

Spatiotemporal Patterns in Cyclic Arrays with and without Time Delay

J. Kosek, P. Pinkas and M. Marek

Prague Institute of Chemical Technology,
Department of Chemical Engineering,
Technická 5, 166 28 Prague 6, Czech Republic.
e-mail: jkk@vscht.cz, pinkasp@vscht.cz, marek@vscht.cz

Abstract

Experimental studies of coupled chemical cells are briefly reviewed and compared with respect to the extent of time delay. Relevance of studies of circulating firing patterns in coupled cells with time delay for information storage are mentioned. Models of arrays of reaction-transport coupled cells with time delay are introduced and studied for excitatory and oscillatory chemical systems in the form of firing patterns arising either as a response to superthreshold concentration stimulation in an excitatory system or resulting from coupling in oscillatory systems, respectively. It is illustrated for Oregonator model of the BZ reaction that a single stimulation of a single excitatory cell with a delayed feedback acting on the input and/or of two or three coupled cells with a delayed mutual mass exchange can cause an excitation of a single pulse, a finite series of pulses (firings) and of an infinite circulating series of firings in dependence on the amplitude of the stimulation, the extent of the time delay and the intensity of the coupling among the cells. The regions of parameter space (intensity of coupling, time delay) for the existence of circulating firings are determined. Existence of periodic, quasiperiodic and chaotic patterns in the form of standing waves in coupled minimal bromate oscillators are also discussed.

1 Introduction

Large number of reaction-diffusion systems of biological origin, for example those forming active (excitable, conducting) tissues in neuro- and cardio- physiology are discrete, consisting from cells (compartments) mutually coupled via electrical and/or mass exchange (chemical) contacts. Propagation of impulses in the form comparable to front and pulse waves is a common feature of such systems (Holden *et al* 1990). Circulating "waves" are of a special importance, particularly in myocardial and brain tissue. For example, the recent results of PET scanning show that working memory is located in the pre-frontal cortex. Working memories are retained by the continuous activity of particular neurons. These neurones stimulate themselves either directly or via a loop involving others. When they stop firing, the memory is lost unless it has been passed on to the hippocampus for more permanent storage (Gelenbe 1991, Amit 1989).

In this paper we study the conditions of existence and properties of circulating excitations ("firings") in several compartmentalized chemical systems. We shall concentrate our attention on the effects of time-delay on the properties of simple circulating spatiotemporal firing patterns. Compartmental chemical systems are now relatively well understood from the point of view of agreement between experimental observations and simulations based on robust mathematical models, after more than 25 years of research.

Studies of model chemical compartmentalized systems have been at first only theoretical. Thus Prigogine and Lefever have studied two coupled cells (Prigogine and Lefever 1967). Scriven and Othmer (Othmer and Scriven 1971,1974) and Martinez and Baer (Martinez and Baer 1973) have analyzed the stability properties of arbitrary network of compartments, mostly by analytical methods. Bunow and Colton (Bunow and Colton 1975) have studied behaviour of linear array of cells with enzyme with substrate inhibited kinetics. They have found asymmetric steady state concentration profiles. Two coupled CSTRs with mutual mass exchange and oscillatory Belousov - Zhabotinski (BZ) reaction have been first studied experimentally in 1975 (Stuchl and Marek 1975). Later, asymmetric steady state concentration patterns and their stability have been investigated in a hexagonal structure of seven reactors (CSTRs) with mutual mass exchange (Stuchl and Marek 1982). Two coupled CSTRs with an oscillatory reaction and direct mass exchange were also studied experimentally by Sawada and coworkers (Fujii and Sawada 1978, Nakijama and Sawada 1981,1988). Two CSTRs coupled electrically were investigated by Crowley and Field (Crowley and Field 1986) and Crowley and Epstein (Crowley and Epstein 1989). Dolník *et al.* (Dolník *et al* 1987) have studied experimentally two coupled CSTRs with mutual mass exchange, oscillatory BZ reaction and concentration forcing of one of them. Breton *et al.* (Breton *et al* 1986) and Marmillot *et al.* (Marmillot *et al* 1991) have studied experimentally multiple steady states in two and three coupled CSTRs with mutual diffusional coupling. They have used a photobiochemical reaction catalyzed by immobilized thylakoids and demonstrated both experimentally and on numerically solved models the occurrence of both stable symmetric and asymmetric steady states in a circular and linear array of cells. Laplante and Erneux (Laplante and Erneux 1992) have studied a one-dimensional array of 16 coupled stirred tank reactors. They have used the bistable chlorite-iodide reaction and studied propagation of the front wave in the system. Weiner *et al.* (Weiner *et al* 1992) studied two identical chemical oscillators (minimal bromate oscillator) coupled by means of the mutual regulation of the flow rate of one reactor by the output of the other and vice versa according to measured Ce^{4+} ions concentration with defined time delay and intensity of coupling. Kosek and Marek (Kosek and Marek 1993) have

studied experimentally propagation of excitation in two continuous stirred tank reactor cells mutually coupled via direct mass exchange through the common wall and modelled the propagation of excitation in a linear array of N -coupled cells via the Oregonator model. Raschman et al. (Raschman *et al* 1986) have studied periodic and aperiodic regimes in linear and cyclic arrays of coupled cells with mutual mass exchange and Brusselator kinetics. Theoretical and computational studies in coupled cells are numerous and have been recently reviewed in two book publications (Scott 1991, Marek and Schreiber 1991). Review of chaotic regimes in coupled and forced excitable and oscillatory cells have been also published recently (Marek and Schreiber 1993).

In the above listed experimental studies of coupled cells three ways of the coupling were realized :

- mass coupling via direct convective-diffusive mass exchange between neighbouring cells,
- electric coupling,
- mass coupling via pumping between the cells.

These ways of coupling differ in the extent of the time-delay in the coupling signal. In the case a) time-delay is low, in the case b) the extent of the coupling-delay can be controlled (e.g. via computer) and the case c) always includes significant time-delay.

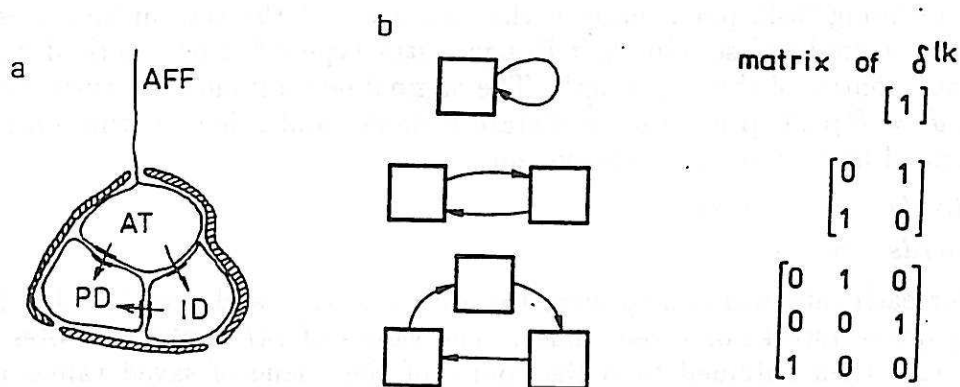


Figure 1:

- Group of synapses, cf. (Sheperd 1979). AFF - afferent axon, AT - synapse of external axon, PD - dendrite of principal neuron, ID - dendrite of intrinsic neuron.
- Configurations studied in this paper.

Recently we have designed an experimental set up of three flow-through CSTRs with the possibility of using all three above ways of mutual coupling. Hence we should be able to study and compare the effects of time-delay introduced by various ways of coupling. In this paper we present first the results of the study of the time-delay on the propagation of excitations and wave-like spatiotemporal patterns in the excitable Belousov-Zhabotinskii (BZ) and discuss also wave regimes in a minimal bromate (MB) oscillatory reaction mixtures modelled by the Oregonator and Minbromator models. We believe that both experimental and connected modelling studies of circulating waves under relatively well defined conditions can be of importance in the understanding of both chemical and electric synapse. A sketch of a group of synapsis according to Ref. (Shaperd 1979) is shown in Fig. 1a. The modelled systems of coupled cells studied in this paper are schematically shown in Fig. 1b.

2 Models of arrays of reaction-transport coupled cells with time-delay

Let us consider a linear or cyclic array of cells. Each cell can exchange mass both with the environment and with its neighbours. Mass balances for the system of N coupled cells with n reaction components may be written in the form

$$dc_i^k/dt = f_i(c_1^k, \dots, c_n^k) + \sum_{j=1}^n d_{ij} \sum_{l=1}^N \delta^{lk} (c_j^l(t - \tau) - c_j^k(t)) \quad (1)$$

Here c_i^k is the concentration of the i -th reaction component in the k -th cell, $f_i : \mathbf{R}^n \rightarrow \mathbf{R}$ are functions describing reaction kinetics and mass exchange with the environment. The rate of transport of the i -th component between the cells is proportional to the difference between the concentrations $c_j^l(t - \tau)$ and $c_j^k(t)$, where τ denotes time-delay in the concentration of the component j exchanged between the l -th and k -th cells. Here $\delta^{lk} = 1$ when the coupling exists, otherwise $\delta^{lk} = 0$. The configurations studied in this paper are schematically depicted in Fig. 1b.

3 Numerical method

Numerical integration of a non-autonomous system of ODEs can be computer time-consuming task, particularly if the dimension of the system increases. We have used a modified semiimplicit Runge-Kutta type 4th order method with an automatic control of the step length. The original non-autonomous system of Eqs (1) $d\mathbf{p}/dt = f(\mathbf{p}, t)$ (\mathbf{p} is a vector of state variables and t denotes time) has been transformed into an autonomous system

$$\begin{aligned} d\mathbf{p}/ds &= f(\mathbf{p}, t) \\ dt/ds &= 1 \end{aligned} \quad (2)$$

After each integration step were the values of t , \mathbf{p} and $d\mathbf{p}/dt$ added into a shifting queue (stack) of saved values. The values of $\mathbf{p}(t - \tau)$ (τ denotes time-delay) were then obtained from the course of the queue of saved values in the proper neighbourhood of the point $(t - \tau)$. The elements of the Jacobi matrix of the system have been evaluated as

$$dp_i(t - \tau)/dp_i = (dp_i(t - \tau)/dt)/(dp_i/dt) \quad (3)$$

where the values of $dp_i(t - \tau)/dt$ were also obtained by a Lagrange interpolation from the shifting queue of saved values.

4 Oregonator model

The well known Oregonator model of the BZ reaction (Field and Noyes 1974) have been used in the form

$$f_1(X, Y, Z) = k_1BY - k_2XY + k_3BX - 2k_4X^2 + k_0(X_0 - X) \quad (4)$$

$$f_2(X, Y, Z) = -k_1BY - k_2XY + f k_5Z + k_0(Y_0 - Y) \quad (5)$$

$$f_3(X, Y, Z) = k_3BX - k_5Z + k_0(Z_0 - Z) \quad (6)$$

where X denotes the concentration of $HBrO_2$, Y the concentration of Br^- , Z the concentration of Ce^{4+} and B the concentration of BrO_3^- , respectively. The values of the parameters used in the modelling of experiments of excitation propagation in two coupled cells, cf. (Kosek and Marek 1993). have been used also in this study, cf. Table 1.

Table 1: Oregonator parameter values.

parameter	value	parameter	value
k_1	2.00 $dm^3.mol^{-1}.s^{-1}$	X_0	0.00 $mol.dm^{-3}$
k_2	2×10^9 $dm^3.mol^{-1}.s^{-1}$	Y_0	1×10^{-6} $mol.dm^{-3}$
k_3	1×10^4 $dm^3.mol^{-1}.s^{-1}$	Z_0	1×10^{-3} $mol.dm^{-3}$
k_4	5×10^7 $dm^3.mol^{-1}.s^{-1}$	B	0.10 $mol.dm^{-3}$
k_5	1.00 s^{-1}	f	1.00
k_0	5×10^{-4} s^{-1}		

5 Firing patterns in the Oregonator model

5.1 Single reaction cell

The most simple model of a reaction cell (an enclosure, cell compartment, a neuron synapse, etc.) can be represented by a single continuous stirred reactor with a delayed feedback, cf. Fig. 1a. We shall study the response of such a reactor to a single superthreshold concentration stimulation with an amplitude A . In the Oregonator model we consider that the amplitude $A < 0$ as we assume that the perturbation corresponds to a decrease of the concentration of Br^- ions caused by an addition of Ag^+ ions into the reactor, cf. experimental procedure and results in (Kosek and Marek 1993).

Global simulation study of the single reactor for values of parameters describing an excitable regime in the reactor has revealed the following types of the behaviour (firing patterns) :

Pattern A : A single excitation ("firing") occurs in the cell, cf. Fig. 2a-c. We can observe in the Figure that single full amplitude excitation occurs and then the excitations decay relatively fast. The successful firing can be identified on the basis of the time course of Ce^{4+} or Br^- ions (proportional to redox potential changes), similarly as in (Kosek and Marek 1993).

Pattern B : A finite cascade of firings, with the firing number n occurs, cf. Fig. 2d. It means that the reactor is able to selfexcite itself and the period of firings ("selfexcitations") is determined by the value of the time-delay.

Pattern C : Permanent firing. For sufficiently large value of the time delay the cell can selfexcite itself continuously ($n = \infty$), cf. Fig. 2e. This situation is analogous to periodically stimulated single CSTR without a time-delay with superthreshold amplitude of the stimulation and the period of stimulation $T > T_R$ (T_R is a refractory period) cf. (Schreiber and Marek 1993).

Pattern D : When the feedback flow (the value of the parameter k_x) increases, it becomes a controlling process and we can observe a single slowly decaying oscillation in the reactor, cf. Fig. 2f.

5.2 Cell arrays

The behaviour described above (patterns A - D) are in principle preserved in cyclic cell arrays. However, the excitation will not propagate for lower values of the mutual coupling (mass transport) coefficient k_x through entire cascade.

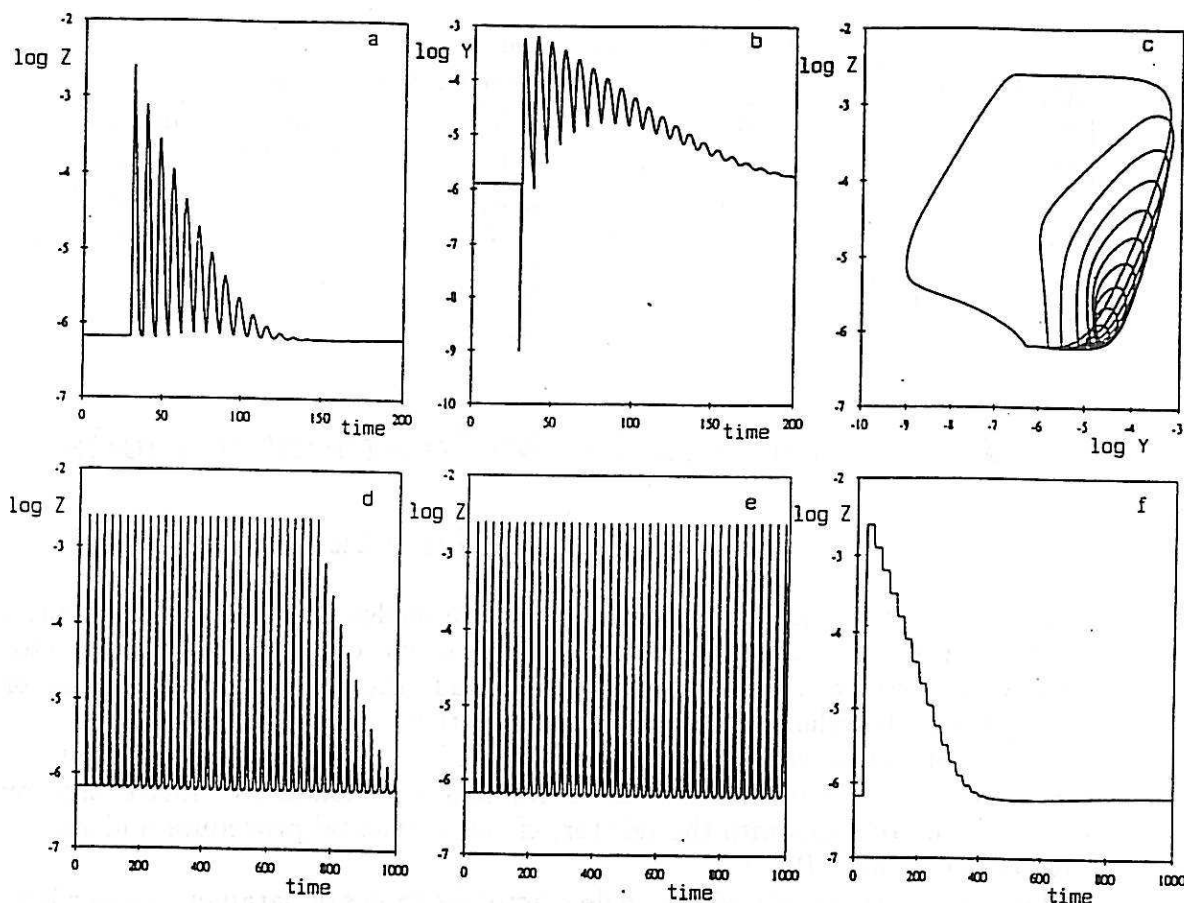


Figure 2: Time course of Z concentration in a single CSTR with delayed feedback, $A = 0.75 \times 10^{-6}$.

a), b), c) Single successful excitation; $k_x = 0.90s^{-1}$, $\tau = 8.0s$. a) $\log Z(t)$, b) $\log Y(t)$, c) $\log Z(t)$ vs $\log Y(t)$.

d) 31 successful excitations; $k_x = 0.90s^{-1}$, $\tau = 24.0s$, $\log Z(t)$.

e) Continuous firing, $k_x = 0.90s^{-1}$, $\tau = 24.5s$, $\log Z(t)$.

f) Mass transport driven regime - very slow single excitation, $k_x = 1.02s^{-1}$, $\tau = 24.0s$, $\log Z(t)$.

Pattern E : For example, for two reaction cells we observe the pattern where the firing occurs in a single cell only, $n_1 = 1$ and $n_2 = 0$ (n_i denotes the number of firings in the i -th cell). This will be denoted as pattern E and it has been discussed in detail for two cells in (Kosek and Marek 1993).

Generally, in the cyclic arrays of two and more coupled cells we can observe firing regimes belonging to the pattern B, where for two cells either $n_1 = n_2$ or $n_1 = n_2 + 1$, $n_1 > 1$ and in the case of three cells either $n_1 = n_2 = n_3$ or $n_1 = n_2 = n_3 + 1$ or $n_1 = n_2 + 1$ and $n_2 = n_3$; $n_1 > 1$.

Examples of the time courses of the variable Z for two cells are in Figs 3a,b and for three cells in Fig. 4a-c.

The overall dependence of the firing numbers n_1 , n_2 in two coupled cells on the time-delay is depicted in Fig. 5. We can observe the sequence of regimes with increasing values of firing numbers n_1 and n_2 and the existence of a limit value of the time-delay τ^* for the permanent firing. For values of time-delay $\tau > \tau^*$ two cells mutually stimulate themselves indefinitely, i.e., $n_1 = n_2 = \infty$.

Typical diagrams of computed regimes in the parametric plane mass transport (coupling) coefficient k_x - time-delay τ are given in Figs 6a-d. For high values

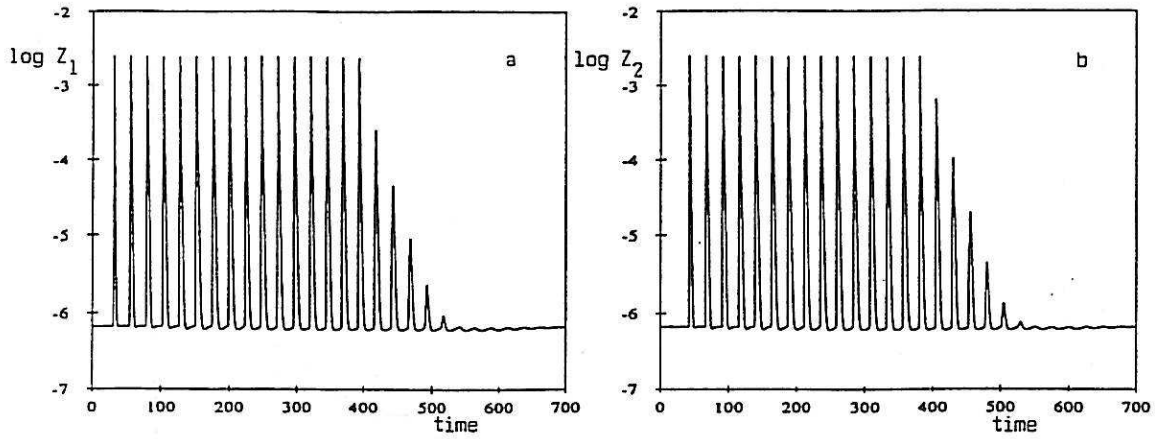


Figure 3: Time course of Z concentration in two coupled CSTRs with a delayed mass exchange, $A = -0.75 \times 10^{-6}$, $k_x = 0.90s^{-1}$, $\tau = 12.0s$.

a) $\log Z_1(t)$ - 16 successful firings.

b) $\log Z_2(t)$ - 15 successful firings.

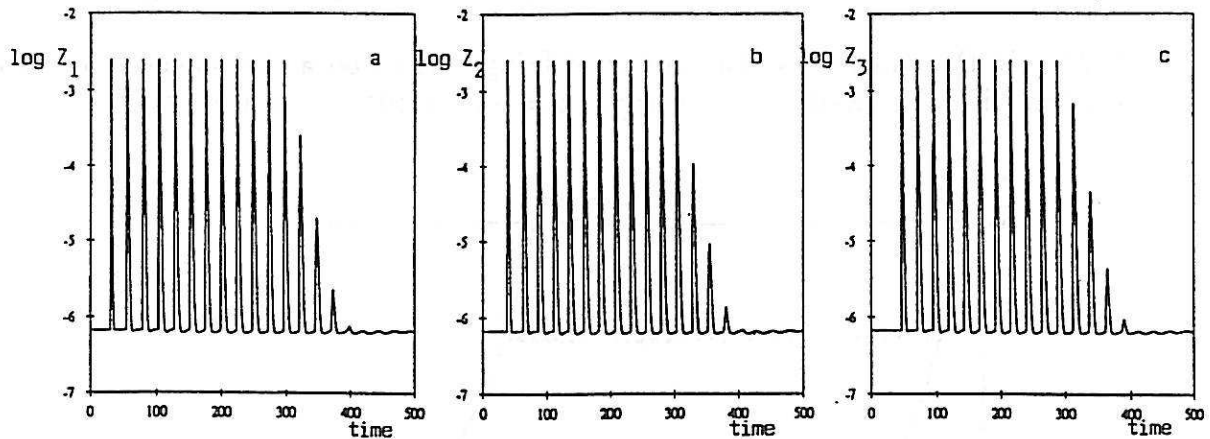


Figure 4: Time course of Z concentrations in a cyclic array of three CSTRs with a delayed mass exchange, $A = -0.75 \times 10^{-6}$, $k_x = 0.90s^{-1}$, $\tau = 8.0s$.

a) $\log Z_1(t)$ - 12 successful firings.

b) $\log Z_2(t)$ - 12 successful firings.

c) $\log Z_3(t)$ - 11 successful firings.

of k_x we can observe slow decay of single excitation (pattern D). In the region of low values of time-delays and intermediate values of k_x a single firing in each cell exists (pattern A). When the value of the time-delay τ is increased we subsequently observe regions with finite number of firings (pattern B) and finally continuous firing (pattern C). In arrays of cells we can observe the presence of the pattern E for lower values of k_x .

When Figs 6b and 6c obtained for different stimulation amplitudes are compared we observe that when higher absolute value of the stimulation amplitude (A) is used, then the regions of the parameter space with patterns B and C are located in narrower range of values of the mass transport (coupling) coefficient k_x . When even higher stimulation amplitudes are used ($A < -0.86 \times 10^{-6}$) then the regions of patterns B and C disappear from the diagrams. Hence we can observe qualitatively similar type of the propagation failure as reported earlier in experimental study of two coupled excitable cells (Kosek and Marek 1993).

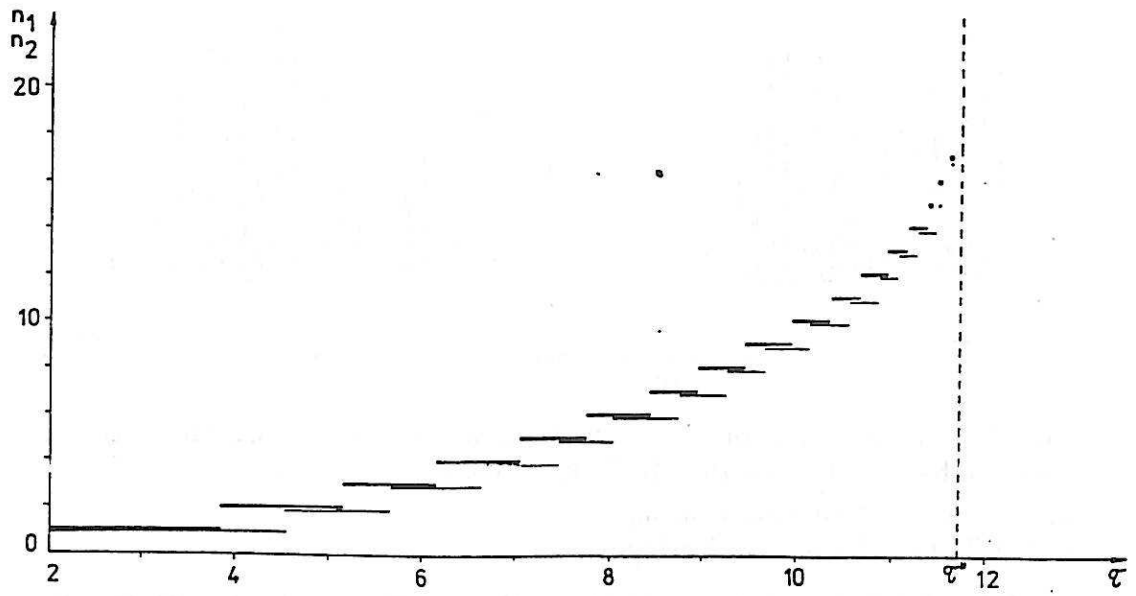
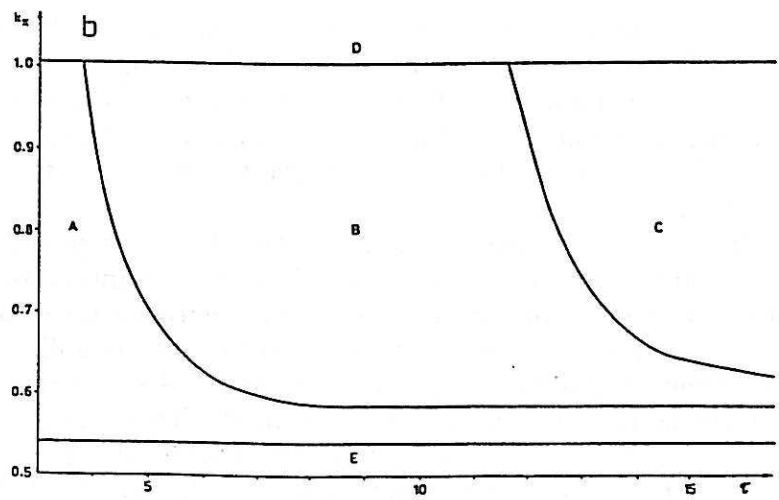
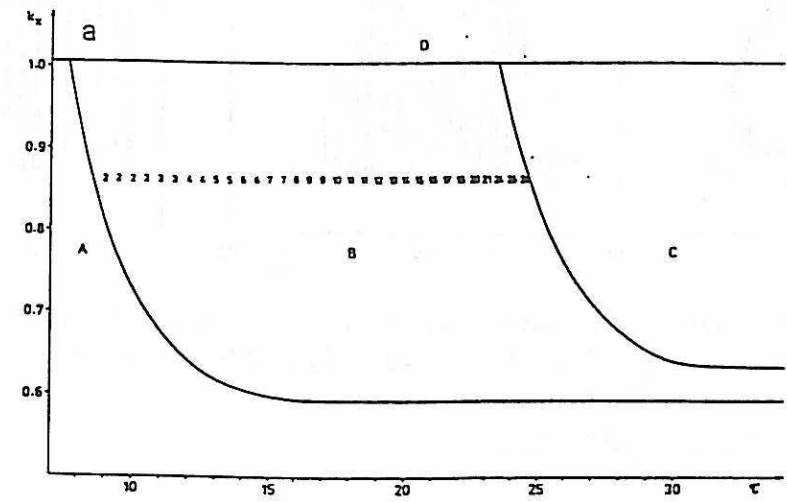


Figure 5: Dependence of the number of firings n_1, n_2 on a time-delay τ for two CSTRs with a delayed mass exchange, $A = -0.8 \times 10^{-6}$, $k_x = 1.00s^{-1}$.



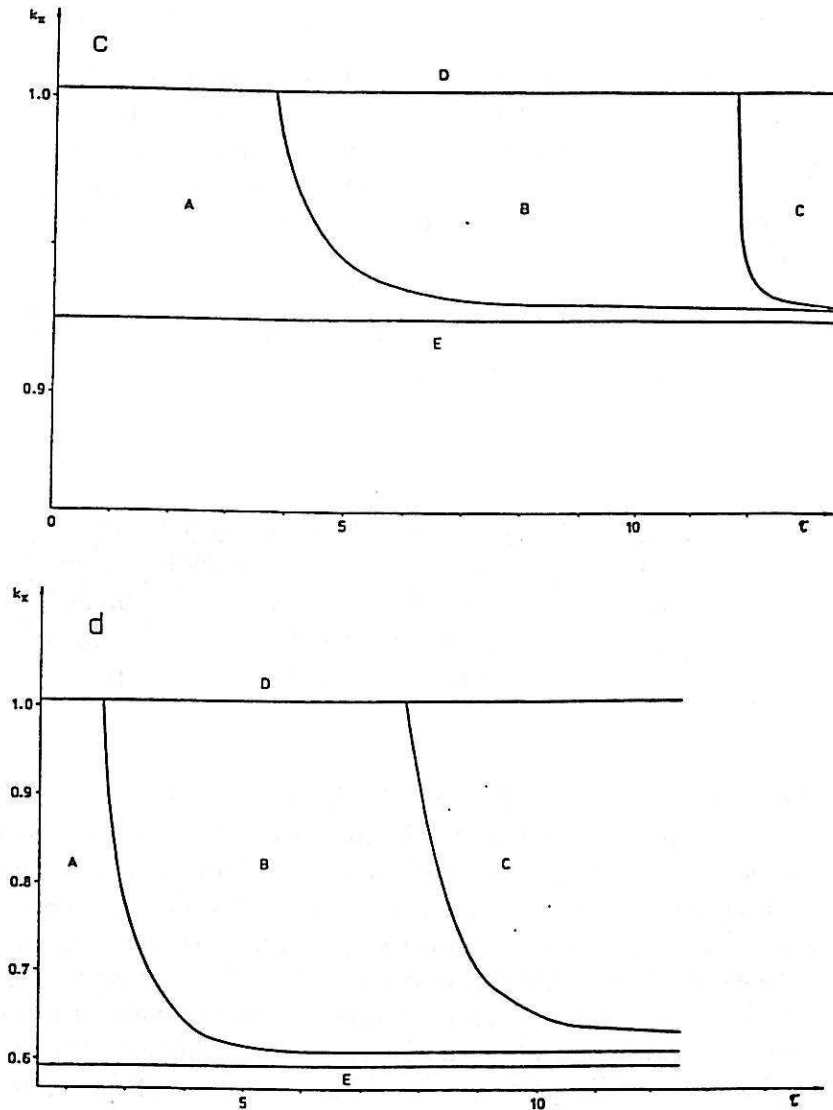


Figure 6: Various firing regimes in the plane mass transport coefficient k_x - time-delay τ . A - single firing in each cell, B - multiple firings in each cell, C - continuous firing, D - mass transport driven regime - single slow excitation, E - single excitation in the stimulated reactor.

- Single CSTR with a delayed feedback, $A = -0.75 \times 10^{-6}$.
- Two CSTRs with a delayed mutual mass exchange, $A = -0.75 \times 10^{-6}$.
- Two CSTRs with a delayed mutual mass exchange, $A = -0.80 \times 10^{-6}$.
- Cyclic array of three CSTRs with a delayed mass exchange, $A = -0.75 \times 10^{-6}$.

6 Minbromator model

The inorganic core of the BZ reaction forms the basis of minimal bromate oscillator (Noyes *et al* 1971). Here we are using the variable version of the model proposed by Schreiber (Schreiber 1992). The model has been used in the form

$$f_1(x, y, w) = [-xy + qy - x^2 - x + K_5 u(x, w)^2 + u(x, w)w - K_6 x(c - w)] / E + K_0(-x) \quad (7)$$

$$f_2(x, y, w) = [-qyv(x, y) - xy - qy]/q + K_0(y_0 - y) \quad (8)$$

$$f_3(x, y, w) = -u(x, w)w + K_6x(c - w) + K_0(w_0 - w) \quad (9)$$

where x is scaled concentration of $H\text{OBr}$, y is scaled concentration of Br^- , w is scaled concentration of Ce^{3+} , t is dimensionless time, K_5 , K_6 , q , E are kinetic parameters, K_0 , c are reactor parameters, w_0 , y_0 are input concentrations of Ce^{3+} , Br^- , and $u(x, w)$, $v(x, y)$ are nonlinear functions arising in the course of the reduction of dimension of this system based on the quasi-steady state assumption and are defined as

$$u(x, w) = [2(2x + K_6x(c - w))]/\{w + \sqrt{w^2 + 8K_5[2x + K_6x(c - w)]}\} \quad (10)$$

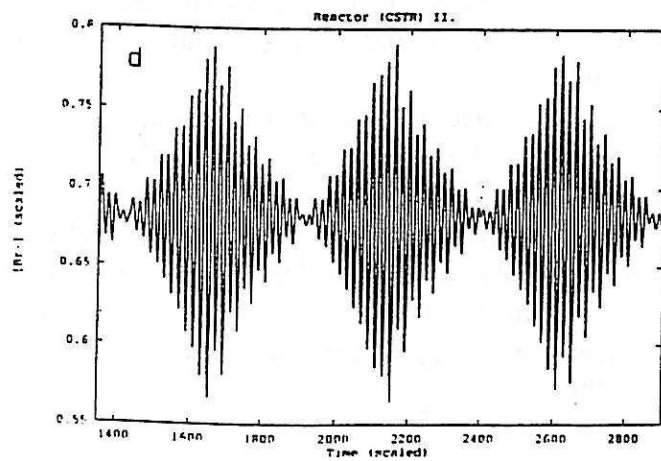
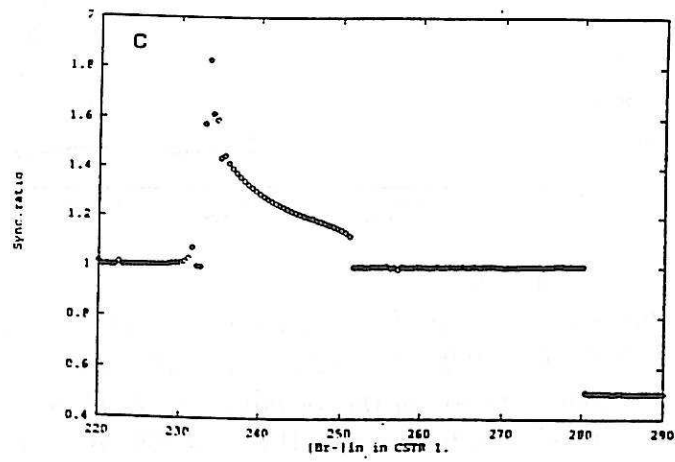
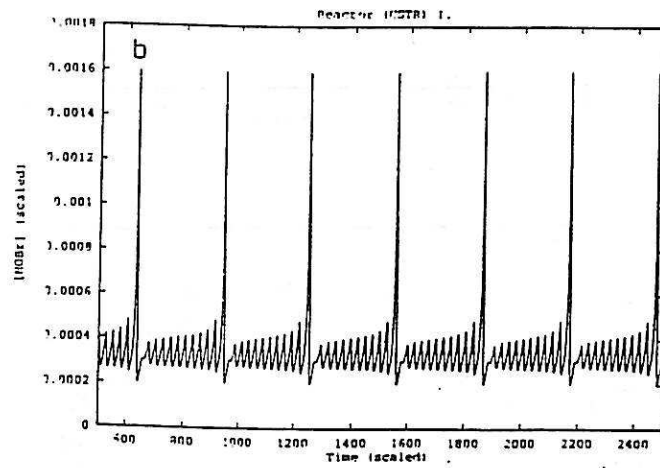
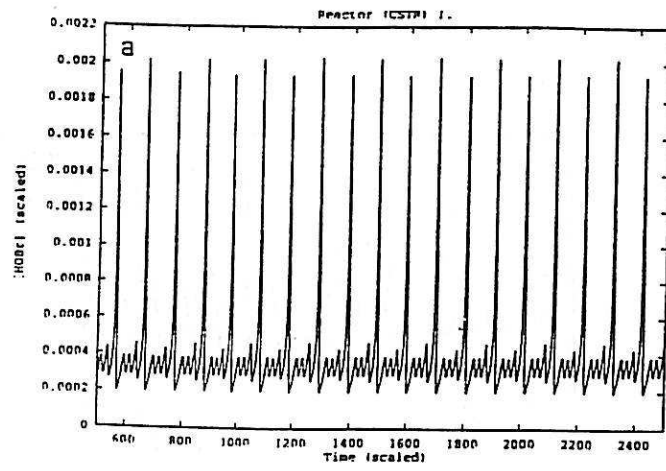
$$v(x, y) = (4x + x^2/y)/(2q) + 1 \quad (11)$$

Table 2: Minbromator parameter values.

parameter	value	parameter	value
E	0.0476	w_0	0.0204
q	9.52×10^{-5}	K_5	0.0893
c	0.0204	K_6	31.2

On the case of coupled cells with the minbromator kinetics we shall illustrate several spatiotemporal patterns which can arise in two and three cell arrays without a time-delay. Both multiple steady states and oscillations may exist in a single cell. Coupling may cause not only appearance of additional unsymmetric steady states (spatial patterns) but also interesting spatiotemporal patterns. If an oscillatory state exists in a single cell and the value of the mass transport coefficients k_x (k_x is scaled coefficient of mass exchange) is varied, then for intermediate values of k_x there exist both periodic, quasiperiodic and chaotic patterns. In Fig. 7a,b are examples of periodic patterns for different values of k_x . The dependence of the ratio of the number of oscillations in the first cell (p) to the number of oscillations in the second cell (q) - p/q - on a parameter (inlet concentration of y) is shown in Fig. 7c. We can observe several steps for similar to devil's staircase-like dependence. Both quasiperiodic (cf. Fig. 7d,e) and chaotic (cf. Fig. 7f) spatiotemporal patterns exist in a certain parametric range. Chaotic attractors may in this case arise both via period-doubling route and via the torus breaking (cf. lobbed Poincare section of the chaotic attractor in Fig. 7f).

Similar periodic, quasiperiodic and chaotic patterns can exist in a cyclic array of three coupled cells. An example of a quasiperiodic pattern is depicted in Fig. 8a,b. We can observe that amplitudes, periods and phases of oscillations in individual cells vary widely.



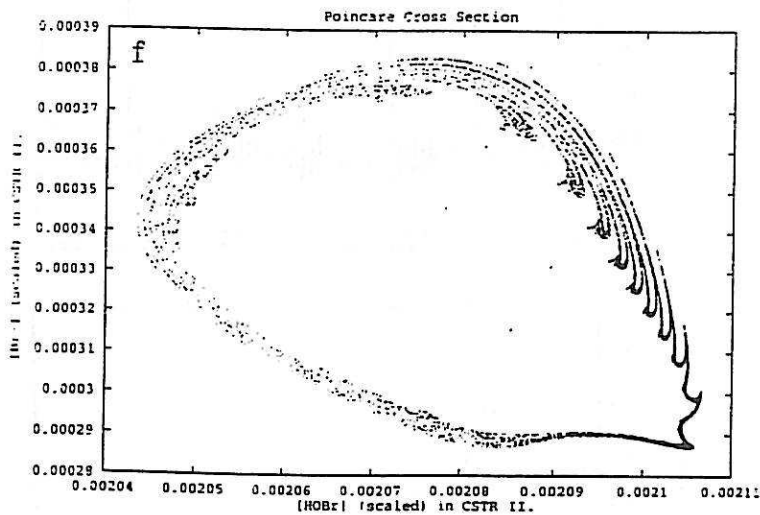
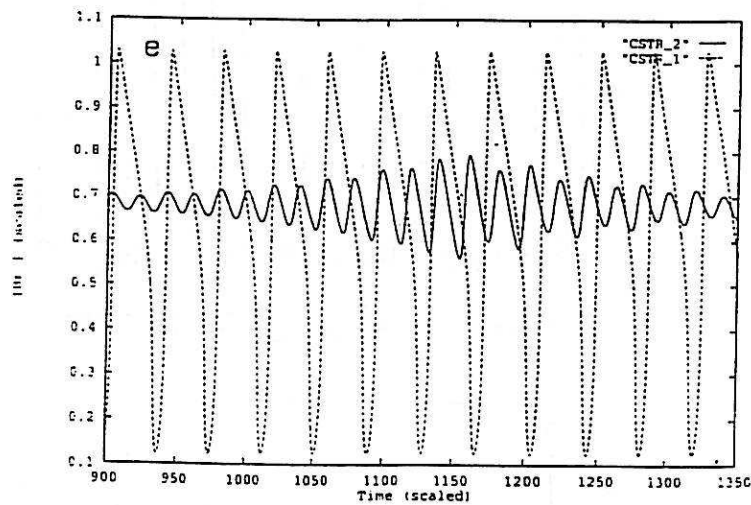


Figure 7: Two coupled cells.

- a) Course of the concentration of the variable. $[HOBr]$ (scaled) vs time (scaled), reactor I : $y_0 = 280$, $K_0 = 0.03$, reactor II : $y_0 = 260$, $K_0 = 0.03$, $k_x = 0.001$.
- b) Course of the concentration of the variable. $[HOBr]$ (scaled) vs time (scaled), reactor I : $y_0 = 280$, $K_0 = 0.03$, reactor II : $y_0 = 260$, $K_0 = 0.03$, $k_x = 0.01$.
- c) Dependence of the resonance ratio p/q on the inlet concentration. Values of parameters : reactor I : $K_0 = 0.03$, $y_0 \in \langle 220; 290 \rangle$, reactor II., $y_0 = 280$, $K_0 = 0.03$, $k_x = 0.001$.
- d) Time course of Br^- concentration, 2nd reaction cell. $[Br^-]$ (scaled) vs time (scaled), reactor I : $y_0 = 280$, $K_0 = 0.03$, reactor II : $y_0 = 280.468$, $K_0 = 0.03$, $k_x = 0.001$.
- e) Time course of Br^- concentration in both reaction cells.
- f) Poincaré section of chaotic attractor arising via torus breaking; values of parameters : $[HOBr]$ (scaled) in 2nd CSTR vs $[HOBr]$ (scaled) in 1st CSTR (Poincaré Cross Section). Reactor I : $y_0 = 280$, $K_0 = 0.03$, reactor II : $y_0 = 280.458$, $K_0 = 0.03$, $k_x = 0.001$.

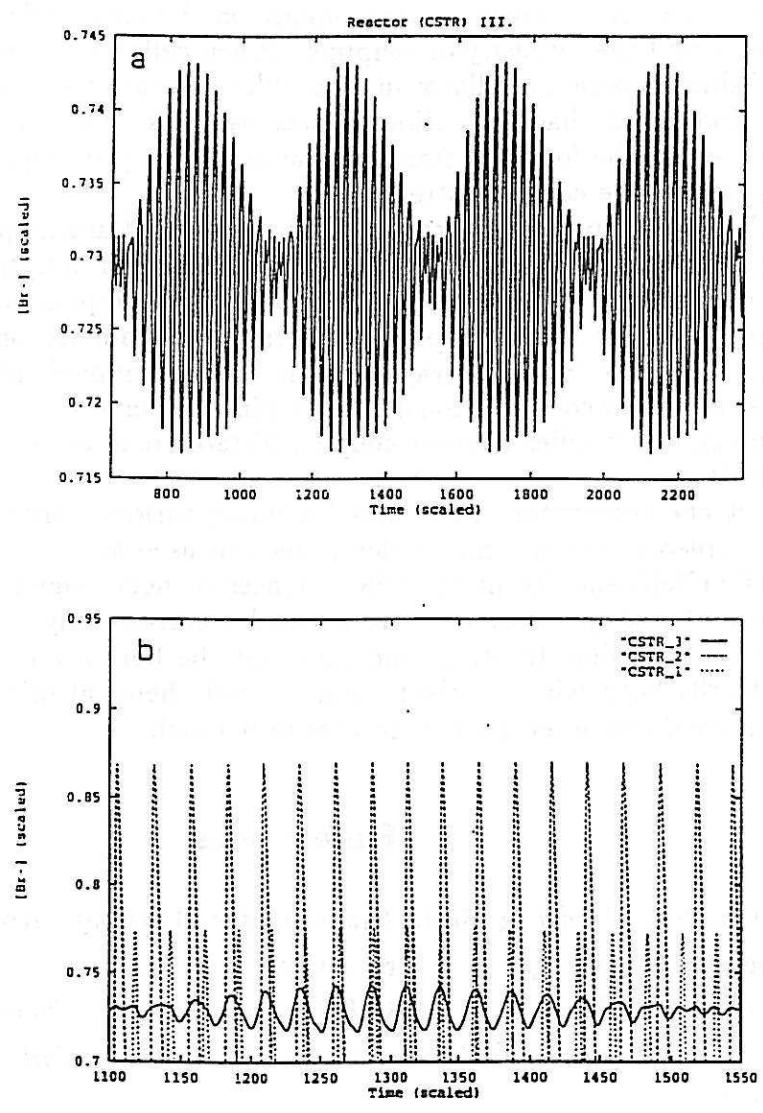


Figure 8:
a) Three coupled cells; quasiperiodic time course of oscillations in a single cell; values of parameters.
b) Time course of oscillations in three cells.
[Br-] (scaled) vs time (scaled), reactor I : $y_0 = 250$, $K_0 = 0.03$, $k_{x12} = 0.001$, reactor II : $y_0 = 260$, $K_0 = 0.03$, $k_{x23} = 0.001$, reactor III : $y_0 = 285$, $K_0 = 0.03$, $k_{x31} = 0.001$, where k_{xij} is the coefficient of mass exchange between i -th and j -th reactor.

7 Discussion and conclusion

Characteristic spatiotemporal patterns may arise in the discrete arrays of coupled cells both when single cell is in excitable and oscillatory state. As it was illustrated for the case of Oregonator model, single stimulation of an excitatory cell can cause excitation of a single pulse, finite series of pulses and infinite circulating series of firings, respectively, in dependence on the amplitude of the stimulations, time-delay and the intensity of coupling. When cells with a simpler chemical system, minimal bromate oscillator in an oscillatory state are coupled, then periodic, quasiperiodic and chaotic spatiotemporal patterns arise. These spatiotemporal patterns are in the forms of standing waves and vary in dependence on the inlet conditions and the coupling strength.

Both types of spatiotemporal patterns can be used under specific conditions for storing an information contained in the incoming signal (amplitude of stimulation, a level of the inlet concentration of characteristic component) and respond with a specific firing or spatiotemporal pattern in dependence on the time-delay or coupling strength. Simple arrays of cells can be coupled into layers or cellular networks and their computational and learning properties can be studied, similarly as in the case of studies of mass coupled bistable reaction systems, cf. (Hjermfelt *et al* 1993).

Intact chemoreceptors structures including various nerve cells have been recently coupled to potentiometer electrodes and used as sensors for specific stimulants, cf. (Belli and Rechnitz 1988). Traces of nerve signal responses, both in a single and multiple unit case are studied quantitatively. These developments make it now possible to study and interpret the behaviour of discrete arrays of coupled cells both with relatively well defined chemical mixtures and still only partly defined chemoreceptor structures in parallel.

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