

Competition and Symbiosis in a Chemical World

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A possible road for the emergence of complexity in artificial inhomogeneous chemical systems is analyzed. We build a reaction–diffusion model inspired from a surfactant-based scheme leading to the formation of micelles and vesicles. Our model only relies on autocatalysis and the existence of a critical concentration. Depending on the parameter values of the extended dynamical system, this simple model already accounts for typical behaviors of living organisms. In particular, competition and different types of symbiotic relationships are reproduced.

1. Introduction

This paper adopts the point of view of a chemical engineer to address the emergence of complex behaviors encountered in biology. Complexity is understood here along the lines of dynamical system theory. It refers to the macroscopic organization which appears spontaneously in far-from-equilibrium systems.^{1–4} Our goal is to tailor classes of molecular structures and external constraints engaged in minimal kinetic mechanisms such that the dynamical and asymptotic properties of an artificial chemical system can mimic some behaviors of living organisms.

We recently examined a road to generate elementary chemical properties assumed to be important for further development of complexity.^{5,6} Simple molecular structures, involving only two coupled reactive groups, were considered. We showed that a given kinetic mechanism, appropriate for describing two-site catalysis, exhibits various thermodynamic and kinetic properties when maintaining the system far from equilibrium and varying only the order of magnitude of the rate constants. In relation to the present account, autocatalysis and tuning of chemical composition in a steady state are the most significant results. Indeed, imposing nonequilibrium conditions in a steady state is a crucial issue to observe the emergence of organized behaviors.^{7–19} We address here this nontrivial engineering task in different physical situations.

We consider a bounded inhomogeneous medium, open to exchanges of matter with the surroundings, and containing some reactive and diffusive species. We wish to build a minimal reaction scheme reproducing various behaviors such as self-organization, growth, competition, and symbiotic relationships when changing only the parameter values, that is, rate constants of the reactions, diffusion coefficients of the chemical species, or concentrations of some species fixed by reservoirs. We intend to show that an elementary “metabolism”, compatible with rather simple molecular structures such as bifunctional molecules,^{5,6} is sufficient to generate chemical “entities” whose interactions determine complex macroscopic behaviors observed in archaic

living organisms. Such chemical entities may be related to autopoietic units that were defined as structures self-maintaining by means of processes that occur within their boundary (a bilayer for instance).^{20,21} Artificial systems based on surfactants leading to the autocatalytic formation of micelles and vesicles were already investigated as possible autopoietic units, both experimentally and theoretically.^{20,22–36} Other related systems exhibiting multimer catalysis were also reported.^{37–48} An account dealing with the competition between vesicles recently appeared in the literature.⁴⁹ The chemical entities considered in this work also have an autocatalytic growth but, in contrast to autopoietic units, they do not exhibit any physical boundary.

The paper is organized as follows. Our generic model is introduced in section 2. Section 3 provides the analytical results obtained either in the case of a homogeneous system or in a finite inhomogeneous medium. The decrease of the diffusion coefficient accompanying the formation of large assemblies is suggested to play an essential role in the ability of a chemical entity to survive. The kinetic scheme is refined in section 4 to include the description of various types of behaviors such as competition and symbiotic relationships between different entities. The conclusions are given in section 5.

2. Presentation of the Model

We wish to mimic nontrivial behaviors observed in living systems, known to be able to self-organize in a permanent regime by opposition to a transient. Sustaining a system in such an organized state requires absorption of food or solar light irradiation that maintains the system far from equilibrium. Depending on the value of control parameters, the asymptotic behavior of nonequilibrium systems may change in the vicinity of so-called bifurcations. Here, we introduce a model able to describe how the concentration in a chemical precursor can control the localized emergence of an explosive evolution. Explosion is characterized by a long induction period followed by a sudden increase of the product concentration toward a stationary state. Hence, an explosive evolution is first slow but then becomes very fast. This type of behavior is typically observed in the presence of autocatalytic reactions such as chain reactions. The name of explosion has been chosen in reference to combustion where many chain reactions begin with the

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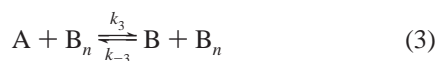
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difficult production of radicals, which then facilitates further production of other radicals. More generally, explosive behavior is observed in the vicinity of a bifurcation associated with bistability. Such a system may possess either two simultaneously stable stationary states of respectively low and high concentration of product or a single stable stationary state of high concentration. In the first case (two stable stationary states), the final state of the system depends on the initial condition. Here, the initial concentration of product obviously vanishes and the system relaxes toward the stationary state of low concentration of product. In the second case (a single stable stationary state of high concentration) the system first evolves slowly before suddenly reaching the stationary state of high concentration.

In relation to this goal, we have been interested in surfactant-based chemical schemes accounting for the formation of micelles and vesicles.^{20,22–32} A simple kinetic model leading to the autocatalytic formation of micelles B_n from a precursor A can be written as^{20,23,24,31,32}



The rate constant associated with forward (respectively backward) reaction (i) is denoted by k_i (respectively k_{-i}). Reaction of A produces the monomeric amphiphiles B at a slow rate, k_1 . Then B monomers rapidly aggregate to form micelles B_n . As soon as micelles are present, they catalyze the formation of monomers B through step (3) associated with rate constant k_3 . Steps (2)–(3) generate autocatalysis since the formation of new micelles is ultimately accelerated by the presence of micelles. Note that the mechanism (1–3) does not picture microscopic events. In particular, the observed nonlinear kinetics has been shown experimentally to be a consequence of phase transfer mediated by a complex between A and the micelle B_n rather than a standard micellar catalysis.^{26–30} In addition, the average number of caprylate monomers per micelle, predicted by molecular thermodynamic theory or determined experimentally,^{26–30} is larger than 20. Such high values of n obviously preclude consideration of step (2) as an elementary process. Nevertheless, it has been shown that more realistic kinetic models, involving elementary processes based on binary collisions between intermediate chemical species B_j with $1 \leq j < n$, may be reduced to the three steps (1), (2), and (3).^{31,32}

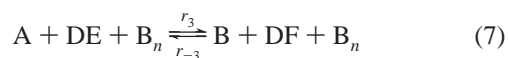
Mechanism (1–3) is a good starting point for the present purpose, that is, using the concentration of precursor A as a control parameter, to determine if the reaction is explosive. Indeed reactions (2) and (3) give rise for $n \geq 2$ to some critical concentration in A above which an autopoietic species B_n develops.^{50,51} Beyond its relevance to model the hydrolysis of esters, this kinetic mechanism could also describe the synthesis of polyfunctional polymers B_n from monomers B, resulting from activation of the monomers A; we already demonstrated that autocatalytic explosive behaviors can be observed when bifunctional molecules are involved.^{5,6} Admitting that species B_n is initially absent from the medium, a small variation of the control parameter A can result, either in the relaxation toward the low-concentration stationary state or in an explosion toward the high concentration stationary state. However, in mechanism

(1–3), detailed balance imposes the following relation between the rate constants of reactions (1) and (3):

$$\frac{k_1}{k_{-1}} = \frac{k_3}{k_{-3}} \quad (4)$$

To enable the stabilization of the chemical system in a nonequilibrium steady state, we need to introduce appropriate constraints violating the detailed-balance condition given in eq 4. Imposing a constant concentration for A is not sufficient to prevent the system from relaxing toward an equilibrium state. It is therefore necessary to control the rate constant values of some reactions. In our model, the forward reactions (1) and (3) are viewed as activation steps accounting for the capability of the chemical entities to extract free energy from the surroundings.⁵² Then, we consider that the standard Gibbs free energies of reactions (1) and (3) are large enough to neglect the formation of B in the absence of a suitable excitation. Under such conditions, we assume in agreement with Hammond's postulate that k_1 and k_3 are extremely small whereas k_{-1} and k_{-3} are extremely large. The low values of k_1 and k_3 are keys to allow for controlling the rates of the forward reactions (1) and (3).

In relation to scenarios of prebiological chemistry,^{53–57} we envisage two different approaches to maintain the system far from equilibrium in a steady state. First, light can be invoked to control the values of the apparent rate constants of the forward reactions (1) and (3). We may admit that, like for photosynthesis, these values are only significant in the presence of an appropriate light source. Under such circumstances, one can easily imagine that medium effects may determine different apparent rate constants of the forward reactions (1) and (3). We already illustrated this strategy in a previous account.⁵ An alternative solution consists of introducing two-site catalysts and reservoirs maintaining constant the concentration of some reactants E and F involved in a “driving” reaction.^{5,6} In the present biological context, ATP and ADP are relevant species for this driving purpose.⁵⁸ One site of a first catalyst C is supposed to be engaged in the reaction of interest, here reaction (1), whereas species E and F act on the second site according to reactions $C + E \rightleftharpoons CE$ and $C + F \rightleftharpoons CF$. Under favorable kinetic conditions, the choice of the concentration of E allows us to control the concentration of species CE and consequently the rate constant value of forward reaction (1).^{5,6} Similarly, we admit that a catalyst, D, with one site engaged in reaction (3), possesses also a site able to react with the same species E and F. Violation of detailed balance requires that D is different from C. From a chemical point of view, it is not necessary to assume that D and C are markedly different catalysts. The kinetic mechanism may be written as



It formally reduces to mechanism (1–3) after introduction of the following apparent rate constants $k_1 \approx r_1 CE$, $k_2 = r_2$, $k_{-2} = r_{-2}$, $k_3 \approx r_3 DE$ where we neglect the noncatalyzed forward reactions (1) and (3). On the contrary, we neglect the catalyzed backward reactions (5) and (7); that is, we choose for instance a sufficiently small concentration for F so that $r_{-1}CF \ll k_{-1}$

and $r_{-3}DF \ll k_{-3}$. Hence, the rate constants of the backward reactions (5) and (7) are independent of the presence of a catalyst. As soon as CE/DE differs from $k_{-1}r_3/(r_1k_{-3})$, the apparent rate constant values violate the detailed-balance condition expressed by eq 4. The importance of this property will be pointed out in the next section when discussing the emergence of bistability in the system.

Except in subsection 3.1, we admit that only small active zones of the medium are illuminated or contain fixed catalysts C and D coupled to reservoirs of species E and F. Consequently, the forward reactions (1) and (3) occur only specifically in space. Outside these active zones, the system is supposed to be in the darkness or deprived of catalysts C and D: the rate constants k_1 and k_3 identify to the extremely small spontaneous rate constants and are neglected. The other rate constants are identical in the entire medium.

Our goal is to build a minimal kinetic scheme capturing the essential features of the phenomenon. All the chemical specificities, which are not absolutely necessary to understand the phenomenon, are ignored. In this respect, the explosive character of the model is already included in the kinetic model for $n = 2$. Higher values of n simply increase the nonlinearities of the model and the suddenness of the evolution toward the final steady state. In the following we consequently impose $n = 2$.

3. Results for a Single Chemical Entity

3.1. Model Behavior in a Homogeneous System in Contact with a Reservoir of Precursor. We assume in this subsection that the forward reactions (1) and (3) may occur everywhere in the medium thanks to the presence of light or catalysts C and D coupled to reservoirs of species E and F. Moreover, we admit that the concentration of precursor A is fixed at a given value at every point of the system. This condition implies that the system is in contact with an ideal reservoir: concentration changes in A governed by reactions (1) and (3) have to be much slower than those originating from direct exchanges of matter with the reservoir and from stirring or diffusion. Then consumption/production of A can be considered as instantaneously balanced by infinitely fast exchanges with the reservoir, allowing us to consider the medium as homogeneous in A. We also assume here that species B and B_n are homogeneously spread in the medium.

Choosing $n = 2$ in a homogeneous medium allows us to extract basic properties of the phenomenon thanks to an elementary analytical approach. Nevertheless, we shall see in the next subsection that this approximation is an oversimplification in the case of an inhomogeneous medium where transport by diffusion becomes essential. With the admission that the three steps ((1)–(3)) can be considered as elementary processes at the chosen level of description, the evolution of monomer concentration, B (respectively, dimer concentration, B_2) reduces to

$$\frac{dB}{dt} = k_1A - k_{-1}B - 2k_2B^2 + 2k_{-2}B_2 + k_3AB_2 - k_{-3}BB_2 \quad (8)$$

$$\frac{dB_2}{dt} = k_2B^2 - k_{-2}B_2 \quad (9)$$

We are interested in the asymptotic state reached by the system in the large time limit. Note that the different constraints prevent the relaxation of the system toward chemical equilibrium. Moreover, since eqs 8 and 9 are nonlinear, the unicity of the stationary state is not ensured. The nonequilibrium stationary states obey

$$-b^3 + qb^2 - b + qp = 0 \quad (10)$$

$$B_2 = \frac{k_{-1}}{k_{-3}}b^2 \quad (11)$$

with

$$\begin{aligned} b &= \sqrt{\frac{k_{-3}k_2}{k_{-1}k_{-2}}}B \\ p &= \frac{k_1k_{-3}}{k_{-1}k_3} \\ q &= k_3A\sqrt{\frac{k_2}{k_{-1}k_{-2}k_{-3}}} \end{aligned} \quad (12)$$

Then the problem reduces to defining the conditions of existence of real solutions to a cubic equation, like for example in the one-variable model introduced by Schlögl.⁵⁹

Originally, the Schlögl model was built to study the analogies between the liquid–gas transition and bistability in an out-of-equilibrium chemical system. The parameter values $p = 1/9$ and $q = \sqrt{3}$ define the so-called triple point used in reference to the terminology of equilibrium phase transition. If $p < 1/9$ and $q > \sqrt{3}$, eq 10 may admit three real solutions, two of them being stable and the third one being unstable.⁵⁹ More precisely, the bistable domain is defined by $p < 1/9$ and $q_1(p) < q < q_c(p)$ with $-2q_1^3 - 2q_1^2\sqrt{q_1^2-3} + 9q_1(1-3p) + 6\sqrt{q_1^2-3} = 0$ and $-2q_c^3 + 2q_c^2\sqrt{q_c^2-3} + 9q_c(1-3p) - 6\sqrt{q_c^2-3} = 0$. For $q < q_1(p)$, the system possesses a single stationary state associated with a low concentration for B and B_2 . Starting from a vanishing (or low) concentration of B and B_2 , the explosive behavior is observed outside the bistable domain, for $q > q_c(p)$, when the system possesses a single stationary state associated with a large concentration for B_2 . Using the expression of parameter p given in eq 12, we deduce that the condition

$$p = \frac{k_1k_{-3}}{k_{-1}k_3} < \frac{1}{9} \quad (13)$$

requires that the apparent rate constants do violate detailed balance expressed by eq 4 to observe explosive behavior. The conditions of existence of the latter⁵⁹ also impose

$$q > q_c \sim \frac{1}{2\sqrt{p}}$$

With use of eq 12, this relation yields

$$A > A_c \sim \frac{k_{-1}}{2} \sqrt{\frac{k_{-2}}{k_1k_2k_3}} \quad (14)$$

where A_c is the critical concentration of the precursor.

In conclusion, if we admit that B and B_2 are initially absent from the medium, the behavior of the system will be completely different depending on whether A is slightly smaller or slightly greater than the threshold A_c : In the first case, the system is bistable and the initial conditions lead to the selection of the stationary state associated with a low value of B and B_2 . In the second case, the system admits a single stationary state associated with a large value of B_2 . The dynamic behavior is explosive: a long induction period precedes the sudden increase of B_2 and its approach to the stationary state. The duration of

the induction time increases as the distance ($A - A_c$) from the bifurcation decreases: this phenomenon is the analogue of critical slowing down observed in equilibrium transitions.^{60,61}

3.2. Model Behavior in a Finite Inhomogeneous Medium in Contact with Reservoirs of Precursor at Its Boundaries.

In contrast to the situation encountered in the preceding subsection, we do not assume that the reservoirs are able to maintain constant the concentrations in precursor A in each point of the medium. We consider now a finite one-dimensional (1d) medium of length L , bounded with two reservoirs, fixing only the concentrations of A at its boundaries. Transport of A in the medium is assumed to be controlled by diffusion. We wish here to study the effects of the diffusion-limited response time of the reservoirs. To this goal, we assume that the free energy-extracting forward reactions (1) and (3) only occur in an active small zone of length $l \ll L$ that is supposed to be located in the middle of the medium. This small active zone corresponds to sites permanently irradiated by light or to the location of the catalysts C and D. Diffusion of A from the boundaries toward the active zone where it is consumed can now be rate-limiting.

At all time t , we impose the following boundary conditions

$$A(x=0, t) = A(x=L, t) = A_0 \quad (15)$$

$$B(x=0, t) = B(x=L, t) = B_2(x=0, t) = B_2(x=L, t) = 0 \quad (16)$$

Initially, the medium is supposed to be homogeneous and filled with A at the same concentration A_0 as in the reservoirs. The initial condition reads

$$A(x, t=0) = A_0, \quad B(x, t=0) = B_2(x, t=0) = 0 \quad (17)$$

The system now possesses three dynamical variables, $A(x, t)$, $B(x, t)$, and $B_2(x, t)$ which vary with space x and time t according to

$$\frac{\partial A}{\partial t} = -k_1 A + k_{-1} B - k_3 A B_2 + k_{-3} B B_2 + D \frac{\partial^2 A}{\partial x^2} \quad (18)$$

$$\frac{\partial B}{\partial t} = k_1 A - k_{-1} B - 2k_2 B^2 + 2k_{-2} B_2 + k_3 A B_2 - k_{-3} B B_2 + D \frac{\partial^2 B}{\partial x^2} \quad (19)$$

$$\frac{\partial B_2}{\partial t} = k_2 B^2 - k_{-2} B_2 + D_2 \frac{\partial^2 B_2}{\partial x^2} \quad (20)$$

where molecules A and B, of comparable size, are supposed to diffuse with the same coefficient D , and where the diffusion coefficient of B_2 is D_2 . Note that the rate constants k_1 and k_3 vanish except in a small active zone. Equations 18–20 are numerically solved after suitable discretization of space and time. We introduce the dimensionless discrete variables $i = x/\Delta x$ and $s = t/\Delta t$, where Δx is the length of a spatial cell and Δt is the integration time step. Equations 18–20 yield

$$A(i, s+1) = A(i, s) - \kappa_1 A(i, s) + \kappa_{-1} B(i, s) - \kappa_3 A(i, s) B_2(i, s) + \kappa_{-3} B(i, s) B_2(i, s) + d(A(i+1, s) + A(i-1, s) - 2A(i, s)) \quad (21)$$

$$B(i, s+1) = B(i, s) + \kappa_1 A(i, s) - \kappa_{-1} B(i, s) - 2\kappa_2 B(i, s)^2 + 2\kappa_{-2} B_2(i, s) + \kappa_3 A(i, s) B_2(i, s) - \kappa_{-3} B(i, s) B_2(i, s) + d(B(i+1, s) + B(i-1, s) - 2B(i, s)) \quad (22)$$

$$B_2(i, s+1) = B_2(i, s) + \kappa_2 B(i, s)^2 - \kappa_{-2} B_2(i, s) + d_2(B_2(i+1, s) + B_2(i-1, s) - 2B_2(i, s)) \quad (23)$$

where the reduced parameters obey $\kappa_i = k_i \Delta t$, $d = D(\Delta t/(\Delta x)^2)$, and $d_2 = D_2(\Delta t/(\Delta x)^2)$. Equations 21–23 are integrated over a sufficiently large time to reach the asymptotic stationary state. For the values of the reduced rate constants chosen, we integrated the equations over 2×10^6 time steps. Convergence of the finite-difference integration scheme is ensured for reduced rate constant values smaller than $A_0 = 1$ and reduced diffusion coefficient smaller than 0.5. In the case of pure diffusion and in a one-dimensional system, the critical value $d = 0.5$ is easily found by imposing that the numerical coefficient $(1 - 2d)$ of the concentration in cell i must be positive.⁶² We checked by doubling the number of cells of the medium that the final state is independent of system size: the height and the width of the stationary profiles are intrinsic properties of the reaction and diffusion processes considered; they do not depend on medium length provided it is sufficiently large.

In the steady state, the model now gives rise to the formation of a spatial singularity both in its composition and in its organization as shown in Figure 1. In the following, we define as a chemical entity (or organism) a set of reactive species resulting from the medium-dependent expression of a chemical mechanism (or metabolism) involving given values of the rate constants. In the present context, the chemical mechanism (1–3) expresses itself as a well-defined entity $\epsilon_{(1-3)}$ whose size and composition depend on the reservoir concentration A_0 . The features of $\epsilon_{(1-3)}$ crucially depend on whether A_0 is smaller or larger than the critical concentration defined in eq 14. When $A_0 \ll A_c$, $\epsilon_{(1-3)}$ essentially contains B at a lower concentration than A_0 . Taking into account the kinetics of reactions (1)–(3) and the values of the diffusion coefficients, the critical concentration determining the formation of B_2 cannot be reached in any point of space. Then $\epsilon_{(1-3)}$ mainly results from realization of reaction (1). In contrast, $\epsilon_{(1-3)}$ is predominantly made of B_2 at a concentration that can be larger than A_0 when $A_0 \gg A_c$. All the reactions (1)–(3) now participate in the emergence and growth of entity $\epsilon_{(1-3)}$. In reference to biology, entity $\epsilon_{(1-3)}$ can be considered as a phenotypic expression of the metabolism (1–3).

To characterize the efficiency of precursor A assimilation and the production of new chemical species B and B_2 , we are interested in the evolution of the total local concentration $C(x, t) = A(x, t) + B(x, t) + 2B_2(x, t)$. Initially, one has $C(x, t=0) = A_0$; an intuitive criterion for assimilation and growth by the entity $\epsilon_{(1-3)}$ is thus

$$C(x, t \rightarrow \infty) > A_0 \text{ for all } x \quad (24)$$

Actually, condition (24) measures to which extent the reservoir of the precursor has been prompted by the system to cause the formation of the products of the metabolism (1–3). Using eqs 18–20 and looking for stationary solutions for C yields

$$D \frac{\partial^2 A(x, t \rightarrow \infty)}{\partial x^2} + D \frac{\partial^2 B(x, t \rightarrow \infty)}{\partial x^2} + 2D_2 \frac{\partial^2 B_2(x, t \rightarrow \infty)}{\partial x^2} = 0 \quad (25)$$

or equivalently

$$DA(x, t \rightarrow \infty) + DB(x, t \rightarrow \infty) + 2D_2 B_2(x, t \rightarrow \infty) = \alpha x + \beta \quad (26)$$

where the value of the two constants α and β follows from the

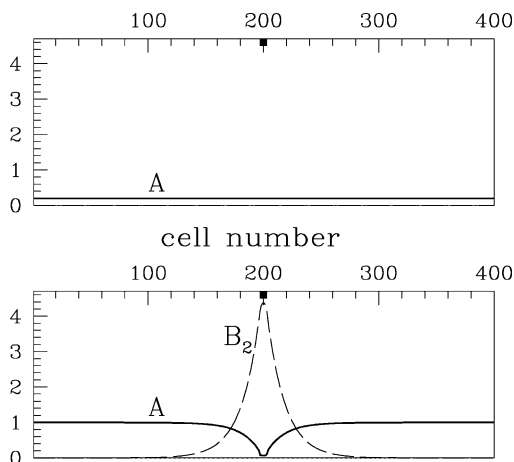


Figure 1. Emergence of an environment-dependent entity $\epsilon_{(1-3)}$. Stationary concentration profiles for chemical species A (thick, solid line) and B_2 (thin, dashed line). Forward reactions (1) and (3) only take place in spatial cells 197–203. The parameter values are the following: $\kappa_1 = 0.00008$ and $\kappa_3 = 0.1$ in the active cells (κ_1 and κ_3 vanish elsewhere), $\kappa_{-1} = 0.1$, $\kappa_{-3} = 0.1$, $\kappa_2 = 0.25$, $\kappa_{-2} = 0.00004$ in each cell ($A_c = 0.22$); $d = 0.1$, $d_2 = 0.01$; $A_0 = 0.2$ (top) or $A_0 = 1$ (bottom).

boundary conditions given in eq 15. It reads $\alpha = 0$ and $\beta = DA_0$, so that eq 26 yields

$$C(x, t \rightarrow \infty) = A_0 + 2 \frac{D - D_2}{D} B_2(x, t \rightarrow \infty) \quad (27)$$

Then the criterion for precursor assimilation defined in eq 24 reduces to

$$D > D_2 \quad (28)$$

expressing that the assembly B_2 has to diffuse more slowly than the small molecules A and B. It is to note that essential properties of reactions (1)–(3), like rate constant values, do not enter into condition (28). The feature which reveals to be fundamental in precursor assimilation and growth of $\epsilon_{(1-3)}$ is thus the formation of large assemblies in relation to the modification of the transport properties it implies. From the latter point of view, the formation of micelles or vesicles from monomeric lipids, or of polyfunctional polymers from suitable monomers, is especially favorable. Hence, the role played by spatial inhomogeneities in the liquid phase appears crucial and condition (28) justifies a posteriori the introduction of the spatial description of the system. We have seen in section 2 that choosing $n = 2$ preserves the explosive character of the chemical scheme. The choice $n = 2$ remains acceptable in an inhomogeneous medium only if one admits that condition (28) is obeyed. In the following, we keep in mind that chemical species B_2 represents a large assembly diffusing considerably less than the species exhibiting the corresponding stoichiometry and we impose $D_2 = D/10$.

We now use the simplicity of the model retained to deduce some analytical properties of the concentration profile of the entity $\epsilon_{(1-3)}$ reached in the limit of large time. When $A_0 < A_c$, entity $\epsilon_{(1-3)}$ essentially contains species B. An upper bound for the concentration of B reached in the middle of the active area at abscissa x_M can be derived using eq 26. We find

$$B(x_M, t \rightarrow \infty) \leq A_0 \quad (29)$$

The profile width $w_{A_0 < A_c}$ of entity $\epsilon_{(1-3)}$ is determined by the

chemical relaxation of B. The latter is essentially governed by reaction (1) whose characteristic time is $\tau_1 = 1/(k_1 + k_{-1})$:

$$w_{A_0 < A_c} = \sqrt{2D\tau_1} \quad (30)$$

In contrast, when $A_0 > A_c$, entity $\epsilon_{(1-3)}$ essentially contains species B_2 . Again eq 26 can be used to derive an upper bound for the concentration of B_2 reached in the middle of the active area at abscissa x_M . It yields

$$B_2(x_M, t \rightarrow \infty) \leq \frac{D}{2D_2} A_0 \quad (31)$$

The profile width $w_{A_0 > A_c}$ of entity $\epsilon_{(1-3)}$ is now determined by the chemical relaxation of B_2 associated with a characteristic time τ_{B_2} :

$$w_{A_0 > A_c} = \sqrt{2D_2\tau_{B_2}} \quad (32)$$

For typical rate constants the backward reaction (2) is the limiting process and one has $\tau_{B_2} \sim 1/k_{-2}$.

Up to now, the numerical calculations were performed with nondimensional values of the concentrations, rate constants, and diffusion coefficients. In a purpose of engineering, it is necessary to evaluate whether the preceding theoretical behavior could be observed in the physical world. The assumption that diffusion controls transport of matter in the inhomogeneous situation implies that L is typically lower than 1 mm for most liquids at room temperature; in fact, one expects other mixing processes such as convection to act beyond that range.⁶³ Taking 10^{-10} – 10^{-9} m² s⁻¹ as a typical order of magnitude for the diffusion coefficient D of a chemical species, the time $\tau_{\text{dif}} \sim L^2/D$ that is required for homogenization by diffusion over the whole medium can be up to the hour range. This derivation can be significant to address the issue of violating detailed balance with the use of reservoirs of species E and F. In fact, it does not exert any constraint if $\epsilon_{(1-3)}$ is autotrophic, that is, the entity is capable of photosynthesis, so that the realization of forward reaction (1) directly results from light absorption. In contrast, τ_{dif} is necessarily the lower limit of the relaxation time of the out-of-equilibrium chemical reaction $E \rightleftharpoons F$ determining the emergence of an heterotrophic entity $\epsilon_{(1-3)}$, if E and F are located together with the nutrient A in the reservoirs at the boundaries. Otherwise, extracting free energy from the out-of-equilibrium process $E \rightleftharpoons F$ would be impossible. Using eqs 30 and 32, it is also possible to estimate the characteristic size of the entity $\epsilon_{(1-3)}$. Taking again $D \sim 10^{-10}$ – 10^{-9} m² s⁻¹, one interestingly obtains the biologically relevant 10- μ m range for a chemical relaxation time of $\epsilon_{(1-3)}$ equal to 1 s.

4. Results for Two Interacting Chemical Entities

We now assume that the medium contains two different active zones, AZ and AZ', respectively containing close but different couples of catalysts (C, D) and (C', D'). Depending on the catalysts, we admit that different entities can be formed from A. They are associated with similar metabolisms obeying reactions (1)–(3), but differ by the nature of the chemical species produced, the values of the apparent rate constants, and/or the diffusion coefficients. In such a model, the catalysts play the role of expression-determining components. For concreteness, a (C, D)-containing active zone, located in the left part of the 1d-medium, is supposed to determine the emergence of entity $\epsilon_{(1-3)}$, made of B and B_2 . Similarly a (C', D')-containing active zone, located in the right part, leads to the formation of

TABLE 1: Different Types of Relationships between Two Organisms (+, Favorable Effect; −, Unfavorable Effect, 0, No Effect)^{64,65}

organism 1	organism 2	interaction type
+	+	mutualism
+	0	commensalism
+	−	parasitism (including predation)
0	0	neutralism
0	−	amensalism
−	−	antagonism (including competition)

entity $\epsilon'_{(1-3)}$, made of B' and B'_2 . To make easier the interpretation of individual entities, we do not consider here the formation of chimeric species $B_i B'_j$ (an example related to lichens is given in the Supporting Information). Indeed, the point we wish to examine is the interaction between entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$ originating either from competition for the precursor A (competition for “food”) or from symbiosis.

Some parameter values and conditions are common to the different situations envisaged in Figures 2, 3, 5, and 7–10. In particular, we consider a 1d medium of 400 cells so that $k_1 = k_3 = 0$ (respectively, $k'_1 = k'_3 = 0$) everywhere except in the left-hand (respectively, right-hand) small active zone of length $l = 7$ cells. In the top figures, 194 cells separate the two active zones, considered as independent for the parameter values chosen. In the bottom figures, the two active zones are separated by only 10 cells. Equations 21–23 are numerically integrated over a sufficiently large time to reach the asymptotic stationary state. We checked again by doubling the number of cells of the medium that the final state is independent of system size: the height and the width of the stationary profiles are intrinsic properties of the reaction and diffusion processes considered; they do not depend on medium length provided it is sufficiently large.

4.1. Interaction by Competition for a Common Precursor.

Competition is a type of organism–organism interaction which can be either between members of the same species or between members of different species. The relationship occurs when commodities such as food are scarce. For the sake of simplicity, competitive behaviors have been classified in different types given in Table 1.⁶⁴ Natural phenomena offer continuous variations between different types of behaviors and the properties of a given class can be seen as caricatural features of natural behaviors. In the most common case, all the members of the relationship are harmed by the competition; one speaks of antagonism between the different organisms.

Figure 2 illustrates interaction between two identical chemical entities. The height of the two stationary profiles of B_2 and B'_2 decreases when bringing closer the two active zones. Figure 2 offers consequently an example of antagonism between the two entities. Clearly, competition could not be studied in a homogeneous medium or when precursor consumption is neglected. Competition originates here from the finite speed of precursor diffusion. The critical value given in eq 14 determined in the case of a constant precursor concentration gives an estimate of the actual critical threshold in an inhomogeneous medium. For the rate constant values chosen in Figure 2, the prediction given by eq 14 underestimates the actual critical value by about 50%. Figures 3 and 4 display interaction between two different entities. For the parameter values chosen, the antagonism is not strong and the behavior is close to neutralism: bringing closer the two active zones does not sensitively change the heights of the peaks represented in Figure 3 but it increases nevertheless the duration of the transient as shown in Figure 4.

As already pointed out, the competition behavior does not depend on whether the entities are identical or not. Much more

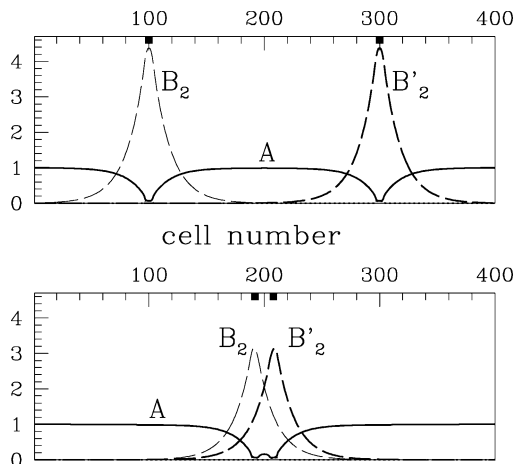


Figure 2. Antagonism due to competition between identical entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Stationary concentration profiles for chemical species A (thick, solid line), B (thin, dotted line), B_2 (thin, dashed line), B' (thick, dotted line), and B'_2 (thick, dashed line). The concentrations of B and B' are too small to be visualized at the scale of the figure. Spatial cells 97–103 and 297–303 (respectively, 189–195 and 205–211) are continuously active in the top (respectively, bottom) figure. The parameter values are the following: $\kappa_1 = 0.00008$ and $\kappa_3 = 0.1$ in the active cells of the left half (κ_1 and κ_3 vanish elsewhere), $\kappa'_1 = 0.00008$ and $\kappa'_3 = 0.1$ in the active cells of the right half (κ'_1 and κ'_3 vanish elsewhere), $\kappa_{-1} = \kappa'_{-1} = 0.1$, $\kappa_{-3} = \kappa'_{-3} = 0.1$, $\kappa_2 = \kappa'_2 = 0.25$, $\kappa_{-2} = \kappa'_{-2} = 0.00004$ in each cell ($A_c = A'_c = 0.22$); $d = 0.1$, $d_2 = 0.01$, $A_0 = 1$.

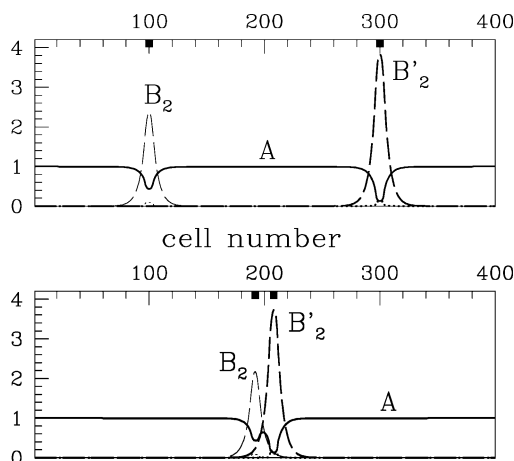


Figure 3. Antagonism close to neutralism between different entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Same caption as Figure 2 except for $\kappa_1 = 0.0005$, $\kappa'_1 = 0.00015$, $\kappa_3 = 0.03$, $\kappa_{-2} = \kappa'_{-2} = 0.0004$ ($A_c = A'_c = 0.52$).

significant is its dependence on the distance from the critical conditions for emergence of the entities. Competition was low in Figures 3 and 4 because conditions rather far from criticality and small diffusion coefficients of chemical species B_2 and B'_2 were chosen. In contrast, Figure 5 explores conditions close to criticality that mimic either an “oligotrophic” system in which the precursor is in low supply or the behavior of entities is rather unsuited to their environment. When the two active zones are far from each other, the two stationary peaks look identical. When the two active zones are close, the left-hand entity $\epsilon_{(1-3)}$, only slightly closer to criticality, disappears while the right-hand entity $\epsilon'_{(1-3)}$ survives and keeps the same properties as in the absence of interaction. This behavior illustrates a type of relationship different from antagonism. The latter is called amensalism in biology: one of the organisms suffers from the interaction whereas the other one is not affected, neither positively nor negatively. Entity $\epsilon'_{(1-3)}$ is the first to grow. It

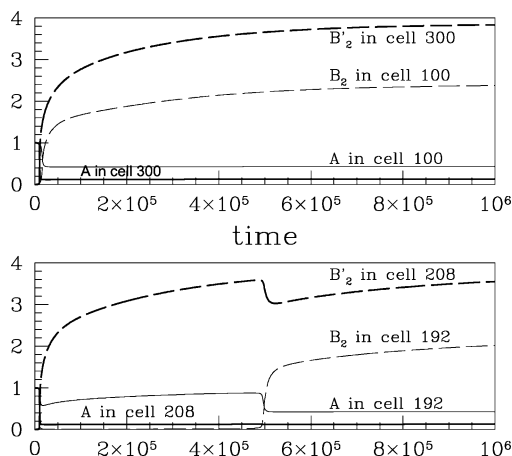


Figure 4. Antagonism close to neutralism between different entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Time evolution of concentrations for chemical species A, B_2 , and B'_2 in cells 100 and 300 for top figure (respectively, 192 and 208 for bottom) located in the middle of the active zones. Same parameter values as in Figure 3.

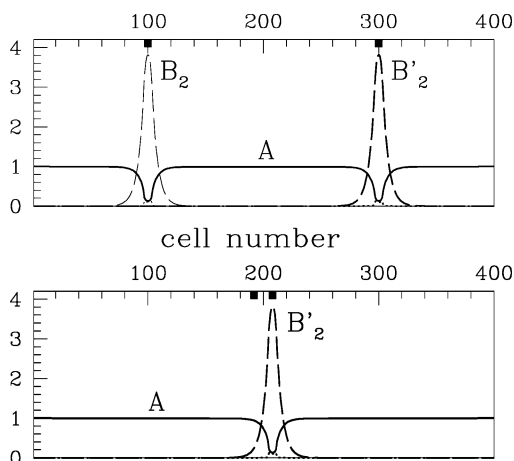


Figure 5. Amensalism between different entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Same caption as Figure 2 except for $\kappa_1 = 0.00011$, $\kappa'_1 = 0.00012$, $\kappa_{-2} = \kappa'_{-2} = 0.0004$ ($A_c = 0.60$, $A'_c = 0.57$).

consumes the precursor A so that the local concentration of the latter seen by $\epsilon_{(1-3)}$ passes under the critical threshold A_c , preventing the growth of chemical species B and B_2 , that is, the growth of the entity $\epsilon_{(1-3)}$. Entity $\epsilon'_{(1-3)}$ possesses traits, here the values of its rate constants, which are only a little more favorable to precursor assimilation. This slightly better adaptation to the environment is decisive here, in the absence of any entity at initial time.

The competition could lead to different results if one entity pre-existed before the appearance of a new active zone in its neighborhood. Then, the “older” entity could survive only because it first consumed the precursor A, preventing the “younger” entity from developing, even if the latter possessed more favorable intrinsic features. This phenomenon is illustrated in Figure 6. The top figure is obtained in the case of a medium with two close active zones which appeared simultaneously as in the different figures already considered. Initially, the medium only contains A. Entity $\epsilon'_{(1-3)}$ is associated with a rate constant k'_1 slightly larger than the value of k_1 associated with entity $\epsilon_{(1-3)}$. Consequently, $\epsilon'_{(1-3)}$ first develops and consumes A. It then prevents the growth of entity $\epsilon_{(1-3)}$, as already observed in the bottom picture of Figure 5. On the contrary, the bottom picture of Figure 6 is obtained when assuming that the left-hand active zone first appears, leading to the formation of entity $\epsilon_{(1-3)}$. Under

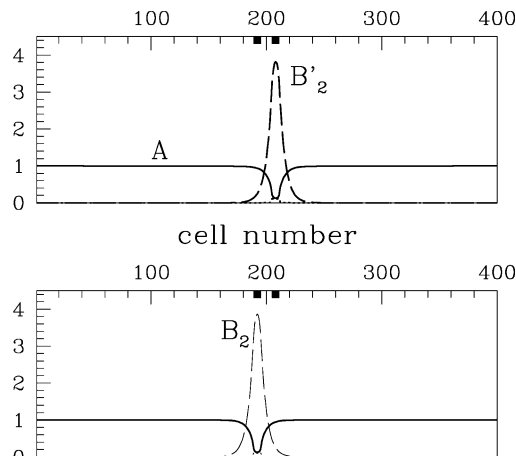


Figure 6. Role of initial conditions in the competition between entities with close properties. Same parameter values as in Figure 5 except $\kappa'_1 = 0.000111$ ($A_c = 0.6030$, $A'_c = 0.6003$). Spatial cells 189–195 and 205–211 are continuously active in the top figure, only entity $\epsilon'_{(1-3)}$ develops. In bottom figure spatial cells 189–195 are first active and entity $\epsilon_{(1-3)}$ reaches a stationary profile before spatial cells 205–211 become active; entity $\epsilon'_{(1-3)}$ never grows.

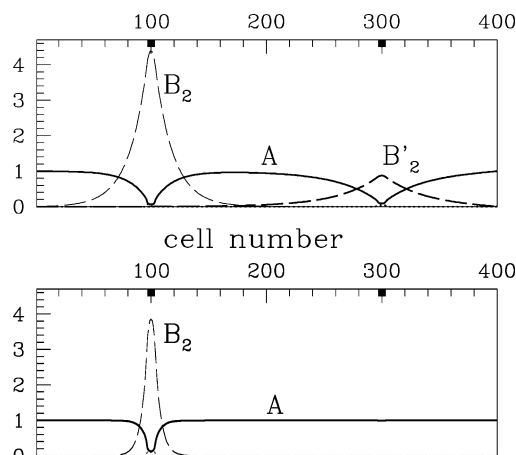


Figure 7. Role of the diffusion coefficient in the competition between different entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Parameter values are identical in the left and right half of the medium except $d_2 = 0.01$ and $d'_2 = 0.05$. $\kappa_3 = \kappa'_3 = 0.1$ in the active cells, $\kappa_{-1} = \kappa'_{-1} = 0.1$, $\kappa_{-3} = \kappa'_{-3} = 0.1$, $\kappa_2 = \kappa'_2 = 0.25$ in each cell, $d = 0.1$, $A_0 = 1$. Top figure: $\kappa_1 = \kappa'_1 = 0.00008$, $\kappa_{-2} = \kappa'_{-2} = 0.00004$ ($A_c = A'_c = 0.22$). Bottom figure: $\kappa_1 = \kappa'_1 = 0.00015$, $\kappa_{-2} = \kappa'_{-2} = 0.0004$ ($A_c = A'_c = 0.52$).

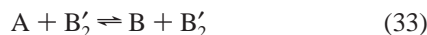
these conditions, when the right-hand zone becomes active, entity $\epsilon_{(1-3)}$ pre-exists. It remains present in the limit of large time and entity $\epsilon'_{(1-3)}$ never grows. In the vicinity of a bifurcation leading to bistability, not only the parameters determine further evolution but also the initial conditions. In reference to biology, such a behavior would imply that the intrinsic properties of a chemical entity are not sufficient to explain that it has been selected in the course of evolution. The fact that an entity first appeared may prevent the development of entities that would have nevertheless presented a better adaptation to the environment. This is a mere consequence of irreversibility in far-from-equilibrium systems.

We examine in Figure 7 the sensitivity of the dynamics to another crucial parameter, the diffusion coefficient of the assembly. We compare the peaks of chemical species B_2 and B'_2 obtained for identical values of the parameters except the diffusion coefficients D_2 and D'_2 . The results illustrate the choice of the criterion for precursor assimilation given in eq 24 and shown to be equivalent to the condition given in eq 28 for the

diffusion coefficients. The increase of the diffusion coefficient of the assembly has a dramatic effect on its formation: for the parameter values chosen in the top of Figure 7, far from the critical threshold, the amount of the most diffusive species is sensitively smaller. In the bottom figure, for parameter values close to the transition, the increase of mobility even leads to the “death” of the corresponding entity.

4.2. Symbiotic Relationships. Beyond the simple competition for the precursor A that only led to antagonism and amensalism, we now propose a slightly modified kinetic scheme directly involving cross-behaviors between the two entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. We wish to introduce the smallest number of new processes allowing us to reproduce the richness of symbiotic relationships observed in biology. By definition, symbiosis is a type of organism–organism interaction where one organism lives in intimate association with another. The commonly admitted different types of symbiotic relationships are given in Table 1.^{64,65} When the coupling between the organisms is suitable, symbiosis may favor the survival of both partners, in particular under difficult conditions. For the simple model built here, less favorable conditions correspond to a smaller diffusion coefficient for the precursor A, a smaller reservoir concentration A_0 , or a smaller value of rate constant k_1 .

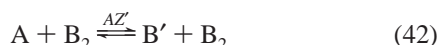
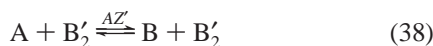
For increasing coupling between the entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$, the following fourth step is added to the kinetic scheme given in eqs 1–3:



Equation 33 expresses that species B'_2 may catalyze the formation of the monomer B; entity $\epsilon'_{(1-3)}$ contributes to the generation of $\epsilon_{(1-3)}$. We thus introduce two new parameters, the rate constants k_4 and k_{-4} associated with forward and backward reaction (33). Note that k_4 vanishes in each cell, except in the active zone of the left half of the medium. The formation of B' is similarly supposed to be catalyzed by the presence of B_2 according to



with rate constants k'_4 and k'_{-4} . Again, k'_4 vanishes everywhere, except in the active zone of the right half of the medium. Hence, the kinetic scheme reduces to



where AZ and AZ' make precise that the corresponding forward reactions only occur in the active zones, generating entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$, respectively. Backward reactions are assumed to occur everywhere.

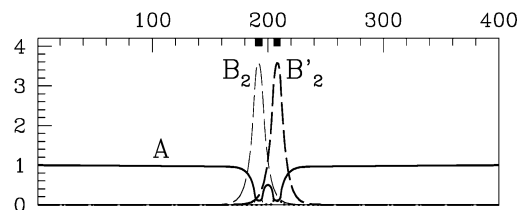
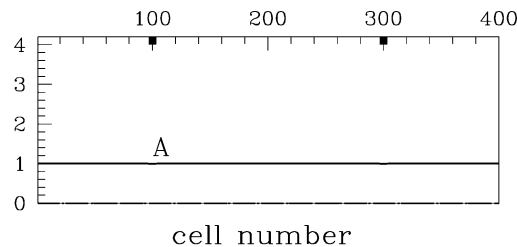


Figure 8. Mutualism between different entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Same caption as Figure 2 except for $\kappa_1 = \kappa'_1 = 0.000105$, $\kappa_{-2} = \kappa'_{-2} = 0.0004$ ($A_c = A'_c = 0.62$), and with an interaction between the two entities characterized by $\kappa_4 = 0.25$ in the active cells of the left half (κ_4 vanishes elsewhere), $\kappa_{-4} = 0.0004$, $\kappa'_4 = 0.25$ in the active cells of the right half (κ'_4 vanishes elsewhere), $\kappa'_{-4} = 0.0004$.

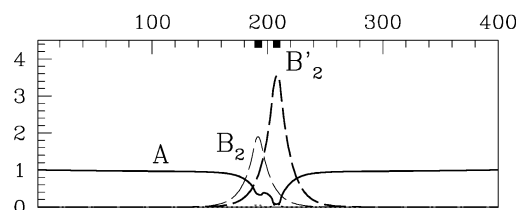
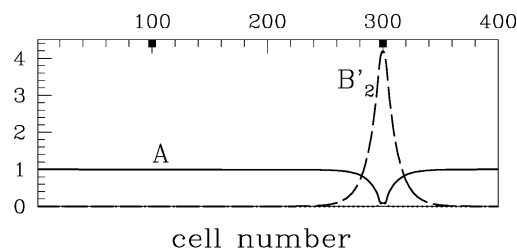


Figure 9. Parasitism between different entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Same caption as Figure 2 except for $\kappa_1 = 0.00004$, $\kappa'_1 = 0.0006$, $\kappa_3 = 0.02$, $\kappa_{-2} = \kappa'_{-2} = 0.0001$ ($A_c = 1.12$, $A'_c = 0.13$), and with an interaction between the two entities characterized by $\kappa_4 = 0.01$, $\kappa_{-4} = 0.0004$, $\kappa'_4 = 10^{-6}$, $\kappa'_{-4} = 10^{-6}$.

An example of interaction with mutual benefits is given in Figure 8. When the two active zones are far from each other, the concentrations of B and B' do not succeed in reaching the critical threshold; entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$ do not grow. When the two active zones are close, the mutual catalysis introduced with steps (38) and (42) makes the growth of both $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$ possible.

Choosing a value of k_4 different from the one of k'_4 , that is, for an asymmetric efficiency of mutual catalysis, we obtain in Figure 9 an example of parasitism. By definition, parasitism is a type of symbiosis in which one organism depends on another in close proximity for its nutrients, protection, or other life functions. The dependent member benefits from the relationship while the other one is harmed by it. Here, when the active zones are distant, that is, in the absence of interaction between the entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$, the critical threshold is not reached for the right-hand entity which does not grow, and the left-hand entity remains alone. When the two active zones are close, the right-hand entity, $\epsilon_{(1-3)}$ (the parasite), develops in the neighborhood of the left-hand one, $\epsilon'_{(1-3)}$ (the host), thanks to mutual catalysis due to step (38). $\epsilon'_{(1-3)}$ suffers from the presence

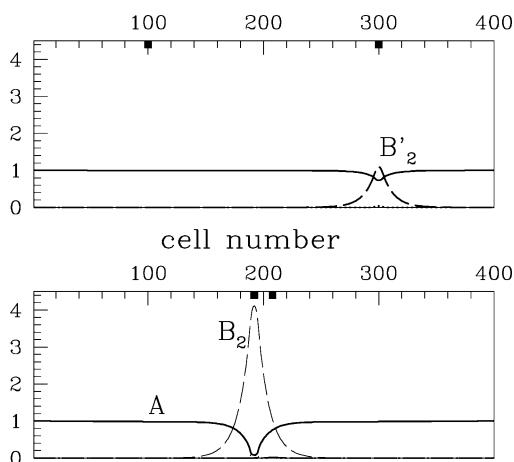


Figure 10. Parasitism with predation between different entities $\epsilon_{(1-3)}$ and $\epsilon'_{(1-3)}$. Same caption as Figure 2 except for $\kappa_1 = 0.00004$, $\kappa'_1 = 0.0005$, $\kappa'_3 = 0.011$, $\kappa_{-2} = \kappa'_{-2} = 10^{-4}$ ($A_c = 0.50$, $A'_c = 0.43$), and with an interaction between the two entities characterized by $\kappa_4 = 0.25$, $\kappa_{-4} = 0.0004$, $\kappa'_4 = 10^{-6}$, $\kappa'_{-4} = 10^{-6}$.

of the parasite in its neighborhood due to the poorer amount of precursor A available. The consequences of parasitism may be so severe that they may cause the death of the host. Such a case of parasitism with predation is given in Figure 10. Although cross-catalysis through reactions (41) and (42) favors the formation of both entities and looks mutualistic, parasitism is observed due to their underlying mutual competition for the source A. The extra success of one entity may even drive the other one to extinction.

5. Conclusion

In this paper, we have built a minimal chemical model inspired from the hydrolysis of an ester and solve the associated reaction–diffusion equations in an inhomogeneous medium maintained far from equilibrium. We show how a limited set of reactions that could involve light or multifunctional catalysts and appropriate reservoirs can lead in a steady state to the formation of a spatially well-defined chemical entity (size and shape of the concentration profile) without requiring any physical boundary like a bilayer membrane. The nature and the extent of the generated entity is strongly dependent on the reservoir concentration in its precursor. The formation of large molecules associated with small diffusion coefficients is shown to be decisive in the entity ability to grow.

Interactions between chemical entities may lead to complex evolutions analogous to typical biological behaviors. We observe that competition for reactants and cross-catalyses are efficient coupling pathways. Considering a same reaction scheme for two interacting entities, we obtain different concentration patterns resulting from symbiotic relationships including antagonism, mutualism, and parasitism when only changing the values of the rate constants of the reactions. These observations are in line with the large morphological diversity of living beings that essentially relies on unity of the constituting polyfunctional macromolecules and metabolisms. In fact, small variations around given molecular architectures do not necessarily induce major alterations of the kinetic mechanism, but may change the values of the rate constants and entirely modify the behavior of the system.

The model developed in the paper can be easily extended to the description of chimeric organisms such as lichens, that result from the mutualistic association of a fungus, not capable of

photosynthesis, and of an autotrophic organism such as an alga or a cyanobacterium. The results show how mutual helps may lead to the colonization of the environment by a chimeric entity, which would have remained localized in the absence of interaction between the host and parasite.

Acknowledgment. This paper is dedicated to the memory of André Adoutte for his illuminating perspective on biological evolution.

Supporting Information Available: Additional information and figures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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