results of the simulations is that the model is capable of producing coexistence in a substantial part of the parameter space, even though the mean-field model (1) predicts competitive exclusion of all the inferior replicator types, and thus the subsequent collapse of the entire metabolic system. The explanation of the possibility of coexistence lies in the local density differences of replicators, leading to local differences of the extinction process through the metabolic function $M(f_s)$. Hence the metabolic function depends on space also, and that can lead to coexistence.

From the point of view of the coexistence, the most important parameters are the community size n (i.e., the number of competitors), the metabolic neighborhood size σ, and the parameters of the flow.

The role of the advection by the flow is twofold. First, it provides empty sites among the grid cells containing replicators, as it transports the competitors onto a fattened-up copy of a filamental fractal. The filaments of various species are separated by empty sites providing thus the competitors with the possibility of replications. Second, the flow mixes the replicators, and thus there are no spaces of large extension lacking one or more type of replicators. This is advantageous for the performance of the metabolic system, which cannot work if one or more replicator types are completely missing from the metabolic neighborhood, as monomers necessary for replication are not produced. Advection makes the replicator set in the metabolic neighborhood more diverse, which increases the value of the metabolic function $M(f_s)$, and hence increases the probability of empty cells to become occupied. A series of snapshots in Fig. 8 shows how the metabolic network superimposed on the chaotic flow works. Here three different types of replicators were placed into the flow, and then they were advected in the flow driven by the two sinking vortices alternately. In the course of time, the species occupied the close vicinity of the fractal curves which were traced out by the particles without any biological activity, cf. Fig. 6.

Another effect of the flow is that it removes a certain amount of the replicators in each time step through one of the sinks. As the amount removed in each step is proportional to the actual population in the region of observation, this effect just rescales the spontaneous decay δ_i of each competitor: $\delta_{i,\mathrm{eff}}=\delta_i+\kappa$, where κ is the *escape rate* of the flow, that is, it characterizes how swiftly the biologically inactive particles would leave the observation region. More precisely, the number of particles remaining in the mixing region after p time steps is $N_p=N_0\exp(-p\kappa)$, where N_0 is the original particle number. As long as we do not choose the strength of the sink to be too large, its actual value was not found to play a crucial role in coexistence.

The role of the number n of different replicators is crucial, however. As we increase the number of competitor types, the probability of finding all of them in the metabolic neighborhood decreases. It can be balanced by increasing the size of the metabolic neighborhood σ, but we were unable to find more than three coexisting competitors. The coexistence of two types of replicators is typical for a wide range of parameter values, whereas the coexistence of three replicators is restricted to a much narrower range of parameters.

The size of the metabolic neighborhood also plays a crucial role in coexistence. If σ is too small, than the probability to have all different replicator types inside the metabolic neighborhood is too small, hence replication is limited, leading to the collapse of the metabolic network. This is in connection with the number of different replicator types; the interplay of these two parameters determine the chance of having a full set of replicator types in the metabolic neighborhood. If, on the other hand, σ is too large, then we end up with a mean-field approximation: the replicators ''feel'' the global averages of replicator densities instead of the local ones, hence the metabolic function becomes independent of space, so we have $M(f_s)\rightarrow m(\mathbf{x})$, and (1) becomes valid. Because this model does not assume that increasing community size has beneficial effect on metabolism, the size of viable communities is limited: too many replicator types

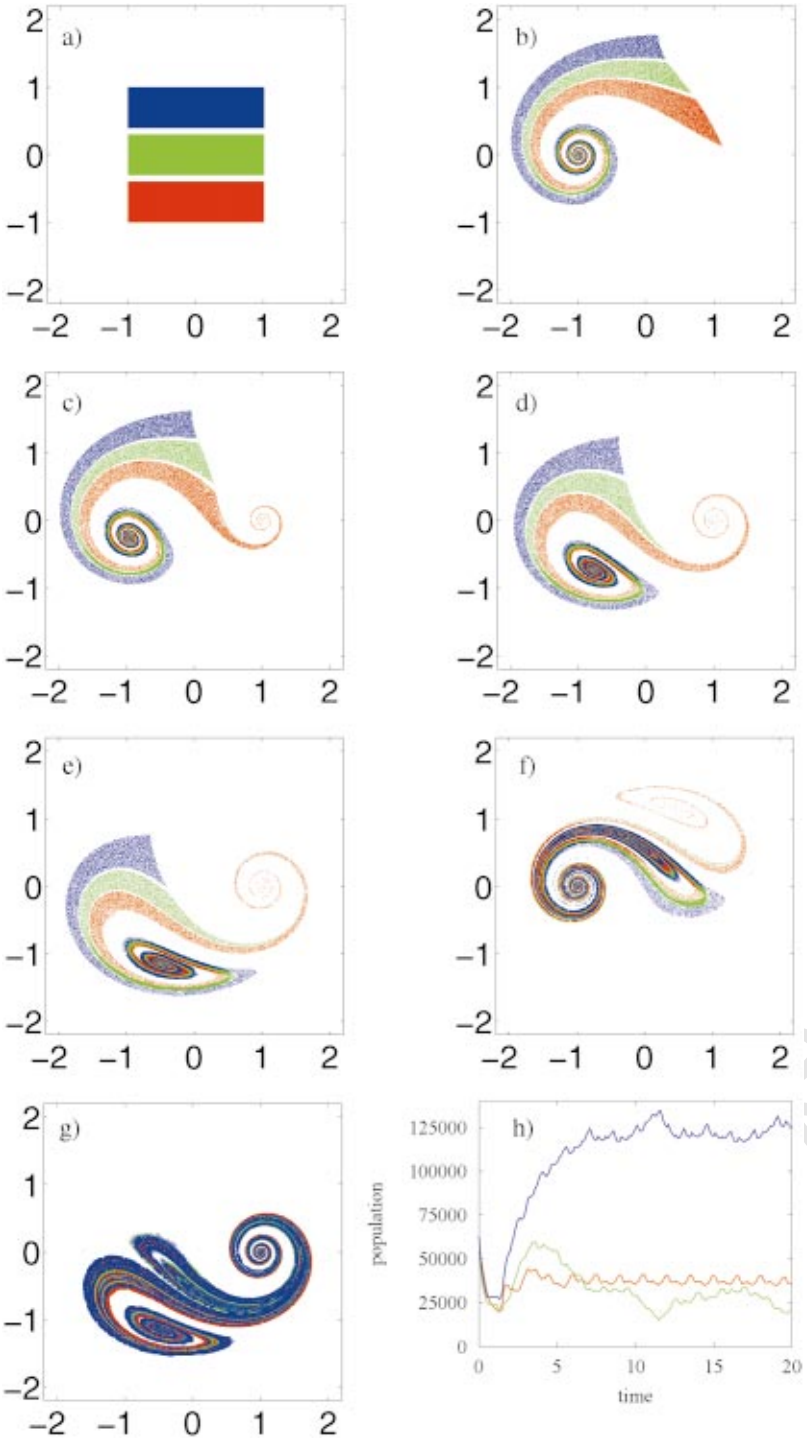

FIG. 8. (Color) Series of snapshots of the metabolic network superimposed on chaotic advection by an open flow. The snapshots were taken at (a) $t=0$, (b) $t=0.5$, (c) $t=0.6$, (d) $t=0.8$, (e) $t=1$, (f) $t=1.5$, and (g) $t=10$. On plot (g) the population size is shown as a function of time measured in units of the flow's period. The simulations were performed on a grid of size 1000×1000 with flow parameters $\eta=0.5$, $\xi=10$. The size of the metabolic neighborhood was $\sigma=10$ for each competitor, and their spontaneous decay was $\delta=0.02$. The replication constants were different for each species; these were $k_1=3$ (red), $k_2=4$ (green), and $k_3=5$ (blue). The potential that an empty site remains empty was $C_e=2$.

need large metabolic neighborhoods, but large neighborhoods act against coexistence. In this sense, it is a worst-case metabolic system, and even in this case it was possible to find coexistence of replicators.

The variation of the replication constants k_i also affects coexistence. As the difference between the replicators' ability to replicate increases, the most fit replicator has the greatest chance to put offsprings into the empty sites, leading to the exclusion of the less fit competitors, hence leading to the collapse of the metabolic network. To the collapse, however, the best had to be about three times as fit as the least fit replicator type.

The weight C_e of an empty site to remain empty has an interesting effect on the coexistence. If we increase this chance, that leads to the decrease of the number of replicators in each step, hence the populations become less dense. This could result in the extinction of the less fit replicators, and thus to the collapse of the metabolic network. It is more surprising that if we decrease C_e, it also might lead to a collapse of the metabolic network. The reason for this is that in the case of small C_e too few empty cells remain, which prohibits replication in the next couple of time steps. It might lead to larger fluctuations in the populations, which can

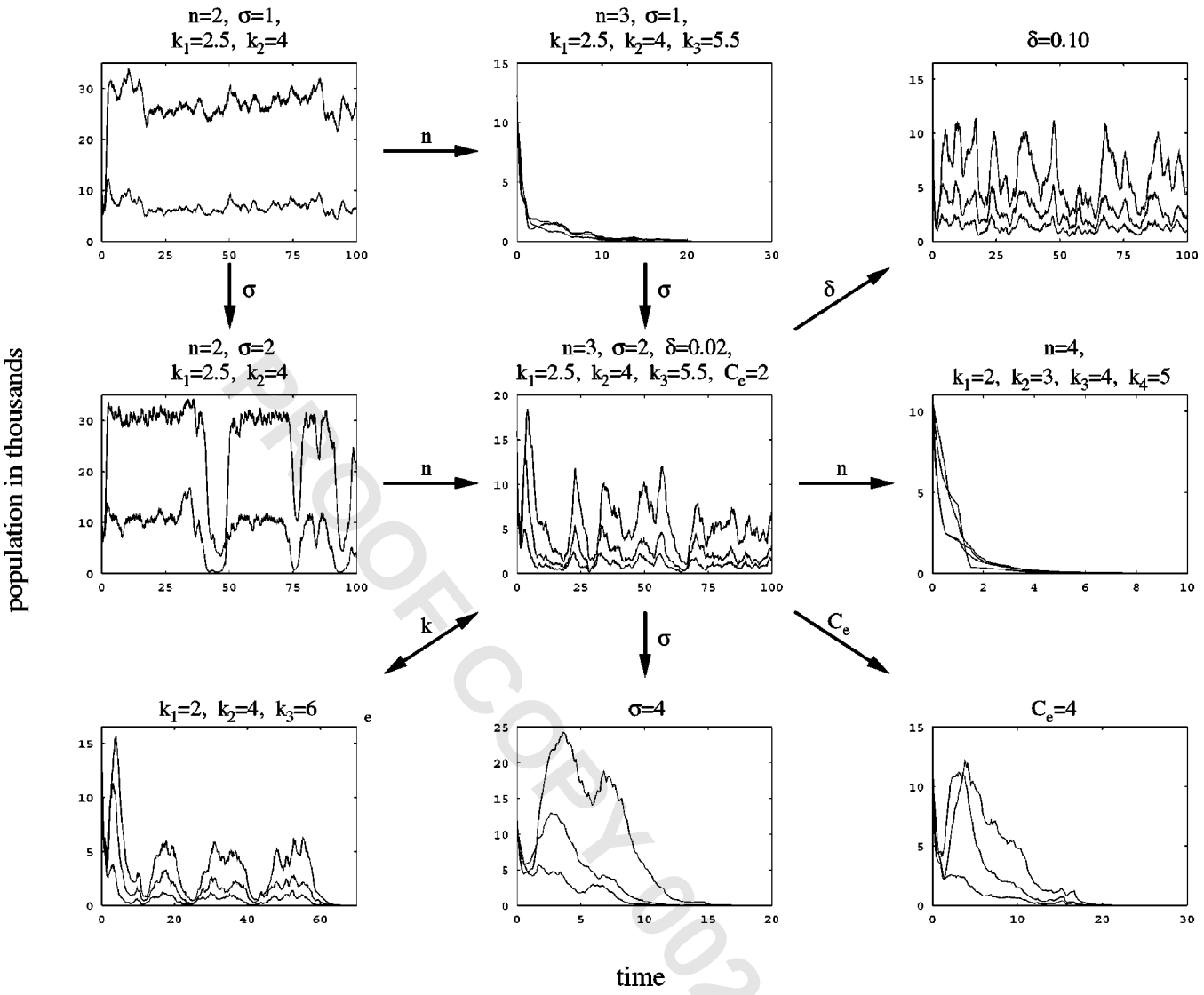

FIG. 9. Time series of population sizes for several parameter settings. The simulations were performed on a grid of size 500×500, the flow parameters were $\eta=0.5$, $\xi=10$. Other parameters are on the figure. Horizontal axes show time measured in units of the flow's period, population sizes are shown in thousands on the vertical axes. Arrows indicate the increase of the parameter of their label. Note that as size σ of the metabolic neighborhood either increases or decreases, the inferior competitor becomes extinct leading to the collapse of the metabolic network. The increase of the community size n has the same effect, and also the increase of C_e acts against coexistence. Note that the spontaneous decay δ has minor effect, and the differences in the replication constants has to be large for extinction.

cause the extinction of the less fit replicator, since it is already present in the smallest abundance.

It was found that the effect of lattice size is not crucial provided that it is large enough to embed a large enough variety of localities. Similar results were obtained with lattice sizes of 200×200, 500×500, or 1000×1000. This observation that the resolution (associated with the ratio of the organism size to the size of the observation region) does not play a role here is consequent with the scale-independence of the governing fractal structures. Unless the size of the replicators is comparable to the size of the observation region, it has no effect. Increasing grid size, that is, increasing the number of competitors in the observation region, just reveals finer and finer, but self-similar structure of the same fractal object inhabited by the macro-molecules. The effect of spontaneous decay was not found to be crucial if it was not extremely high. It had to be more than $\delta>0.1$ to lead to extinction; typically it had to be as high as 0.2.

The effect of parameter variance on the populations is illustrated in Fig. 9.

It is also important to check whether the metabolic network superimposed on the chaotic mixing by the flow is persistent in the case of the appearance of *parasites*. Defining a parasite in the metabolic system is quite simple: it will be a new replicator that receives metabolic help from the cooperative system, but does not contribute to metabolism. In biochemical terms, a parasite uses the monomers produced by the cooperative replicators but does not catalyze any elementary reaction of monomer production. If the replicators can mutate and can thus produce parasitic (as well as other, possibly cooperative) variants, the long-term viability of the metabolic replicator system critically depends on the system's resistance to such parasites.

The parasite is introduced into the system as an extra

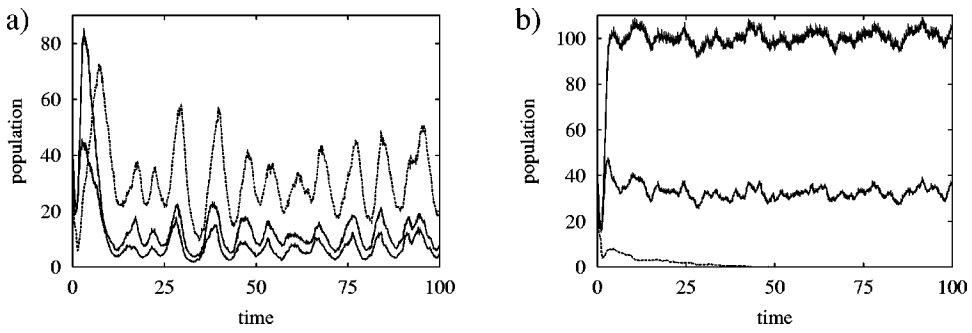

FIG. 10. Parasite with two cooperating replicators. (a) Parasite (dashed) coexists with the cooperating replicators (solid lines); (b) parasite (dashed) dies out, but the collaborative replicators (solid lines) coexist. The simulations were performed on a grid of size 1000×1000 with flow parameters $\eta=0.5$, $\xi=10$. The size of the metabolic neighborhood was (a) $\sigma=2$ and (b) $\sigma=1$. Spontaneous decay was $\delta=0.02$, replication constants were $k_1=3$, $k_2=4$, and for the parasite $k_p=5$. The potential for an empty cell to remain empty was $C_e=2$.

replicator with the largest replication constant k_p: it is the fastest replicator, $k_p>k_i$ $(i=1,\ldots,n)$. The parasite can replicate just like the others to empty sites on the grid, provided that all cooperative types of replicators are present in its metabolic neighborhood. The others, however, do not need the parasite to be present for their replication. It means that the local copy number $f_s(p)$ of the parasite inside the metabolic neighborhood was omitted from the local metabolic function $M(f_s)$.

The main observation in the simulations was that even a fast parasite could not kill a system that otherwise was viable. In some cases the parasites were coexisting with the cooperative replicators [Fig. 10(a)], in other cases it was the parasite that was excluded [Fig. 10(b)] although it was the best competitor, but in both cases the metabolic system proved to be stable against the appearance of a parasite.

V. CONCLUSIONS

Similar to the surface models, the coexistence of metabolic replicators is possible in open chaotic flows because of the local variation of the metabolic function $M(f_s)$. This inhomogeneity follows from the strong but imperfect mixing in the open chaotic flow and the local interactions among the molecules as well. While replicators with a small kinetic constant tend to go extinct very fast in the mean-field model, a rare replicator within the flow is more likely to be complemented by the more common types in its metabolic neighborhood than the other way around. Consequently, the speed of replication is increased for rare molecules in the flow. This *advantage of rarity* principle[1,14] is responsible for the coexistence of metabolic replicators in this spatial model. Of course if metabolic neighborhood size is too small, then there is too small a probability to find all the necessary molecules for the metabolism within the same metabolic neighborhood. On the other hand, too large a neighborhood size averages out the inhomogeneities, and thus obliterates the advantage of rare replicator types (second column of Fig. 9). Thus, if the physical environment defines a metabolic neighborhood size, then there must be a maximal number of metabolically coupled replicators which can coexist.

We have shown that selfish parasites cannot destroy this system. We have observed two different outcomes with parasites introduced into the system: (i) either the introduced parasite becomes extinct, or (ii) the parasite coexists with the cooperative molecules (Fig. 10). We can conclude from the simulation experiments that the first situation emerges when the number of coexisting replicators is at the maximum for a given neighborhood size. Then the parasite could not find all the cooperative replicators in its metabolic neighborhood, and thus it dies out. The invading parasite persists only if it has a reasonable chance to find all the metabolically active replicators nearby. This is the case when the number of coexisting replicators is smaller than the maximum set by metabolic neighborhood size, so that the parasite ''fits into'' the system, without doing much harm to it. Such a coexistent parasite is free to mutate into a new member of the replication network, or even into a ''replicase.'' Thus, the parasite can be considered as a preadapted replicator that can be converted for some function useful to the whole system by further evolutionary changes.[1]

We found that the number of coexisting species was maximum three. This number, however, depends on the size of the replication and the metabolic neighborhoods, on the strength of mixing, and most importantly on the biological model we use. This limit on the maximum number of coexisting replicators was due to the fact that the metabolic model used here was a worst-case model where more replicators present require larger a metabolic neighborhood, which acts against coexistence. This model did not include the realistic beneficial effect of larger community size on metabolism, which would increase the number of coexisting species.

We observed that those areas of the parameter space where coexistence was maintained form compact, connected sets. Also, the coexistence depends only weakly on the parameters of the flow, that is, on the parameters of the environment. This means that the metabolic system, even in this worst-case form, is *resistant* to small perturbations, and small change in the parameters did not lead to the extinction of competitors, and hence to the collapse of the metabolic network. This underlines that the main effect the metabolic networks needs to maintain coexistence is the *spatial inhomogeneity*.

ACKNOWLEDGMENTS

The financial support from the OTKA (Hungarian Scientific Fund) Grant Nos. T029789, F029637, and T032423 are gratefully acknowledged. GK and IS were supported by the Bolyai Grant. GK is indebted to the Dr. Imre Korányi Fellowship of the Cholnoky Foundation.

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