

COMPLEX DYNAMICS, HYPERCHAOS AND COUPLING IN A MICROBIOLOGICAL MODEL

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ABSTRACT

Interacting populations of bacteria and phages (i.e vira) play an important role for many biotechnological applications. The homogeneous and well-controlled bacterial cultures used in modern cheese production, for instance, are often extremely sensitive to attacks by phages, and considerable efforts are invested in the search for more resistant cultures.

In order to examine different strategies in this search we have simulated a variety of growth, competition and selection processes that may arise in interacting populations of bacteria and phages. Our model considers a culture containing several variants of the same bacterium, each sensitive to a specific phage. The culture grows in a chemostat with a continuous supply of nutrients. Surplus bacteria and vira are removed through dilution. Depending on the rate of dilution, the model exhibits periodic behavior, quasiperiodic behavior, deterministic chaos or hyperchaos.

To study phenomena related with incomplete mixing in the chemostat we have coupled behaviors associated with different compartments. In particular, we have investigated how the behavior changes when we introduce a diffusive coupling of a periodic attractor to a quasiperiodic and a hyperchaotic attractor, respectively.

INTRODUCTION

The dairy industry uses acidifying bacteria in the production of, e.g., cheese and cultured butter. The cultures applied today are quite homogeneous and for that reason they are often very sensitive to attacks by bacteriophages (Hugenholtz 1986). One of the purposes of the present work is to simulate different processes occurring in the interaction between populations of bacteria and phages in a chemostat reactor and in that way propose strategies for the development of new bacteria cultures.

Our model considers different variants of the same bacterium, each sensitive or resistant to particular phage populations. In a phage attack, the phage adsorbs to the bacterial surface and attempts to transfer the viral DNA into the cell. This can lead to i) a lytic response, in which the phage programs the bacterium to produce a number of phages whereafter the cell is lysed, ii) a lysogenic response, in which the viral DNA is inserted into the bacterial chromosome with the result that the bacterium becomes partly resistant to new phage attacks, or iii) a failing response, in which the phage is destroyed by the bacterial immune system before additional vira are produced (Schwartz 1980). Under stress the lysogenic bacterium may either release the viral DNA or be lysed after production of phages.

Simulations have shown a variety of interesting dynamic phenomena. For different parameter values, periodic, quasiperiodic, chaotic and even hyperchaotic solutions are found, and in general several stationary solutions exist simultaneously. Besides, the

model has certain symmetry properties which control the form of the solutions. We have also coupled systems with different dynamic behaviors, associated with different rates of dilution, through diffusion of nutrients between two compartments.

To illustrate the various solutions we have used three-dimensional phase plots, where the concentrations of three variants of bacteria are depicted against each other, and Poincaré sections illustrating the distribution of intersection points on a two-dimensional surface that cuts the attractor transversely. In addition, to test the model for chaos and hyperchaos, we have made calculations of Lyapunov exponents. These measure the average exponential rate of convergence or divergence of two nearby trajectories in phase space. If the largest Lyapunov exponent is positive, two closeby orbits diverge at an exponential rate, implying that two almost similar sets of initial conditions may give very different solutions. A system with one positive Lyapunov exponent is chaotic, and a hyperchaotic system has two positive Lyapunov exponents.

THE MODEL

We consider three variants of the same bacterium, each being sensitive to a particular phage population and resistant to the phages that infect the other bacteria. Other than that, the bacteria have identical properties. The delay associated with the lytic response is accounted for, whereas the possibility of a lysogenic response is neglected. The bacteria interact through competition for a common substrate required for their growth. The model is deterministic.

The following differential equations describe the model:

$$\frac{dB_i}{dt} = \frac{v_i \cdot S \cdot B_i}{\kappa_i + S} - B_i \left(\rho + \sum_{j=1}^3 \alpha_{ij} \omega_j P_j \right) \quad (1)$$

$$\frac{dIB_{i1}}{dt} = B_i \sum_{j=1}^3 \alpha_{ij} \omega_j P_j - \rho IB_{i1} - \frac{3}{\Lambda_i} IB_{i1} \quad (2)$$

$$\frac{dIB_{i2}}{dt} = \frac{3}{\Lambda_i} (IB_{i1} - IB_{i2}) - \rho IB_{i2} \quad (3)$$

$$\frac{dIB_{i3}}{dt} = \frac{3}{\Lambda_i} (IB_{i2} - IB_{i3}) - \rho IB_{i3} \quad (4)$$

$$\begin{aligned} \frac{dP_j}{dt} = & \varphi_j - P_j \sum_{i=1}^3 \alpha_{ij} B_i - \rho P_j \\ & - P_j \sum_{i=1}^3 \sum_{k=1}^3 \alpha_{ij} IB_{ik} + \frac{3}{\Lambda_j} \beta_j IB_{j3} \end{aligned} \quad (5)$$

$$\frac{dS}{dt} = \rho(\sigma - S) - \sum_{i=1}^3 \frac{S \cdot B_i \cdot v_i \cdot \gamma_i}{S + \kappa_i} \quad (6)$$

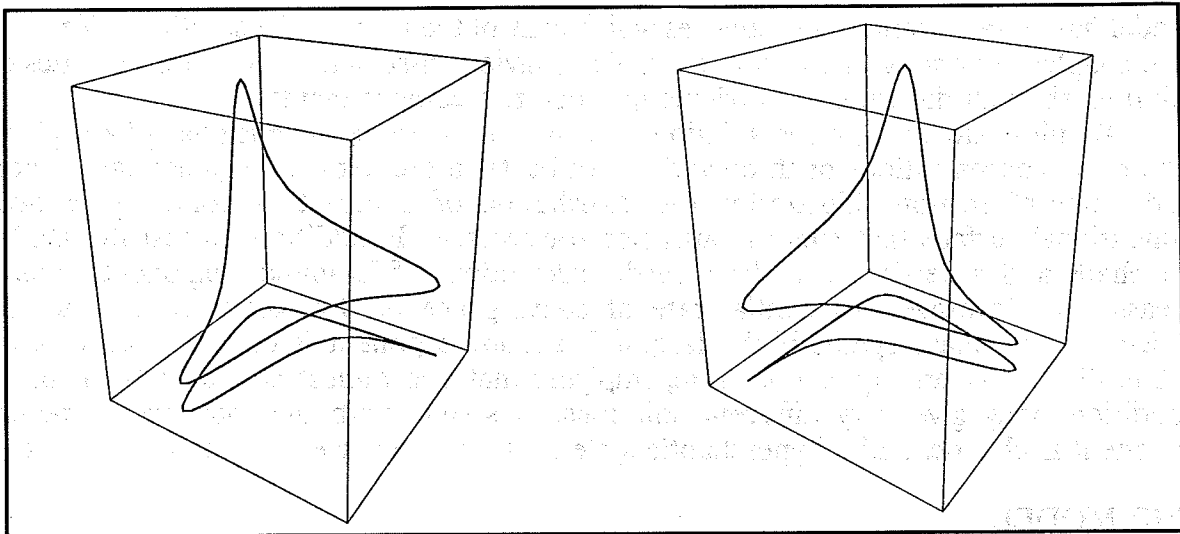


Figure 1 Three-dimensional phase plots of the symmetric periodic solutions. $\rho = 0.0065 \text{ min}^{-1}$.

B_i and P_j denote the concentrations of bacteria of variant i and of phages that infect bacteria of variant j , respectively. S is the concentration of substrate in the chemostat. α_{ij} (10^{-9} l/min) and ω_{ij} (0.8 for $i = j$, else 0.005) are constants defining the adsorption and infection processes between B_i and P_j , κ_i (10000 mg/l) and ν_i (0.024 min^{-1}) are constants of the Monod equation describing the growth of the bacterial populations in absence of viral attacks (Monod 1949), and γ_i (0.01 mg) is the substrate consumed in the formation of each bacterium. ρ is the rate at which a suspension of substrate is supplied to the chemostat, and the contents of the chemostat are diluted. The delay associated with lysis of infected bacteria ($\lambda_i = 30 \text{ min}$) is simulated as a third order delay. IB_{ik} is the concentration of infected bacteria of variant i at level k in the delay chain. β_i (100) is the number of phages released in each lysis of an infected cell. σ (10000 mg/l) is the concentration of the supplied substrate, and φ_j (0.1 l^{-1}) represents a continuous pollution by phages from external sources.

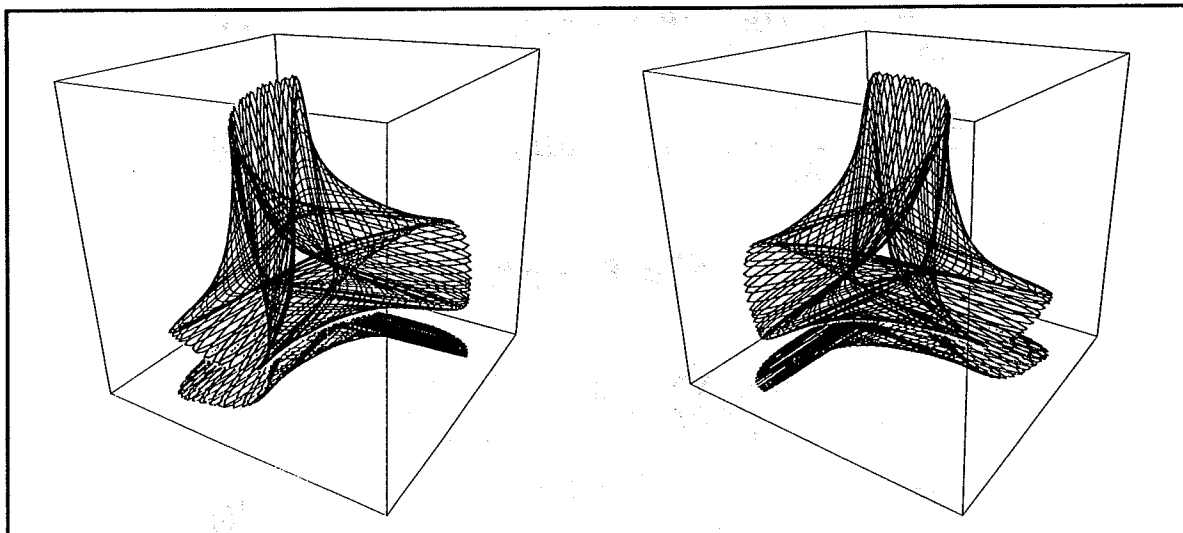


Figure 2 Three-dimensional phase plots of the two symmetric quasiperiodic solutions. $\rho = 0.0055 \text{ min}^{-1}$.

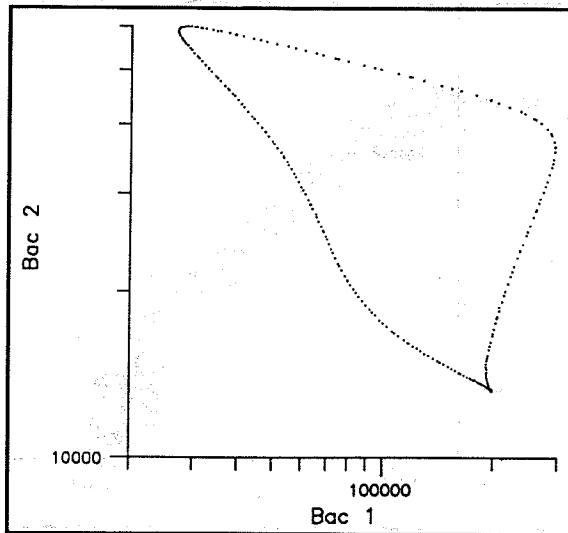


Figure 3 Poincaré section of a quasiperiodic torus. $\rho=0.0057 \text{ min}^{-1}$.

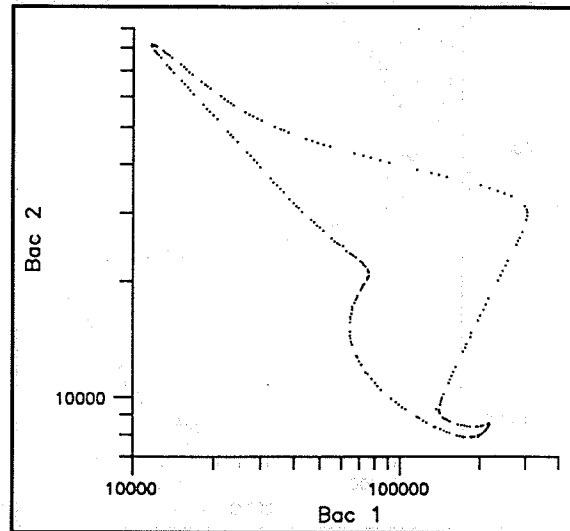


Figure 4 Poincaré section of the deformed quasiperiodic torus. $\rho=0.0052 \text{ min}^{-1}$.

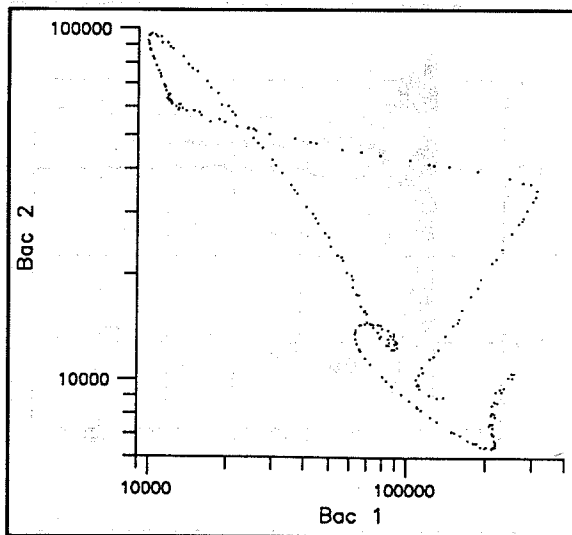


Figure 5 Poincaré section of a chaotic attractor. $\rho=0.0051 \text{ min}^{-1}$.

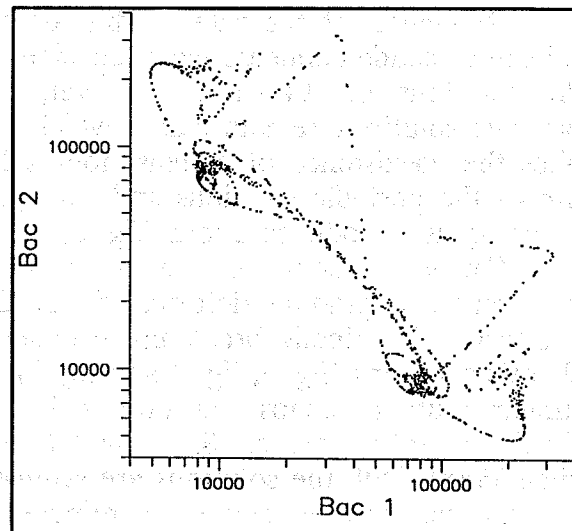


Figure 6 Poincaré section of the fused attractor. $\rho=0.004925 \text{ min}^{-1}$.

DYNAMICS OF THE MODEL

For realistic parameter values, the model exhibits a very complex dynamic behavior. In the following illustrations, the rate of dilution is used as bifurcation parameter since it is the parameter with the largest influence on the behavior (Nielsen and Stranddorf 1991).

For high values of the rate of dilution we have found only periodic solutions. As a consequence of the structure of the model, symmetric solutions exist simultaneously (fig. 1). The solution chosen by the system depends on the initial conditions and the boundaries between those initial conditions that lead to one and those that lead to the other solution are probably fractal.

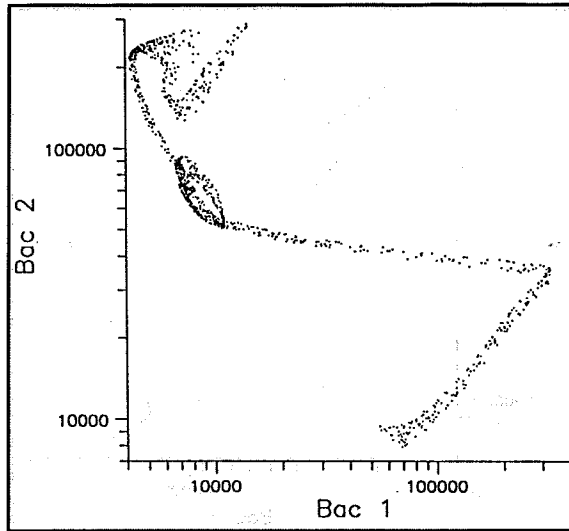


Figure 7 Poincaré section of the attractor that has started to collapse. $\rho=0.00485 \text{ min}^{-1}$.

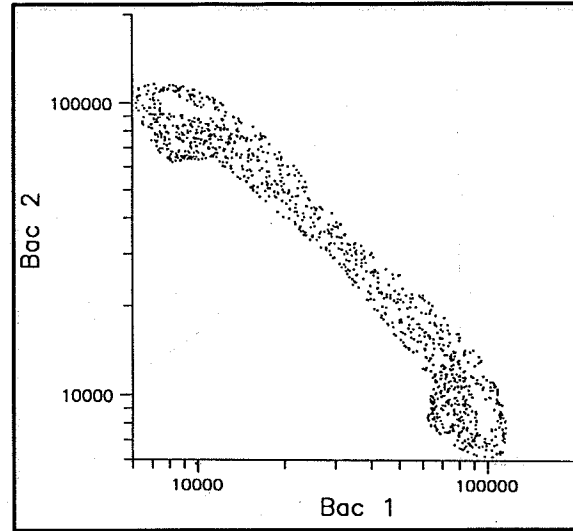


Figure 8 Poincaré section of the totally collapsed attractor. $\rho=0.00480 \text{ min}^{-1}$.

Reduction of the rate of dilution results in a sudden appearance of quasiperiodic solutions on two-tori. However, the periodic solutions remain stable which implies the coexistence of at least four solutions - the periodic solutions and two symmetric quasiperiodic solutions (fig. 2).

Further reduction of the rate of dilution causes a gradual deformation of the two-tori which finally break up, producing chaotic solutions (fig. 3, fig. 4 and fig. 5). A similar route to chaos was observed in a simple migration model (Sturis and Mosekilde 1988). Still, the solutions are symmetric. As the rate of dilution continues to decrease, however, the symmetric chaotic solutions suddenly melt together. Fig. 6 shows a Poincaré section of the resulting compound attractor - this section has the form almost like a butterfly. Shortly after the fusion, the attractor starts to "collapse". Fig. 7 and 8 show how the wings of the butterfly one by one are folded in response to small reductions in the rate of dilution. The Poincaré section changes type, instead of a one-dimensional non-closed curve the section covers an area. This makes it probable that the solution is hyperchaotic (Killory et al. 1987), a proposition which is verified through calculation of the five largest Lyapunov exponents (Wolf et al. 1985). Fig. 9 shows the convergence of these exponents as the simulation time increases. The fact that two exponents are positive indicates that the solution is hyperchaotic.

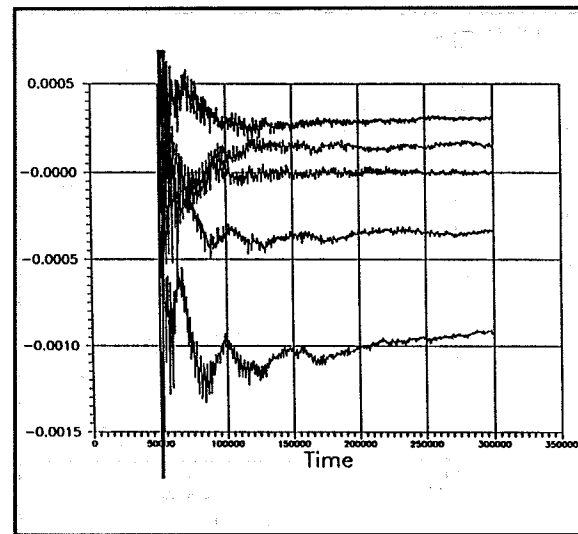


Figure 9 Convergence of the five largest Lyapunov exponents for $\rho=0.0040 \text{ min}^{-1}$.

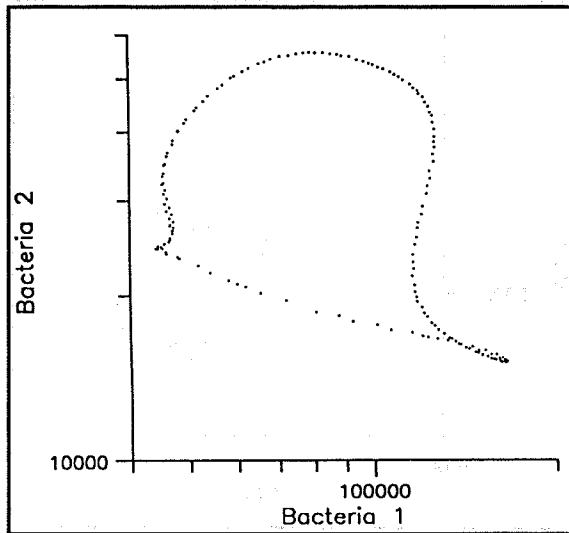


Figure 10 Poincaré section of the solution in chamber A.
 $D=0.0002 \text{ min}^{-1}$ and $\rho=0.0056 \text{ min}^{-1}$.

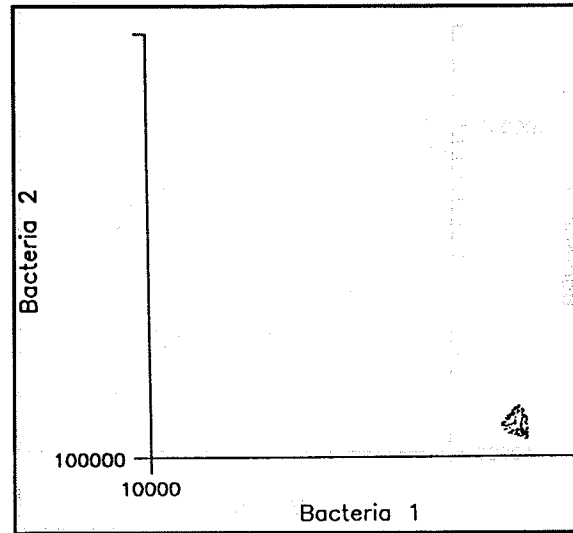


Figure 11 Poincaré section of the solution in chamber B.
 $D=0.0002 \text{ min}^{-1}$ and $\rho=0.0060 \text{ min}^{-1}$.

DIFFUSIVELY COUPLED SYSTEMS

In practice, the chemostat may not be fully mixed. With different rates of dilution in different parts of the chemostat, spatially separated attractors exist which interact through diffusion of substrate.

One way to model this phenomenon is to couple two separate chemostat reactors with different rates of dilution. The two subsystems are connected by a substrate permeable membrane which serves as a substrate difference equalizer.

The differential equations for the concentrations of the bacteria, the phages and the infected bacteria are the same as in the uncoupled system, with the exception that we have two equations for each concentration, one for chamber A and one for chamber B. The concentrations of substrate in the two chambers are described as:

$$\frac{dS_a}{dt} = \rho_a(\sigma_a - S_a) - D(S_a - S_b) - \sum_{i=1}^3 \frac{S_a \cdot B_{ia} \cdot v_i \cdot \gamma_i}{S_a + \kappa_i} \quad (7)$$

$$\frac{dS_b}{dt} = \rho_b(\sigma_b - S_b) - D(S_b - S_a) - \sum_{i=1}^3 \frac{S_b \cdot B_{ib} \cdot v_i \cdot \gamma_i}{S_b + \kappa_i} \quad (8)$$

where the indices a and b refer to the chambers A and B and D measures the efficiency of the diffusion.

Coupling of a periodic and a quasiperiodic attractor.

One could speculate whether the effect of such a coupling is stabilizing or destabilizing. Coupling of a quasiperiodic (chamber A) and a periodic solution (chamber B) reveals a surprising result since it shows stabilizing as well as destabilizing effects.

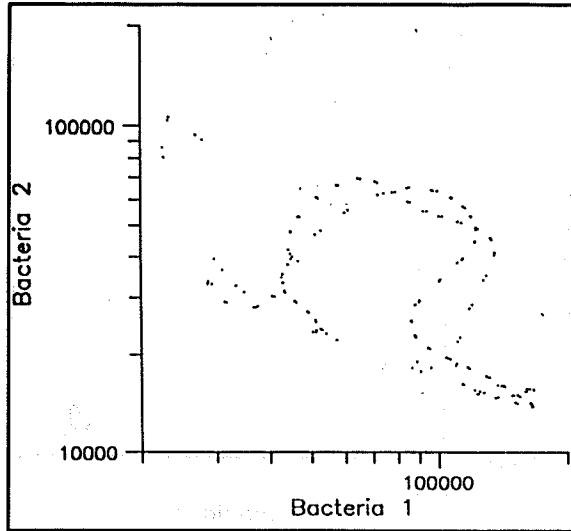


Figure 12 Poincaré section of the solution in chamber A.
 $D=0.002 \text{ min}^{-1}$ and $\rho=0.0056 \text{ min}^{-1}$.

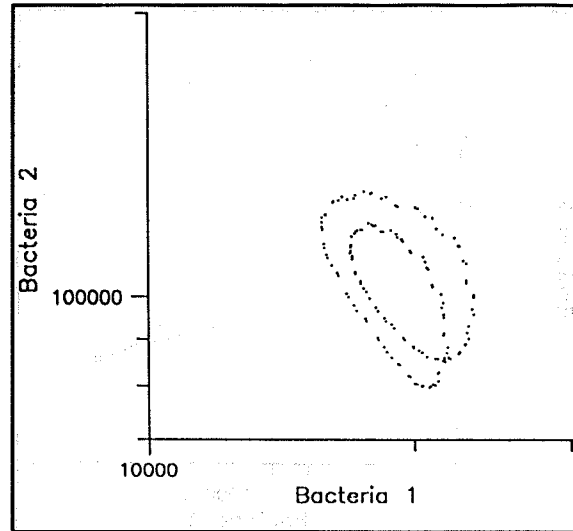


Figure 13 Poincaré section of the solution in chamber B.
 $D=0.002 \text{ min}^{-1}$ and $\rho=0.0060 \text{ min}^{-1}$.

More complex possibilities have been suggested as outcomes of the coupling of strange attractors. It has also been suggested that these outcomes are controlled by relations between the sum of the Lyapunov exponents for the two systems and the efficiency of the diffusion (Pikovsky 1984; Kristensen 1990).

The effect of the diffusion is rather large. Already with $D=0.0002 \text{ min}^{-1}$ the Poincaré sections show significant changes compared to the uncoupled situation. The Poincaré section of the attractor in chamber A shows a closed curve which indicates that the solution is quasiperiodic (fig. 10). The situation in chamber B appears to be more

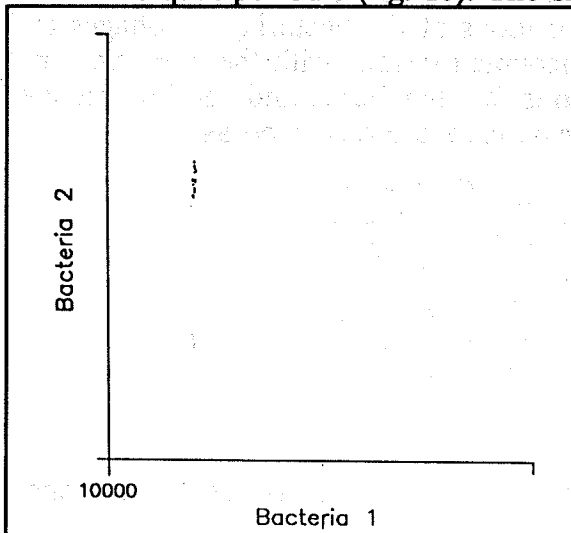


Figure 14 Poincaré section of the solution in chamber A.
 $D=0.02 \text{ min}^{-1}$ and $\rho=0.0056 \text{ min}^{-1}$.

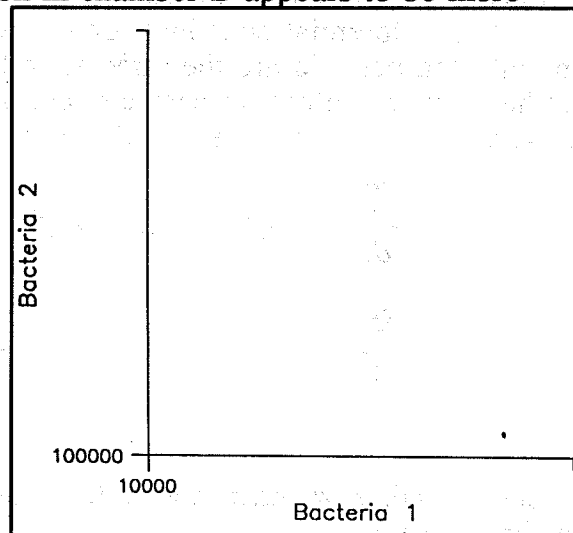


Figure 15 Poincaré section of the solution in chamber B.
 $D=0.02 \text{ min}^{-1}$ and $\rho=0.0060 \text{ min}^{-1}$.

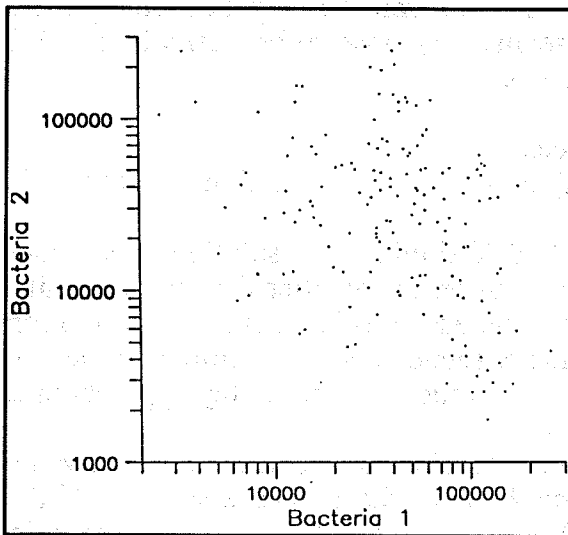


Figure 16 Poincaré section of the solution in chamber A.
 $D=0.0002 \text{ min}^{-1}$ and $\rho=0.0046 \text{ min}^{-1}$.

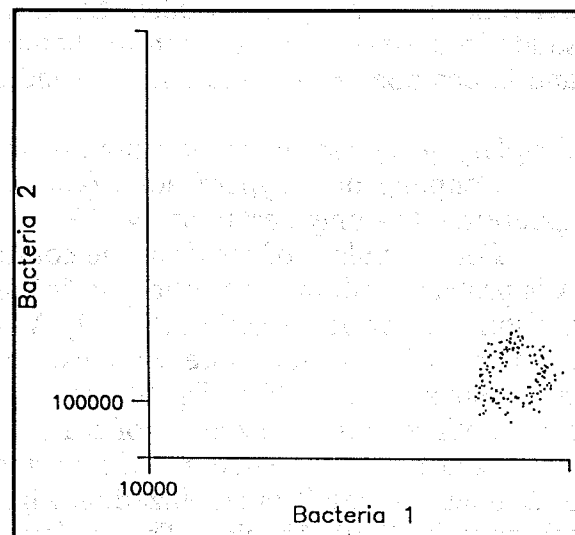


Figure 17 Poincaré section of the solution in chamber B.
 $D=0.0002 \text{ min}^{-1}$ and $\rho=0.0060 \text{ min}^{-1}$.

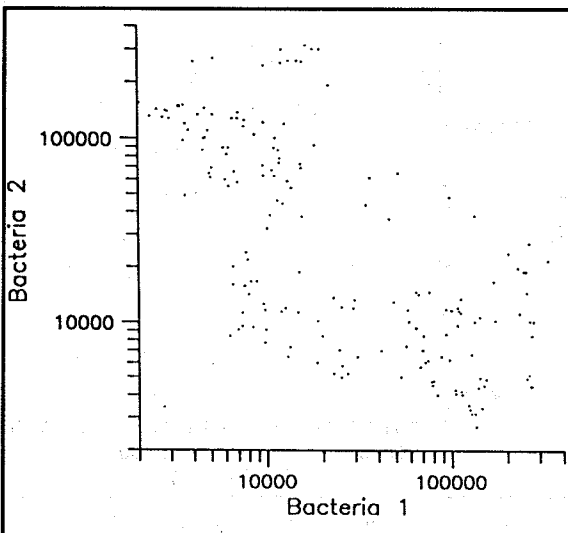


Figure 18 Poincaré section of the solution in chamber A.
 $D=0.001 \text{ min}^{-1}$ and $\rho=0.0046 \text{ min}^{-1}$.

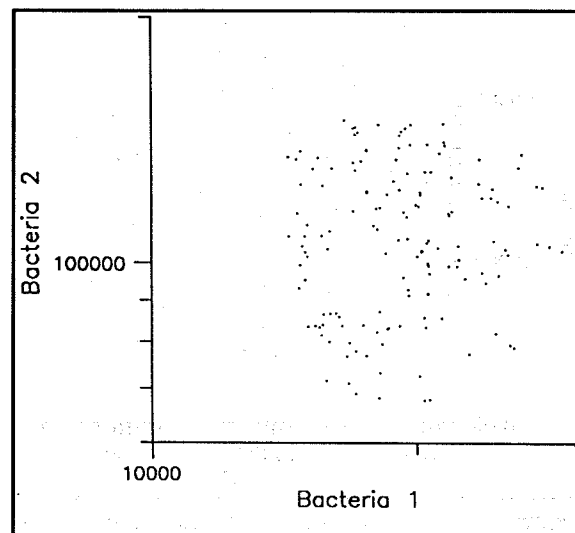


Figure 19 Poincaré section of the solution in chamber B.
 $D=0.001 \text{ min}^{-1}$ and $\rho=0.0060 \text{ min}^{-1}$.

complex and examination of the Poincaré section (fig. 11) reveals that the solution is neither quasiperiodic nor periodic. We may describe this solution as a *disturbed periodic solution*. It would probably be more correct to describe it as a chaotic solution. It seems, however, to be a solution which attempts to be periodic but is disturbed again and again, and for that reason it cannot reach the periodic attractor perfectly and gives a chaotic impression.

When D is increased to 0.002 min^{-1} the situation changes. The solution in chamber A is folded but apparently remains quasiperiodic (fig. 12) and also the solution in chamber B has become quasiperiodic. (fig. 13). When $D=0.02 \text{ min}^{-1}$ a very harmonic

ber B has become quasiperiodic. (fig. 13). When $D=0.02 \text{ min}^{-1}$ a very harmonic picture suddenly appears. The solution in chamber A seems very close to be periodic (fig. 14) and in chamber B the solution is periodic (fig. 15).

Coupling of a periodic with a hyperchaotic attractor.

Coupling of a hyperchaotic (chamber A) and a periodic solution (chamber B) apparently has only destabilizing effects.

For low values of the diffusion constant ($D=0.0002 \text{ min}^{-1}$) the solution in chamber A is probably still hyperchaotic (fig. 16) and the solution in chamber B again looks like a disturbed periodic solution (fig. 17). When D is increased to 0.001 min^{-1} , the solution in chamber B becomes more complex. The Poincaré sections of the solutions in the two chambers are more alike (fig. 18 and 19) and both solutions are probably hyperchaotic, since both sections show areas of scattered dots.

Contrary to the coupling of a periodic and a quasiperiodic solution, a high value of D does not result in stabilization. Fig. 20 and 21 show the Poincaré sections of the solutions for $D=0.018 \text{ min}^{-1}$. The sections are almost similar and they look hyperchaotic. Unfortunately it has not yet been possible to calculate the Lyapunov exponents for the coupled system to verify this.

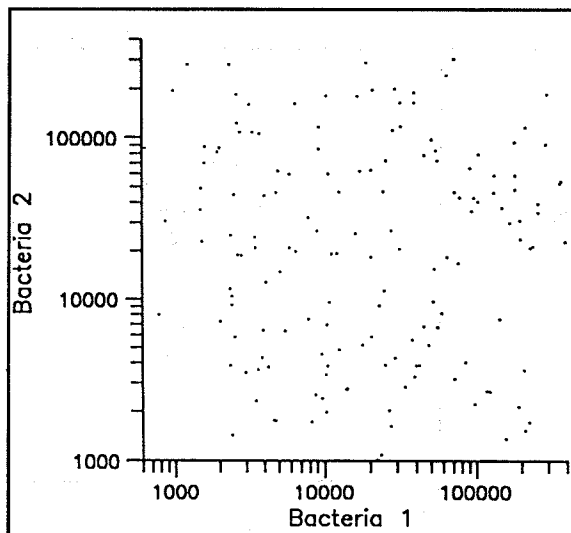


Figure 20 Poincaré section of the solution in chamber A.
 $D=0.018 \text{ min}^{-1}$ and $\rho=0.0046 \text{ min}^{-1}$.

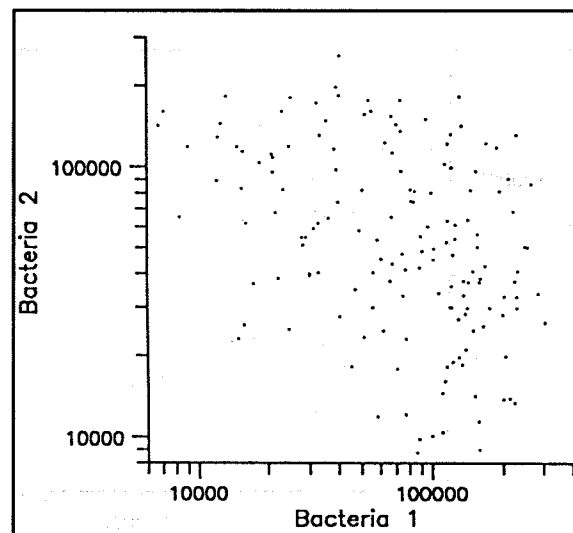


Figure 21 Poincaré section of the solution in chamber B.
 $D=0.018 \text{ min}^{-1}$ and $\rho=0.0060 \text{ min}^{-1}$.

CONCLUSION

Our simulation results show that the model with only three bacterial variants exhibits periodic, quasiperiodic, chaotic and hyperchaotic solutions.

Hyperchaos has only been detected in a few systems (Roessler 1987; Thomsen et al. 1991), and it is interesting to find this kind of behavior in a realistic model of a microbiological system. One could imagine that hyperchaos is a natural form of interaction in biological and ecological systems.

One of the most controversial problems in this connection is related to the question of introducing additional species. Will a multi-species system be more regular

in its behavior than a system with only a few species? Some preliminary simulations of ours indicate that this is in fact the case.

The effect of coupling can be either stabilizing and destabilizing. Surprisingly, coupling of a periodic and a quasiperiodic solution has both effects. For low values of the rate of dilution, the effect is destabilizing and for high values it is stabilizing. Coupling of a periodic with a hyperchaotic solution apparently has only destabilizing effects. We had expected coupling to have stabilizing effects, at least for a high diffusion constant, just like a high rate of dilution results in stabilization. It would be interesting to calculate the Lyapunov exponents of the systems and to see if the connections between them and the diffusion constant can explain the observed results. Further investigations should be made to study the effects of coupling.

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