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Emergence of Mutualism Application of a Differential Model to Endosymbiosis.

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Abstract

A population dynamics approach based on a system of differential equations allows us to establish conditions for the emergence of mutualism for cases such as coelenterates-algae symbionts. A central assumption of the model is that a host organism is able to discriminate, via some molecular recognition mechanisms, among different invading organisms and preferentially reject *parasites* rather than *bona fide symbionts*. Large differential rejection rates allow the emergence of mutualism. Different attractors of the population dynamics correspond to the emergence of mutualism, predominance of "selfish" species, or coexistence of many species.

1 Introduction

1.1 The paradox of mutualism

Mutualistic systems are known to occur in nature, e.g., lichen made of algae and fungus, corals-zooxanthellae and Hydra-Chlorella. Exchanges among the partners are beneficial for the species involved, which live together in close association. The benefits exchanged can be food, energy, protection-habitat and transport (pollination) {Boucher, James and Keeler, 1982}. According to {Begon, Harper and Townsend, 1986} most of the world's biomass is composed of mutualists: organisms in forests, meadows and corals are involved in symbiotic associations.

The emergence and stability of mutualism constitutes a paradox in terms of individual selection of the fittest. The paradox is the following: since giving food to the other symbiont should be costly for the donor, we expect the donor to be disadvantaged in terms of fitness with respect to a more selfish species which would give nothing.

The purpose of this paper is to describe a mathematical model which accepts the premises of this assertion but refutes its conclusion. An important part of the argument is that selection occurs not only at the level of individual organisms, but also at the level of their mutualistic associations.

The next section presents the elementary processes involving individual organisms. Section 3 is a summary of simulation results. We also extend the model to the case when the benefit enjoyed by endosymbionts is protection by the host. The conclusions of this study are discussed in section 4.

2 Building-up of the model

2.1 Phylogeny and interactions

The system is made of five populations, whose interactions and phylogeny are represented on Figure 1.

Populations C and B are unrelated and are not involved in any interaction with other populations. They can be considered as primeval organisms. Their respective fitnesses are γ and β . Population A differs from population B by one mutation. Population A can be considered as a *host* for populations D and E. It produces some nutrients that can be used by D or E. D is a guest of A and is a *selfish* organism, it is further called an *egoist*. It uses nutrients produced by A, but does not give anything in exchange to A. E is a *bona fide symbiont* of A. It uses nutrients produced by A and in exchange provides A with nutrients. Both D and E are called endosymbionts when they are inside A.

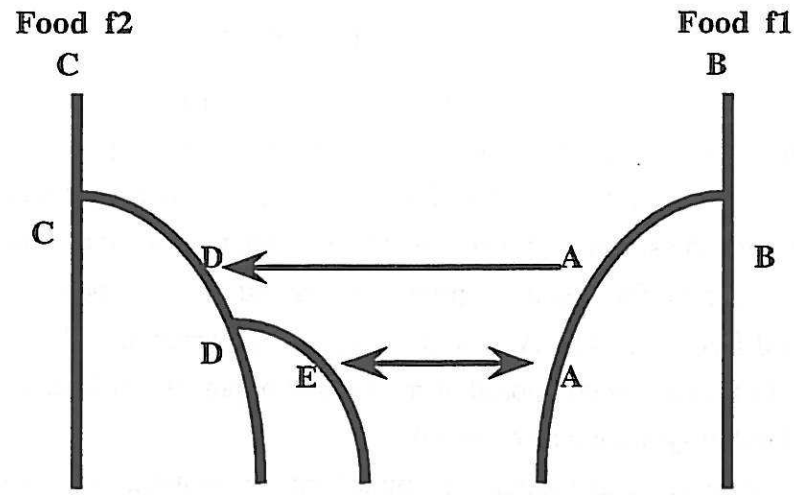


Figure 1 : Phylogeny and interactions of the 5-species system.

The organisms of the populations C, D and E use resources 2, available in quantity f_2 . The organisms of the populations A and B use resources 1, available in quantity f_1 . Horizontal arrows figure exchanges among organisms.

2.2 The elementary processes

The ecosystem is made of free organisms A, B, C, D and E and couples AE and AD, when A is infested respectively by E or D. To simplify the model, we have first supposed that the host A offers only one site where E or D are able to bind. This simplification limits the set of possible associations to couples AD and AE. Changes in population sizes are due to elementary processes represented in Figure 2. Those elementary processes are: reproduction which depends on a fitness coefficient, death which occurs with a rate d , mutation which occurs with a rate m and association and dissociation which depend on kinetic constants.

Choosing the kinetic constant of dissociation of D superior to the kinetic constant of dissociation of E ($ks_d > ks_e$) allows E to spend more time inside A than D. This results in a larger time average fitness of E. The basic hypothesis is that the host normally rejects "guests" at a certain rate, but it can somehow appreciate the degree of cooperation of E and reject it less frequently than D. This selective rejection of D might be due to some molecular recognition mechanism, which are known to exist in polypes and sponges, or simply because the increase in the level of nutrient produced by E decreases the rejection rate of E by A.

The only "advantage" of E with respect to D in this model is : $ks_e < ks_d$. We then want to check when, i.e. for what set of parameters, this condition is sufficient to overcome the advantage in fitness of D over E and bring the emergence of mutualism.

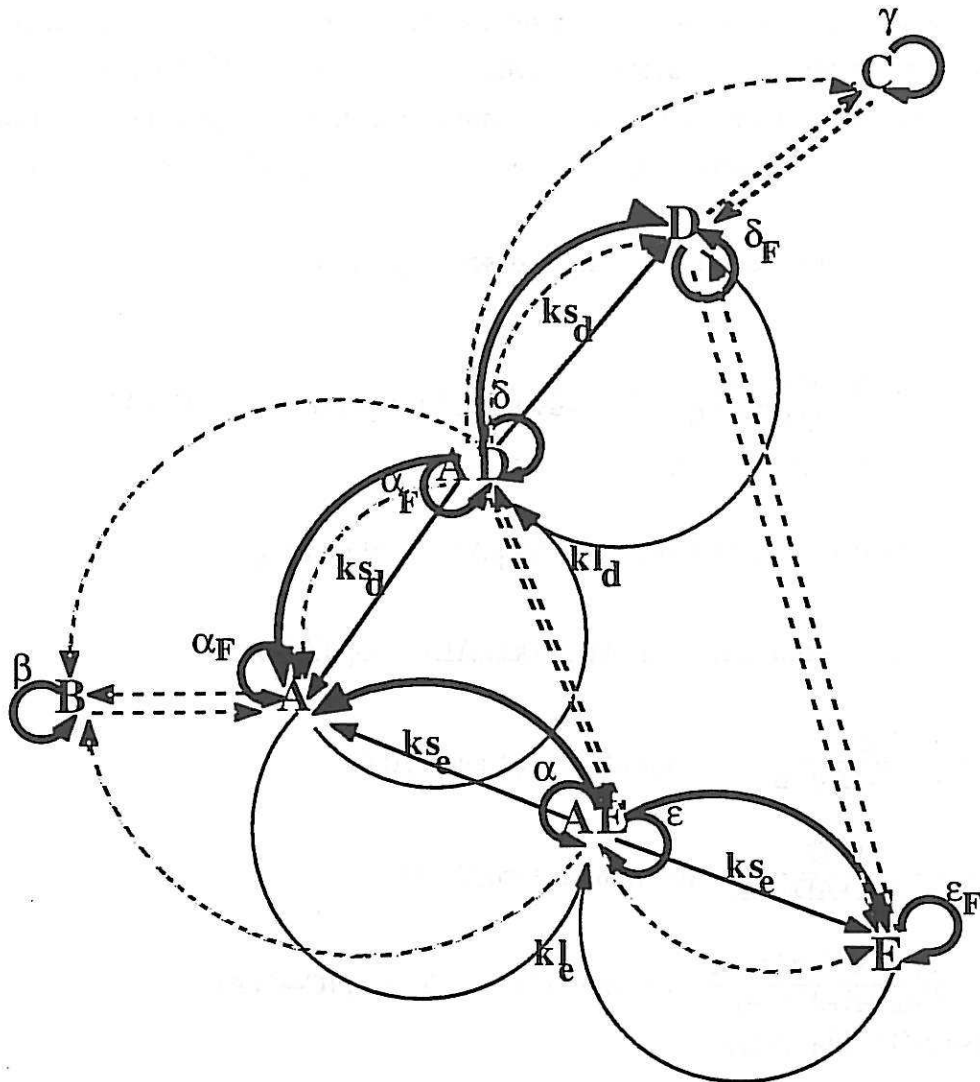


Figure 2: Set of the elementary processes that modify the populations.

Thin continuous lines represent fast association processes between hosts and guests organisms with kinetic constants k_{le} , k_{se} , and fast dissociation processes with kinetic constants k_{ld} and k_{sd} . Bold lines represent reproduction and death processes (with rate d). The greek letters represent the fitness coefficients associated with the reproduction processes of the organisms, which are either free or associated with another organism belonging to a different species. In the case of reproduction of one of the symbionts of AD or AE, the other one is liberated. For each one of AE or AD two processes can then occur. $AE \rightarrow A + AE$ (reproduction of A with fitness α); $AE \rightarrow E + AE$ (reproduction of E with fitness ϵ); $AD \rightarrow A + AD$ (reproduction of A with fitness α_F); $AD \rightarrow D + AD$ (reproduction of D with fitness δ).

3 The model

3.1 The differential system

We propose here a differential equation model introduced in {Weisbuch, 1984}. This model takes into account the dynamics of association-dissociation of organisms which we described in the previous section. This dynamics is representative of the processes

existing among coelenterates-algae symbiosis and we study the range of parameter values for which this aggregation dynamics gives rise to mutualism. With respect to the Volterra-Lotka approach, this model does not exhibit divergences of populations in the case of positive interactions among organisms and is analytically soluble in the low mutation rate limit.

The set of differential equations describing the corresponding population dynamics is:

$$\frac{dA}{dt} = \frac{(\alpha_F \cdot (A+AD) + \alpha \cdot AE) \cdot f1}{A+AD+AE+B} - (d + m \cdot n) \cdot A + d \cdot (AD+AE) + m \cdot (B+AD) + (ks_e \cdot AE) + (ks_d \cdot AD) - kl_e \cdot (A \cdot E) - kl_d \cdot (A \cdot D) \quad (3.1)$$

$$\frac{dAD}{dt} = -2 \cdot (d + m \cdot n) \cdot AD + (m \cdot AE) - (ks_d \cdot AD) + (kl_d \cdot (A \cdot D)) \quad (3.2)$$

$$\frac{dAE}{dt} = -2 \cdot (d + m \cdot n) \cdot AE + (m \cdot AD) - (ks_e \cdot AE) + (kl_e \cdot (A \cdot E)) \quad (3.3)$$

$$\frac{dB}{dt} = \frac{\beta \cdot B \cdot f1}{A+AD+AE+B} - (d + m \cdot n) \cdot B + m \cdot (A+AE+AD) \quad (3.4)$$

$$\frac{dC}{dt} = \frac{\gamma \cdot C \cdot f2}{C+D+E+AD+AE} - (d + m \cdot n) \cdot C + m \cdot (D+AD) \quad (3.5)$$

$$\frac{dD}{dt} = \frac{(\delta_F \cdot D + \delta \cdot AD) \cdot f2}{C+D+E+AD+AE} - (d + m \cdot n) \cdot D + (d \cdot AD) + m \cdot (C+E+AD) + (ks_d \cdot AD) - kl_d \cdot (A \cdot D) \quad (3.6)$$

$$\frac{dE}{dt} = \frac{(\epsilon_F \cdot E + \epsilon \cdot AE) \cdot f2}{C+D+E+AD+AE} - (d + m \cdot n) \cdot E + d \cdot AE + m \cdot (D+AE) + ks_e \cdot AE - kl_e \cdot (A \cdot E) \quad (3.7)$$

These equations simply sum the contributions of the processes listed in section 2.2 and set the time variation of each population.

3.2 Simulation results

The initial conditions are such that populations are at equilibrium for the populations B, C, A, D and AD, mutant E being absent; for instance: A=0.01, AE=0, AD=0, B=80000, C=20000, D=60000. At time t=0, E is introduced in the system, with population E=0.01.

For each set of parameters¹, the initial conditions, determined by numerical

¹ d (frequency of death)=10⁻². m (mutation rate)=10⁻⁵. n (number of genes)=3. f1 (food shared between A and B)=80. f2 (food shared between C, D and E)=100.

simulations of the differential system in the absence of E, are those corresponding to the eventual emergence of mutualism, when a true symbiont E is introduced among an ecosystem at equilibrium containing only primeval species B,C and "egoists" D plus the host species A.

Varying parameters and initial conditions three types of attractors are obtained by numerical integration of system (equations (3.1) to (3.7)). All attractors are point attractors. The most sensitive parameters, in terms of dynamical behavior, are the difference in fitness ($\delta - \epsilon$) and in the rejection rate ($ks_D - ks_E$) between species D and E. The resource parameters f_1 and f_2 simply change the scale of populations. Three time scales, fast, intermediate and slow, are fixed by respectively ks_D , d and m . d/m determines the ratio between dominant and less fit species populations.

For small ks_D , i.e., when D spends in A an amount of time comparable to E, AE does not prevail over AD. The "egoist" D benefits from the nutrients it gets from A, and develops faster than E. A does not benefit from D and is not able to grow faster than B. Finally the primeval population B remains at the higher level. A small population of host A is mainly infested by "egoists" D, which gives a small but sufficient advantage to D to overcome C.

Emergence of mutualism is observed for large ks_D , i.e. when D is rapidly expelled from A. A gets support from E and is able to overcome B. The symbiotic organism AE becomes predominant over the primeval populations C and B. The primeval organisms populations are only maintained by the mutations.

For some values of the fitness parameters a coexistence region is observed for intermediate values of ks_D . In this region, one observes coexistence of the couples AD and AE. The fitness of A in these couples is comparable to that of B, which coexists with them. A high population of free D is also maintained.

The three regimes can be observed on Figure 3 which shows the equilibrium levels of the populations when ks_D increases. The transition value of ks_D between the three dynamics depends upon the difference in fitness between D and E.

This diagram is complicated because the regime that is reached depends not only on the parameters, but also from the initial conditions. The discontinuities in populations are due to the non-linearity of the equilibrium equations, obtained by setting to zero the time

α_F (free organisms A)=8. β (organisms B)=10. γ (organisms C)=8. δ_F (free organisms D)=8. ϵ_F (free organisms E)=7. α (organisms A in AE)=12. δ (organisms D in AD)=12. ϵ (organisms E in AE) is between 8 and 12.

kl_D (organisms D)=1. kl_E (organisms E)=1. ks_D (organisms D) is between 0.1 and 12. ks_E (organisms E)=0.1.

derivatives. For the same set of parameters several solutions exist , one or two of which are attractors. Dependence on the initial conditions and hysteresis are then observed.

One consequence of this hysteresis is that the conditions for the stability of mutualism when facing the invasion of a new "egoist" is less stringent than the condition for the emergence of mutualism facing the same "egoist" already established. The emergence of mutualism implies a transition from a different attractor and is achieved for larger ks_d (or a smaller $\delta - \epsilon$) than its failure against an invading "egoist" which implies a dynamics starting from the mutualism attractor. In the second case the transition is achieved for a lower ks_d (or a larger $\delta - \epsilon$).

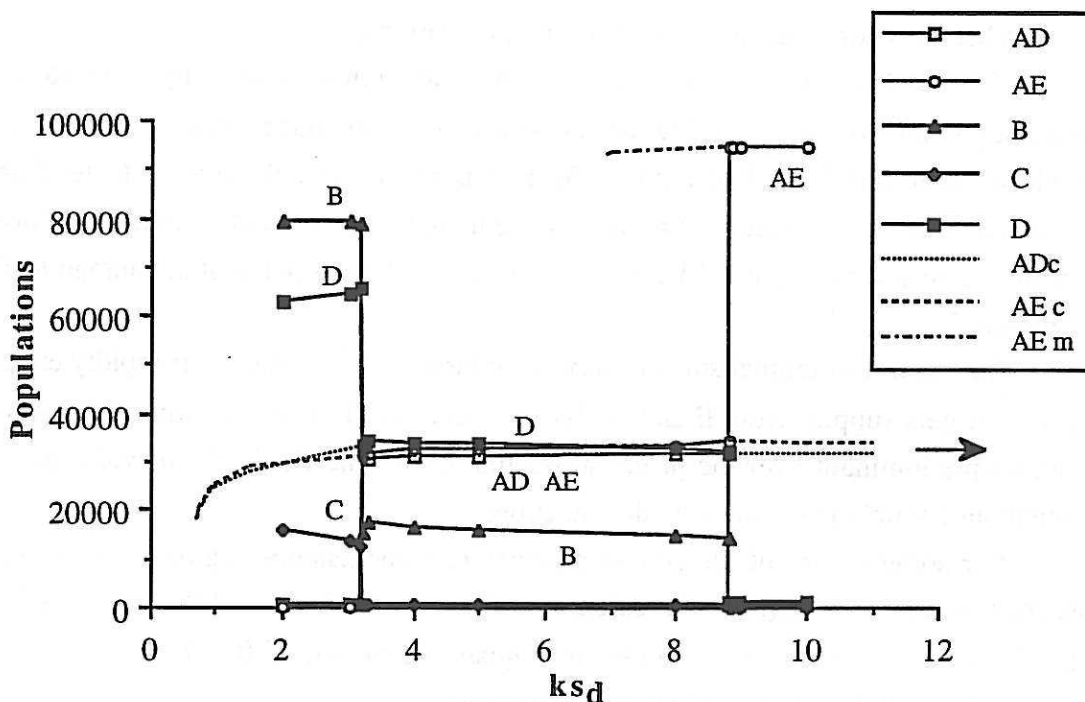


Figure 3: Equilibrium populations measured at time $t=100000$ as a function of ks_d for $\epsilon=10$.

The three regimes, predominance of the ancestors, coexistence and emergence of mutualism are separated by sharp transitions. Populations of A and E, very small, are not represented on the diagram. Continuous lines were obtained from initial conditions in the absence of E species (emergence conditions). The dotted lines are obtained with initial populations of the attractors: AD_c and AE_c corresponding to the coexistence attractor and AE_m to the mutualism attractor. The arrow indicates that the coexistence attractor exists up to larger values of ks_d .

We also performed analytical analysis (slow manifold analysis) which allowed us to interpret the simulation results and to predict the transitions among the different dynamical regimes. We won't give the details of this analysis here but they can be found in {Weisbuch and Duchateau, 1993}.

Figure 4 is a summary of the limits of stability of the different attractors obtained

from numerical simulations and algebraic analysis of the slow manifold.

The abscissa of this diagram is the ratio of the maximum population on each branch (hosts and parasites): $\frac{f1.\alpha}{f2.\epsilon} \cdot \frac{d^*}{d}$. The second fraction correspond to the case where the host A offers protection to the symbiont E, thus decreasing its death coefficient d with respect to free species (see section 4). The ordinate is the dissociation constant ks_d .

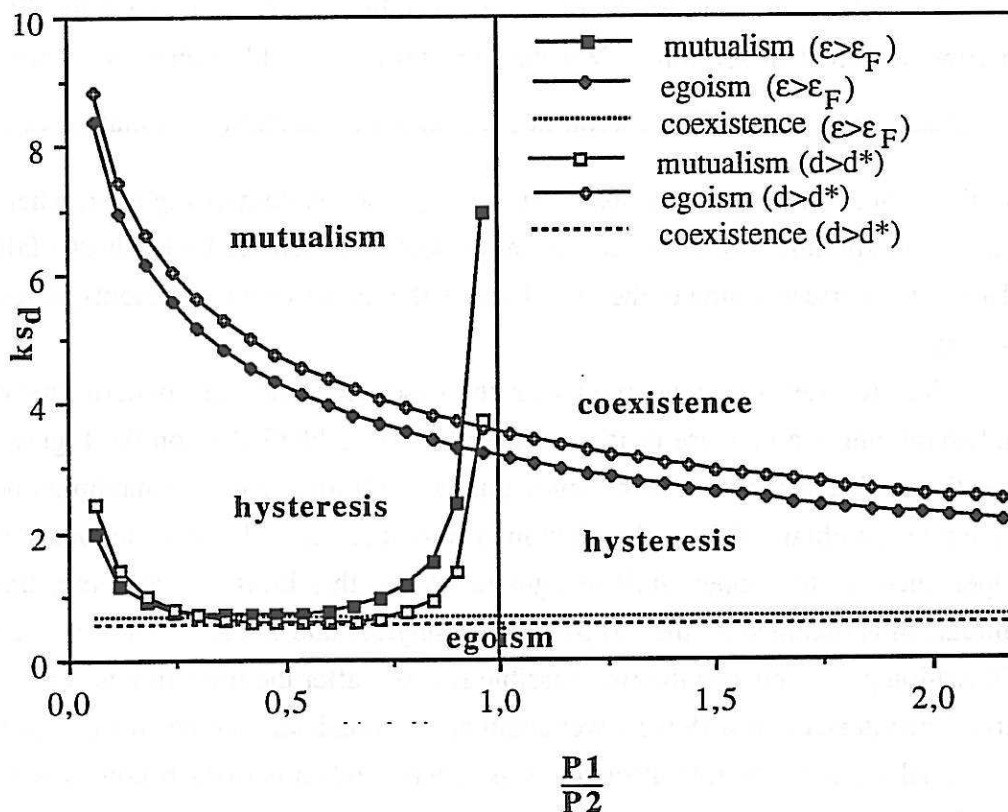


Figure 4: Limits of stability in the plane $(\frac{P1}{P2}, ksd)$

The transition from egoism to coexistence or mutualism depends on the saturation ratio relating the maximum populations of A species, $P1=f1.\alpha.d^*$, to E species, $P2=f2.\epsilon.d$. The vertical line at $P1=P2$ is a limit to the existence of mutualism which is only possible in the left part of the diagram. The limits of stability of the three regimes are drawn when the endosymbionts enjoys either an increase in fitness (black dots) or in lifetime (open dots). The upper decreasing curves are the upper stability limits of egoism (losanges), and the lower curves are the lower stability limits of mutualism (squares). The horizontal straight lines are the lower stability of coexistence. In the lower ks_d regions egoism, and in the upper regions mutualism or coexistence, according to the possibility of saturation of the host by the symbionts, are the unique possible attractors. In between, which attractor is reached depends on the initial conditions (hysteresis).

Mutualistic associations sometimes involve protection in exchange for food, for instance in the case of damselfish and anemon, or coelenterate and algae. This protection against predators might be described in our model by changing the death rate inside the

host with respect to the death rate outside, i.e., the endosymbiont enjoys an increase of its lifetime when it is inside the host.

We have done series of simulations and algebraic computations on the slow manifold to study the "extreme" case when the only benefit enjoyed by the endosymbionts D and E is a reduction of their death rate d^* with respect to their death rate d when they are free ($d=0.01$, $d^*=0.007$). Fitnesses are maintained constant inside and outside the host ($\delta_F = \delta = 8$, $\epsilon_F = \epsilon = 7$). All other parameters are the same as for previous cases.

The 30% decrease in death rate for endosymbionts is comparable to the 30% increase in fitnesses used in section 3. We then expect comparable behaviors when the other parameters such as the dissociation rate ks_d and the maximum population ratio $\frac{f1.d^*.\alpha}{f2.d.e}$ are the same, which is indeed observed on the phase diagram of Figure 4, where the open dots - corresponding to the model where protection is offered by the host - fall aside the black dots - corresponding to the model where the fitness of the symbionts increases inside the host.

We are presently concerned with the case when the only benefit enjoyed by the endosymbiont is a increase of its fitness ($d^*=d$) (the black dots on the Figure 4). Let us note the vertical asymptote of the lower mutualism limit when both maximum populations are equal (as obtained from the slow manifold analysis). The monotonously decreasing upper curve is the upper limit of egoism. When this limit is overcome, transition to mutualism is obtained on the left part of the diagram and to coexistence on the right. The bifurcation point between the two possible regimes after the transition is very close to the left of the intersection with the lower stability of mutualism. In other words, nearly as soon as mutualism is a possible attractor, it is reached when egoism becomes unstable. The condition for this scenario is the possibility for the symbionts to saturate the available hosts. Otherwise, mutualism is impossible and transition to coexistence is observed. The diagram of Figure 3 with several reachable attractors is in fact only obtained for a small parameter region in the vicinity of the equality of maximum populations.

4 Conclusions

Let us summarize the results and discuss the biological significance of the model.

Mutualism does not contradict Darwinian theory of selection of the fittest, provided that one compares species according to their effective fitness, which takes into account the benefits enjoyed by the symbionts while they are associated.

Mutualism can be established when a recognition mechanism allows the host to discriminate among parasites and *bona fide* symbionts. One is then led to look for possible recognition mechanism in biological associations. In the case of rumen/enterobacteria association {Begon, Harper and Townsend, 1986}, the evident candidate for the recognition function is the immune system. For the rhizobium of legumes associating the legume cells and nitrogen fixing bacteria, lectins able to recognize the polysaccharides on the cells walls of the bacteria also are rather convincing molecular mechanisms {Lis and Sharon, 1986}. Other molecular recognition mechanisms have been documented in very simple organisms (spongiae, tunicates, coelenterates) which could be involved in symbiotic associations {Douglas, 1988; Taylor, 1973}. Negative electric charges on the surface of symbiotic chlorellae cell walls allow hydrae to recognize them {McNeil, Hohman and Muscatine, 1981}. Another mechanism, which seems to apply to the *Hydra/Chlorella* system, is the detection by the *Hydra* of maltose released by the *Chlorella* (maltose is the benefit enjoyed by the *Hydra* from the *Chlorella*) {Hohman, McNeil and Muscatine, 1982; McAuley and Smith, 1982; Muscatine and McNeil, 1989}.

The differential model that we have built allows to predict the possible emergence of mutualism according to the individual characteristics of the organisms. It applies to most endosymbiotic systems, where association times are smaller than organisms lifetime. It takes into account exchanged benefits such as food and protection.

The model we presented here considers only the binary associations but in most cases the host offers a number of sites, p , to the endosymbionts. This is the case, for instance, for coelenterates and algae. In {Weisbuch and Duchateau, 1993} we have shown that the multiple-site model is equivalent to the simpler model we described here, in the time range of interest to us.

Hosts and endosymbionts might have different lifetimes, in Nature. We have shown in {Weisbuch and Duchateau, 1993} that if we take into account this difference the qualitative features of the model, such as the existence of the three dynamical regimes, are preserved (when the death ratio is changed up to a factor of 10).

The possibility of a coexistence regime with both egoists and true symbionts present with comparable populations was an unexpected result of the model. We are tempted to consider that the possible saturation of the host by the symbionts is the normal case which excludes the possibility of observing coexistence. On the other hand, coexistence could be a possibility in those many systems where we cannot figure out the benefits of the association for each individual organism involved, e.g. lichen where the benefit for the algae is not obvious {Begon, Harper and Townsend, 1986} or intestinal flora in insects or mammals. Since the coexistence situation is less favorable to the host than complete

mutualism, we might imagine that further mutations would select host organisms with larger rejection rates of "egoists". The real existence in biological systems of the coexistence regime is still an open question worth investigating.

Acknowledgments

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