## ON THE STABILITY OF COUPLED CHEMICAL OSCILLATORS

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Received 17 April 1984 Revised 3 July 1984

The coupling of chemical oscillators is investigated in the case of the Brusselator model. The stable steady states obtained by coupling two, three and more Brusselators in parallel, in a diffusion like manner are discussed. Results are given for identical, identical with perturbation (i.e. almost identical), and completely dissimilar oscillators.

Parameter domains in which stability and multistability can be found are analyzed. These domains usually increase with the number of cells – thus a bigger system of oscillators has a greater chance to be stabilized. The symmetry patterns of the stable domains are discussed.

#### 1. Introduction

In a previous paper [1] the behaviour of chemical oscillators coupled by a diffusion like process was examined. It was found that all tested oscillators have a region of coupling rates that bring them to a stable steady state.

This behaviour was found to be quite general, namely all the examined oscillators and models have this property, regardless of the nature of their non-linearity, and regardless of whether the oscillations are conservative or of the limit cycle type.

In this work we examine this approach to stability in more detail, in order to have more insight into this unexpected phenomenon. Moreover, the coupling problem is also examined in the case of more than two cells, and in this way we investigate the approach to stability of large number of coupled cells.

In a certain way a poorly mixed CSTR may behave in a manner similar to coupled, perfectly mixed, oscillators. In this sense the investigation of coupled oscillators may give us more insight as to what happens in a real CSTR.

The importance of such an investigation is enhanced by the fact that similar models are used not only in chemical and chemical engineering problems, but also in other fields such as population of various species in ecology, morphogenesis and neurophysiology. Imagine two nerve cells, each pulsating due to some set of chemical reactions, coupled by diffusion to each other. If the diffusion rate is right, the two cells may be stabilized and stop pulsating.

In the field of ecology one can imagine two sites each having same prey-predator mechanism which causes the number density of the species to oscillate. If the species are capable of moving from site to site at a proper rate, the two sites may become stable with a constant and different number of species in each. Similar examples can be found in other fields.

The examined oscillator was taken to be the Brusselator [2]. It contains only two components, and thus the computations with increasing number of coupled cells are not too difficult. Moreover, the case of the single cell can be solved analytically, as is well documented in the literature [2–5]. In fact the original paper of Lefever and Prigogine [2] regarding this model, deals a little with the problem of coupling such oscillators, and their study serves as a starting point for the present one.

Tyson [3] studied the problem of Brusselators coupled in series, namely, the products of one cell

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serve as input to the second cell. In this study, in contrast, the cells are coupled in parallel – each cell is controlled by its own parameters and its components are exchanged between neighbor cells as described below.

A further study of coupling of two Brusselators is given by Schreiber and Marek [6, 7], who study the approach to chaos in the case of coupling two similar oscillators with different coupling rates.

The main interest of this paper, as stated above, is stability of the coupled oscillators; very little will be said on the oscillations, whether periodic, quasiperiodic or chaotic.

## 2. The Brusselator-single cell

This oscillator was given ample attention in the literature and only the highlights will be given here.

The model is given by the following reactions:

$$A \xrightarrow{k_1} X, \tag{1}$$

$$2X + Y \xrightarrow{k_2} 3X, \tag{2}$$

$$X \xrightarrow{k_3} Y,$$
 (3)

$$X \xrightarrow{k_4} P$$
, (4)

with the appropriate rate constants. The resulting differential equations can be written in dimensionless quantities as

$$\dot{x} = -(B+1)x + x^2y + A \tag{5}$$

$$\dot{\mathbf{v}} = \mathbf{B}\mathbf{x} - \mathbf{x}^2 \mathbf{v}. \tag{6}$$

These equations depend only on the two parameters A and B. A is equivalent to the rate in which x is produced from the outside, while B is the rate in which the species y is produced from x, via reaction (3), while the term  $x^2y$  gives the rate of x production from both x and y, via reaction (2). This is the only non-linear term in this set.

The steady states  $\dot{x} = \dot{y} = 0$  are given by  $x_{ss} = A$  and  $y_{ss} = B/A$ . The eigenvalues  $\lambda$  at the steady state obey the characteristic equation:

$$\lambda^2 - (B - 1 - A^2)\lambda + A^2 = 0. \tag{7}$$

As B is increased past  $1 + A^2$ , a supercritical Hopf bifurcation [8, 9] occurs, and the steady state looses its stability, i.e., both eigenvalues will have now positive real parts and the system starts oscillating in a limit cycle [3-5]. The rate constants depend on the chemicals which are not written explicitly in the model and are assumed to be kept constant. Thus the parameters A and B are controllable constraints, to be determined by the experimentalist. It is assumed, in what follows, that all the cells to be coupled are in their oscillating regime, i.e.,  $B > A^2 + 1$  in all cases.

### 3. The coupling

The cells are coupled to their nearest neighbors, thus the system takes the form

$$\dot{x}_1 = -(B_i + 1)x_i + x_i^2 y_i + A_i + k(x_{i+1} - x_i) + k(x_{i-1} - x_i),$$
(8)

$$\dot{y}_i = B_i x_i - x_i^2 y_i + k(y_{i+1} - y_i) + k(y_{i-1} - y_i),$$
(9)

for  $1 \le i \le n$ , where n is the number of coupled cells. Only one coupling term will appear for the edge cells, i.e.,  $k(x_2 - x_1)$  or  $k(x_{n-1} - x_n)$  for i = 1 or i = n respectively. Matter is transferred from one cell to the next in a diffusion-like manner, i.e., proportional to the concentration difference.

As the number of cells increases to infinity, the system is best described by reaction-diffusion partial differential equations, where the diffusion constant takes the place of the coupling rate. There are many papers [12–20] (of which we cite but a few) dealing with pattern formation and dissipative structures due to such reaction and diffusion processes.

Most of these papers deal with the case of different diffusion constants for each species while the other parameters, such as A and B, are the same. In this work, in contrast, we have used the same coupling rate for all species but different parameters for the different cells.

The case of different coupling rates k for the x and the y species is dealt with in some previous work [2, 6, 7]; however, in this work the same coupling is used for all species. Taking the same coupling rate -k, for all species seems to be more appropriate to describe experiments where material transfer occurs by pumping or similar method.

As stated above, all cells are in their oscillating regimes – i.e.,  $B_i > 1 + A_i^2$ . The main interest of the paper is the formation of a stable-nonoscillating-system out of the oscillating cells. The stable system thus formed, will be non-homogeneous and the concentrations of the various species will be different in the different cells. In what follows we shall limit the discussion to a few subspaces of the 2n + 1 parameter space  $(n \ A$ 's  $n \ B$ 's and one coupling rate).

## 4. Calculations and general results

Newton's method was used to locate the zeros of eqs. (8) and (9) and thus to find the steady states of the system. When these were found, the eigenvalues of the Jacobian matrix were computed, and thus the turning points and double points (where the Jacobian determinant becomes zero, i.e., one eigenvalue becomes zero) and Hopf's bifurcation points (where the real part of a conjugate pair of eigenvalues becomes zero), were found. (The exact mathematical definitions of turning points, double points, etc. is discussed in refs. 8 and 9. The definitions given here will suffice for our purposes).

The steady state will be stable if all the eigenvalues have negative real part. We shall denote the number of eigenvalues with positive real part by p. Thus a stable steady state will be one for which

p = 0, otherwise the steady state will be unstable and the system will oscillate.

Two cases can be solved immediately.

- a) If the coupling rate k is very small, the number of eigenvalues with positive real parts will be p = 2n. Each cell will be nearly on its own and will oscillate very near its own limit cycle with its own period, determined by its parameters  $A_i$  and  $B_i$ . The system will move on an n-tori in a 2n-dimensional space.
- b) If the coupling rate k is very high, then all the coupled cells become essentially one cell with average  $\overline{A} = (A_1 + A_2 + \cdots + A_n)/n$  and  $\overline{B} = (B_1 + B_2 + \cdots + B_n)/n$  and with appropriate limit cycle and period. Thus p = 2 and all the other 2n 2 eigenvalues will be negative. The system will move quickly to a two-dimensional subspace in the 2n-dimensional space and remain there in a limit cycle. The negative eigenvalues come in pairs as multiples of k. Thus the negative eigenvalues for high k values are: -2k for 2 cells, -k and -3k for 3 cells and -0.5857864k, -2k and -3.4142138k for four cells (each value appears twice).

As k increases, p must, therefore, change from 2n to 2. In many cases, to be described below, it passes through p=0 thus creating a stable system. This observation may seem contrary to intuition, by which we tend to assume that coupling or diffusion, between the different parts of the system, tends to "wash out" the differences and to "homogenize" the system. In spite of the intuition, the coupled system made of individual oscillators may be frozen and remain in a stable steady state due to its inherent non-linearities. We shall not be concerned with the oscillations and other rich dynamics created by the seemingly simple diffusion-like mechanism.

## 5. Two identical cells

This problem can be tracked more easily and so it will be dealt with first. If  $B_1 = B_2 = B$  and  $A_1 = A_2 = A$  then the characteristic equation for

the homogeneous solution (i.e., same steady state in both cells),  $y_1 = y_2 = B/A$ ,  $x_1 = x_2 = A$ , is found to be

$$[\lambda^{2} + \lambda(A^{2} + 1 - B) + A^{2}][\lambda^{2} + \lambda(A^{2} + 1 - B + 4k) + A^{2}(1 + 2k) + 2k(1 - B) + 4k^{2}] = 0.$$
(10)

The first parenthesis is the same as the one for the single cell (eq. (7)) and does not depend on the coupling rate. If the independent term in the second parenthesis equals zero, i.e.,

$$4k^2 + 2k(A^2 + 1 - B) + A^2 = 0. (11)$$

then  $\lambda = 0$  and a turning point or a double point is obtained. Since  $B \ge A^2 + 1$  in order to obtain oscillations, then physically possible solutions to equation (11) are possible only if  $B \ge (A+1)^2$ . Two cases may arise: a) eq. (11) has no possible solution, i.e.,  $B \le (A+1)^2$ ; then p goes directly from 4 to 2 at  $k = (B - 1 - A^2)/4$ . In this case, the homogeneous solution is the only possible one; it will be unstable for all coupling rates, and the system will always oscillate. The pattern of oscillations may become quite complicated [6, 7], but is outside the scope of this work. b) Eq. (11) does have physically possible solutions; then at these k's, p changes from 4 to 3 and from 3 to 2. These two points are double points, namely, another solution, an inhomogeneous one, starts there [9]. This inhomogeneous steady state may become stable in a certain range of coupling rates depending on the parameters. Fig. 1 shows the two steadystate solutions, the homogeneous and the inhomogeneous ones, as a function of the coupling rate for the case B = 10, A = 2.

In this case eq. (11) is seen to be solved for k = 0.5 and k = 2.0. Between these points, p = 3, while below and above these points p = 4 and p = 2 respectively. Since these points are double points, another, inhomogeneous, solution starts there [9]. This inhomogeneous solution is, of course, doubly degenerate, since the indices 1 and 2 are interchangeable. The locations of the turning points, double points and Hopf bifurcations, where

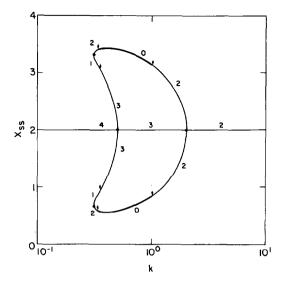


Fig. 1. Concentration of X species vs. coupling rate for two identical cells with B=10, A=2. Numbers give the value of p- the number of eigenvalues with positive real part. Range of stability, i.e., p=0, is emphasized. Dots show double points and turning points at k=0.5 (4,3), k=2 (3,2), k=0.312906 (2,1); arrows show bifurcations at k=0.332800 (2,0), k=1.01157 (2,0), k=0.348742 (3,1); the numbers in parenthesis are the two values of p at the point. Above the line x=2 (i.e., the homogeneous solution) the concentrations refer to cell 1, and below it to cell 2. Since the cells are identical, the figure is symmetric about this line.

the value of p changes, are given in the figure caption. For 0.332800 < k < 1.01157 this inhomogeneous solution is seen to be stable with p = 0. The two cells, although with the same parameters, will not have the same concentrations. For example, in our case the inhomogeneous solution at k = 0.5 (the lower double point) is  $x_1 = 3.4142$ ,  $y_1 = 3.1716$ ,  $x_2 = 0.58579$ ,  $y_2 = 8.8284$ , as compared to the unstable homogeneous solution of  $x_1 = x_2 = 2$ ,  $y_1 = y_2 = 5$ .

The system under these constraints may either move towards the stable steady states or move along a limit cycle, depending, of course, on the initial conditions. We have not calculated the attraction basins, i.e., the sets of initial conditions for the stable states or for the oscillating ones. This is a very interesting, important and difficult problem which is not dealt with in this work.

If the parameters of the cells are changed to B=10, A=1, a figure very similar to that of figure 1 is obtained. Once, however, p becomes 2 as k increases, it remains so. There is no Hopf bifurcation to p=0 and the system will not be stable anywhere in this case. In other words, coupled identical cells both of which are oscillating with A=2, B=10, between the cited coupling rates, may either oscillate or come to a stable steady state with no oscillations, depending on the initial conditions. On the other hand if B=10 and A=1, the coupled cells will always oscillate regardless of the initial conditions and regardless of the coupling rate.

# 6. Multiple identical cells

As in the case of two identical cells, stable steady states can be obtained when more than two cells are coupled. Table I gives typical concentrations for k = 0.5, B = 10, and A = 1 and A = 2.

The main observation is that the coupled identical oscillators may be "frozen", the symmetry broken, and an inhomogeneous stable dissipative structure [2,4] is formed. Moreover, the coupled oscillators may be "frozen" in more than one stable steady state, as can be seen for example in

the case of A = 2, n = 4. In this case we obtain two symmetrical concentrations made up from the two possible combinations of the inhomogeneous solutions of two coupled cells, namely, abba and baab. It is obvious that if the situation ab is a solution for two cells, then both abba and baab must be a solution for four coupled cells, since the middle coupling terms will be zero [the terms such as  $k(x_3 - x_2)$  will be zero since  $x_3 = x_2$ ]. It can be shown that in these symmetrical combinations, four of the eigenvalues are the same as those of two cells, while the other four are different. It turns out that all the symmetrical combinations have a range of stability, very similar, but not identical, with the subset from which it is built. For example, the first symmetrical stable steady state with B = 10, A = 2, and n = 4 have a range of 0.3328003 < k < 1.011568, exactly as the two cells case, while for the second one 0.3331850 < k< 1.011568. The upper bifurcation point is the same while the difference between the lower ones is minute.

Similar results are obtained for any even number of cells. Thus we can form six cells as *abbaab* and similar combinations for eight cells and more made up from two cells. Also eight cells can be formed by combining two groups of four cells with B = 10 and A = 1, and so on.

Table I Concentrations at stable steady state of identical cells with B = 10 at k = 0.5

A	n	Cell 1	Cell 2	Cell 3	Cell 4	Cell 5
1	2		no stable SS			
1	3		no stable SS			
1	4	x = 3.432	0.3382	0.1199	0.1097	_
		y = 3.251	11.21	14.97	16.76	
1	5	x = 0.3408	4.005	0.4193	0.1249	0.1101
		y = 7.893	2.910	11.19	15.01	16.81
2	2	x = 3.414	0.5858		_	
		y = 3.172	8.828			
2	3		no stable SS			
2	4	x = 3.414	0.5858	0.5858	3.414	_
		y = 3.172	8.828	8.828	3.172	
2	4	x = 0.5858	3.414	3.414	0.5858	
		y = 8.828	3.172	3.172	8.828	_
2	5	-	no stable SS			

There is no known way to calculate the range of parameters in which this stability will occur; however, detailed computations and symmetry considerations show that the number of coexisting stable states increases with the number of cells.

### 7. Two almost identical cells

The parameters of the two cells differ slightly from each other, thus the homogeneous solution no longer exists. We note also that the degeneracy, that occurred in the case of the identical cells, namely, that cells one and two could be interchanged, is lifted. Three steady states are now possible: (I) is derived from the previously inhomogeneous solution. (II) is derived from the previously inhomogeneous solution – degenerate with I. (III) is derived from the previously homogeneous solution. These results are shown for the case  $B_1 = 9.9$ ,  $B_2 = 10$ ,  $A_1 = A_2 = 2$  in fig. 2.

States I and II are very near those of the unperturbed cells – compare to fig. 1.

Thus, for example, at k = 0.5 the three steady states are (I)  $x_1 = 3.4178$ ,  $y_1 = 3.1393$ ,  $x_2 =$ 0.582198,  $y_2 = 8.8106$ ; (II)  $x_1 = 0.60897$ ,  $y_1 = 8.755$ ,  $x_2 = 3.391$ ,  $y_2 = 3.1909$ ; and (III)  $x_1 =$ 1.4868,  $y_1 = 6.1944$ ,  $x_2 = 2.5132$ ,  $y_2 = 4.1414$ . States I and II may become stable with p = 0while state III is always unstable. These numbers should be compared to the ones given in the previous section for the case of identical unperturbed cells. The perturbation thus lifts the degeneracy - the concentrations of states I and II are seen to be very similar when the indices 1 and 2 are interchanged - and creates two different and in this case stable solutions in the ranges 0.328359 < k < 1.03829 for I and 0.35935 < k < 0.980602 for II.

As the perturbation increases, the range of existence of the "closed" solution i.e. II and III decreases, until it disappears completely, in this case for  $B_1 = 9.5$ ,  $B_2 = 20$ , and only one, inhomogeneous solution remains.

Fig. 2 shows also states II and III for a larger perturbation, namely,  $B_1 = 9.55$ . State I in this

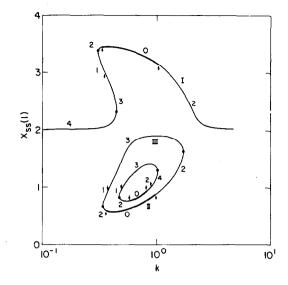


Fig. 2. Perturbation of two cells: concentration of X species in the first cell vs. the coupling rate for  $B_1 = 9.9$ ,  $B_2 = 10$ ,  $A_1 = A_2 = 2$  and  $B_1 = 9.55$ ,  $B_2 = 10$ ,  $A_1 = A_2 = 2$  (inner plot). (I) Dots at (turning points) k = 0.308958 (2,1) and k = 0.446053 (4,3); arrows (bifurcations) at k = 0.328359 (2,0), k = 1.03829 (2,0), k = 0.347018 (3,1). (II) Dots at k = 0.334663 (2,1), k = 1.678616 (3,2); arrows at k = 0.3593503 (2,0), k = 0.9806022 (2,0). Inner circle dots at k = 0.4690119 (2,1), k = 1.037833 (4,3); arrows at k = 0.5908347, k = 0.8072446 (2,0), k = 0.893693 (4,2). (III) Dots: same as II. Arrows at k = 0.368558 (3,1). Inner circle: k = 0.4872504 (3,1).

case is very similar to that of the smaller perturbation and is not shown.

In state II of the "inner circle" one notices a region of p = 4 near the upper turning point. This may change the dynamics of the system and the attraction basins of the various domains, but it does not have any bearing on the stable states.

We note also the possibility of coexistence of multiple steady states. Between the lower turning point of states II and III (k = 0.33466) and the upper turning point of state I (k = 0.44605), five steady states can coexist, with p = 0, p = 1, p = 2, p = 3 and p = 4. A variety of oscillations and possibly chaos in addition to the two stable steady states can be realized, depending on the initial conditions.

Similar results were obtained [1] for more complicated models such as the Field-Körös-Noyes (FKN) mechanism [10] of the Belousov-

Zhabotinskii reaction. In that case the model contains eight independent species and seven reversible reactions, i.e., 14 rate constants. In spite of the extra complexity, the essential features remain the same. A coupling range in which five steady states coexist, and another one in which two different and inhomogeneous stable steady states are possible (compare fig. 2 with fig. 5 of ref. 1).

In the Brusselator, as well as in the more complicated FKN mechanism, two coupled oscillators can stabilize each other at two different states provided the parameters, the coupling rate and the initial conditions, permit.

# 8. Two coupled oscillators - general case

The results obtained here are very similar to those obtained previously for the case of large perturbation, when, obviously, only one inhomogeneous steady state exists. As the coupling rate increases, p goes from 4 to 2. Depending on the parameters, this transition can be a direct one (for example, for  $B_1 = 3$ ,  $B_2 = 4$ ,  $A_1 = A_2 = 1$  the transition is at k = 0.2345765), or follow a series of turning points and bifurcations similar to those depicted in fig. 2, in which case a stability region will be found (for example, for  $B_1 = 3$ ,  $B_2 = 10$ ,  $A_1 = A_2 = 1$ , p = 0 between 0.03199288 < k < 0.8609949).

In all cases studied, the bifurcations are supercritical; thus between the above limits the system will be stable.

In fig. 3 the limits of the stability region are shown as a function of  $B_2$  for two different values of  $B_1$ , namely  $B_1 = 3$  and  $B_1 = 3.9$  and  $A_1 = A_2 = 1$ . As the coupling rate increases at constant  $B_2$ , a Hopf bifurcation from p = 2 to p = 0 occurs at the lower line and another one from p = 0 to p = 2 at the upper line. Thus inside the curves (to the right) the system of two coupled Brusselators will be stable at p = 0, while outside (to the left) p > 0 and the coupled system will oscillate.

For each curve there is a critical point of  $B_2$  and k. When  $B_2$  is below that point the coupled sys-

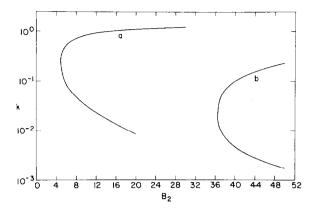


Fig. 3. Two cells: coupling rate for Hopf bifurcation from p=2 to p=0 vs.  $B_2$  at (a)  $A_1=A_2=1$ ,  $B_1=3$ ; (b)  $A_1=A_2=1$ ,  $B_1=3.9$ . System is stable inside the plots and unstable outside.

tem will oscillate, while if  $B_2$  is above that point, the system will be stable for some values of k. The value of  $B_2$  at the critical point rises with  $B_1$ , while the value of k decreases.

The critical  $B_2$  is plotted against  $B_1$  in fig. 4. It is seen that the line rises asymptotically to infinity at  $B_1 = 4$ . Between the line  $B_2 = B_1$  and the plotted

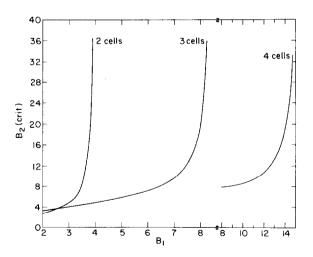


Fig. 4. Critical  $B_2$  (see text) vs.  $B_1$  for 2, 3 and 4 cells. Above the line, the system can be stable for some values of k. Below the line the system is never stable. Constant constraints:  $A_1 = A_2 = 1$ ,  $B_2 = B_3 (= B_4)$  in case of 3 (and 4) cells.

line or above  $B_1 = 4$  no stability is possible. Above the plotted line the coupled system will be stable for some coupling rates.

## 9. Three cells

Fig. 5 shows the complicated series of turning points and bifurcations that occur as p goes from 6 to 2 as the coupling rate increases. The existence of a stable steady state between the supercritical Hopf bifurcations is clearly marked. In addition, a variety of oscillations with a very complicated dynamics exists in this and similar systems.

Fig. 6 depicts stability regions in four exemplary cases in all of which  $A_1 = A_2 = A_3 = 1$ :

a)  $B_1 = 4.1$  with  $B_2 = B_3$  as the variable parameter. Results, similar to those shown in figure 3 for the two cells case, show also a critical  $B_2 = B_3$  below which no stability is possible while above it, stability occurs between the marked coupling rates. This critical value depends on  $B_1$  (as shown in fig. 4), and goes to infinity at  $B_1 = 8.6$ .

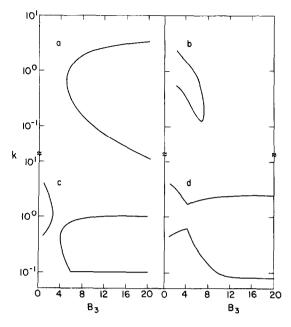


Fig. 6. Three coupled cells: coupling rate for Hopf bifurcation from p=2 to p=0 vs.  $B_3$ . At  $A_1=A_2=A_3=1$  in all cases: a)  $B_1=4.1$ ,  $B_2=B_3$ ; b) B=2,  $B_2=B_1+2$ ,  $B_3=B_1+4$  (abscissa is  $B_1$ ); c)  $B_1=6$ ,  $B_2=3.5$ , d)  $B_1=4.1$ ,  $B_2=10$ , system is stable inside the plots and unstable outside.

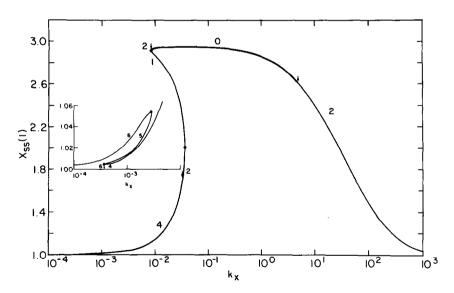


Fig. 5. Concentration of x species in the first cell of three coupled cells vs. the coupling rate  $B_1 = 3$ ,  $B_2 = 30$ ,  $B_3 = 100$ ,  $A_1 = A_2 = A_3 = 1$ . The inset shows an enlargement of the lower left corner. Dots (turning points) at  $k = 0.3872425 \times 10^{-3}$  (5, 6),  $k = 0.285393 \times 10^{-2}$  (6, 5), k = 0.0363274 (2, 1),  $k = 0.833739 \times 10^{-2}$  (1, 2). Arrows (bifurcations) at  $k = 0.3872825 \times 10^{-3}$  (6, 4),  $k = 0.322566 \times 10^{-1}$  (4, 2),  $k = 0.8339906 \times 10^{-2}$  (2, 0),  $k = 0.4952748 \times 10^{1}$  (0, 2).

Table II Critical coupling rate and  $B_2 = B_3$  as a function of  $B_1$ .  $A_1 = A_2 = A_3 = 1$ .

$B_1$	2.10	3.00	4.10	5.00	6.00	7.5	8.0	8.5
$B_2 = B_3$ (crit.)	3.21	4.01	4.99	5.87	7.07	12.5	19.8	71.8
k (crit.)	0.86	0.69	0.54	0.44	0.31	0.14	0.077	0.019

Table III Critical coupling rates and  $\Delta B$  as a function of  $B_1$ .  $A_1 = A_2 = A_3 = 1$ .

D	2.1	2.0	4.0	۷.0	7.0	7.06	7.5	9.0	0.3
$\boldsymbol{B}_1$	∠,1	3.0	4.0	0.0	7.0	7.05	1.5	8.0	8.2
$\Delta B$ (crit.)	0.85	1.07	0.93	0.85	1.95	2.00	3.75	8.85	14.3
k (crit.)	0.97	0.84	0.67	0.32	0.19	0.18	0.13	0.072	0.05

One notes that under these conditions no single pair of cells can be stabilized, yet the three cells will be stable.

The critical coupling rate, i.e., the coupling at the critical  $B_2 = B_3$ , falls roughly with the rise of  $B_2 = B_3$ . Table II shows this result.

b)  $B_2 = B_1 + 2$ ,  $B_3 = B_1 + 4$ , and  $B_1$  is the variable parameter. In other words, there is a constant difference  $\Delta B = 2$  between each pair of cells. In this case stability is obtained for low values of the variable parameter, i.e.,  $B_1$ , and above  $B_1 = 7.05$  no stability is possible. The stability range is in this case to the left of the critical parameter. In table III critical  $\Delta B$  and k are given as a function of  $B_1$ .

The critical value of  $\Delta B$  rises very sharply with  $B_1$  and beyond  $B_1 = 8.3$  no stability is possible for the three cells in this pattern. As the critical  $\Delta B$  rises, the critical coupling rate falls, in the same fashion as before.

- c)  $B_1 = 6$ ,  $B_2 = 3.5$ , and  $B_3$  is the variable parameter. In this case two, disconnected, ranges of stability are obtained. One range in the low  $B_3$ 's and the other at high  $B_3$ 's. In the gap  $2.5 < B_3 < 4$  no stability is possible.
- d)  $B_1 = 4.1$ ,  $B_2 = 10$ , as a function of  $B_3$ . In this case the gap between the two stability ranges has disappeared the two ranges have merged into one and stability can be found for any value of  $B_3$ .

## 10. Four and more cells

Two cases were studied:

a)  $B_2 = B_3 = \cdots = B_n$  as the variable parameter while  $B_1$  is kept constant. The plots of k vs.  $B_2$  are the same as in case a) above. For each  $B_1$ , there is a critical  $B_2$  below which there is no stability. A plot of  $B_1$  vs. critical  $B_2$  for the four cells case is shown in fig. 4. Again  $B_1$  increases, the critical  $B_2$  rises to infinity, in accord with the previous cases, at certain limiting value of  $B_1$ . Table IV shows the dependence of the limiting  $B_1$  on the number of cells.

Roughly speaking, the limiting  $B_1$  equals the square of the number of cells. As before, the increase of the critical  $B_2 = B_3 = \cdots = B_n$  goes together with the decrease of the critical k.

b)  $B_{i+1} = B_i + \Delta B$  with  $\Delta B = 2$  and  $B_1$  as the variable parameter. Similar to case b) in the three cells problem. The obtained plots are similar to those of case b) of the three cells problem. Above some critical  $B_1$  stability is no longer possible. The critical value of  $B_1$  increases while the critical coupling rate decreases with the number of cells as shown in table V. The value of  $B_1k/n$  is roughly constant.

As the number of cells increases the range of stability increases but small gaps of instability (similar to plot (c) of fig. 6) may be formed. For

Table IV Limiting  $B_1$  as a function of the number of cells.  $A_1 = A_2 = \cdots = A_n = 1$ .  $B_2 = B_3 = \cdots = B_n$ .

n	2	3	4	5	6	7
$\boldsymbol{B}_1$	4	8.6	15.2	24.3	35.3	48.2
-						

Table V Critical  $B_1$  and k with  $\Delta B = 2$ ,  $A_1 = A_2 = \cdots = A_n = 1$ , as a function of the number of cells

n	2	3	4	5	6	7
$B_1$	3.015	7.05	13.75	23.65	33.53	46.48
k .	0.24	0.19	0.13	0.103	0.087	0.074

example there are instability gaps when  $6.05 < B_1 < 7.55$  and  $8.35 < B_1 < 9.45$  for six and seven cells respectively.

At certain values of  $B_1$ , more than one stable configuration is possible at the same, or nearly the same, coupling rates, as in the problem of two cells with perturbation (fig. 2).

## 11. Discussion

The stability domains described are not exhaustive. Obviously the huge number of parameters defies such complete description. General conclusions can, however, be drawn from the presented material, in spite of such obvious limitations.

In the first place, the very fact that the coupling of oscillators can in some cases cause stability or different dynamics [6, 7] is of utmost experimental importance. Suppose the mixing between two or more parts of the same vessel is not perfect. In this case the parts behave essentially as the coupled cells described above, with some unspecified coupling rate. Such a system can suddenly come to a steady state (or have a totally different dynamics), although a better mixing will resume the oscillations. Such situations should obviously be eliminated in any experimental device, and care must be taken to ensure perfect mixing [11].

Most domains of stability, although quite varied in shape and location occur, usually about an order of magnitude around unit coupling rate. In other words, since the time in this dimensionless description is given in units of the reciprocal of the rate of reaction (4), the coupling rate which causes stability will be roughly of the same order of magnitude as the rate of disappearance of the X species. This point is illustrated quite well in the figures, in which ranges of stability are indicated.

The range of parameters in which the system of coupled cells may become stable increases with the number of cells. In a large number of coupled cells it is easier to find a set or sets of parameters which allow stability. This point is illustrated, for example, in fig. 4 and in tables IV and V. It is seen how the range of parameters in which stable steady state is enlarged with the number of cells.

This point may have a very important neurological implication [12]. A set of coupled nerve cells oscillating in unison, or otherwise, may reach stability just because more cells are added to the system, even if the extra cells have parameters which permit oscillations. It is possible, as seen in Table II, by adding a fourth cell to three others, to bring the whole system to a halt.

This conclusion is probably true for other oscillators as well. It was shown [1] earlier that this stabilization property is not a peculiarity of the Brusselator, but is also true for other oscillators. We can thus safely assume that increasing the number of coupled cells of any oscillator will have the same property.

Whether an addition of cells will stabilize the system or not, depends of course on the particular dynamics of the system. Thus adding the extra cells at one point of the trajectory may stabilize the system, while adding them at another point may not. A related point is the perturbation needed to bring a system from its oscillatory state to its stable one. This point can be answered only by finding the attraction basins of each steady of the states – a rather difficult task.

The problem of finding the conditions that the parameters must fulfill [1] in order for the system to have a stable steady state is still left unanswered. However, our computation shows that the answer must depend on the number of cells.

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