A coupled chemical burster: The chlorine dioxide–iodide reaction in two flow reactors

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The dynamical behavior of the chlorine dioxide–iodide reaction has been studied in a system consisting of two continuous flow stirred tank reactors (CSTRs). The reactors are coupled by computer monitoring of the electrochemical potential in each reactor, which is then used to control the input into the other reactor. Two forms of coupling are employed: reciprocally triggered, exponentially decreasing stimulation, and alternating mass exchange. The reaction, which exhibits oscillatory and excitatory behavior in a single CSTR, displays neuronlike bursting behavior with both forms of coupling. Reciprocal stimulation yields bursting in both reactors, while with alternating mass exchange, bursting is observed in one reactor and complex oscillation in the other. A simple model of the reaction gives good agreement between the experimental observations and numerical simulations.

I. INTRODUCTION

The problem of two coupled chemical oscillators has been investigated for almost 20 years. A distinction among coupled systems is often made according to the nature of the coupling.1 The most thoroughly studied experimental systems in chemistry are those that are physically coupled through mass transport.2–9 Another form of physical coupling can be accomplished by electrical connection of two continuous flow stirred tank reactors (CSTRs).10 Such systems are analogous to biological neurons coupled through gap junctions.11 Chemical coupling represents a substantially different way of linking two (or more) subsystems which are capable of independent oscillation and which have one or more species in common.1 This form of coupling resembles in some ways synaptic coupling of neurons,11 with the common species playing the role of the neurotransmitter in carrying information from one subsystem to the other.

Coupled chemical oscillators display a wide variety of dynamical behavior such as synchronization, frequency locking, quasiperiodicity, chaos, birhythmicity, extinction of oscillation and rhythmogenesis.12 Bursting behavior, i.e., regular alternating periods of quiescence and of oscillations, is a common feature of neural oscillators. Bursting can occur in isolated single neurons, and in pairs or in larger networks of synaptically coupled neurons. The sharp voltage maxima occurring in bursting neurons are known as action potentials; they serve as a means of transmitting information from cell to cell. A bursting signal from a typical neuron is shown in Fig. 1.

Bursting can also be found in coupled chemical systems, but until now most observations of this phenomenon have been made in the Belousov–Zhabotinsky reaction in a single reactor system.14–16 Recently, bursting behavior has been observed in the chlorine dioxide–iodide reaction in a CSTR.19 When the excitatory steady state in a single flow reactor is stimulated by superthreshold injection of a solution of chlorite ion or of chlorine dioxide, transient oscillations are observed following a period of very low iodide concentration. Under periodic stimulation the system produces bursts of oscillations resembling those found in neurons with postinhibitory rebound,20 a situation in which immediately after a period of inhibition (hyperpolarization), the neuron is for a time more excitable than in the absence of inhibition. This dynamical resemblance has encouraged us to attempt to stimulate in chemical systems situations that may occur in systems of neurons. For the present study we have chosen the chlorine dioxide-iodide reaction in a system consisting of two coupled CSTRs.

One form of coupling introduced here and referred to as alternating coupling by mass transfer is a modification of physical coupling with mass exchange. We allow mass transfer in only one direction at any given time. This arrangement resembles in some ways the coupling of neurons through gap junctions, though the analogy is by no means perfect. The other form of coupling that we employ does not correspond to either simple physical or chemical coupling. This configuration, which we call connection by reciprocal stimulation, is intended to be an approximation of mutual inhibitory synaptic connection.

In this paper, we first describe the experimental and numerical realization of these coupling schemes. Next, we present experimental and numerical examples of bursting behavior observed in this system. The conditions and parameters that play the most important role in producing bursting behavior are then analyzed together with a comparison of the experimental and numerical results.

II. RECIPROCALLY TRIGGERED, EXponentially DECREASING STIMULATION

In reciprocally triggered, exponentially decreasing stimulation the amount (or strength) of the stimulus decreases exponentially with time. The initiation of the stimulus delivered to one reactor cell is triggered by an event in the other cell, and the connection is reciprocal. For exam-
ple, when the concentration of a chosen species in reactor 1 increases above a certain value, then an additional input flow from a supplementary reservoir into reactor 2 is activated. The concentration level that causes the beginning of stimulation is called the trigger value. The additional flow decreases exponentially with time until the concentration in cell 2 reaches its trigger value, at which time stimulation of cell 2 ceases and stimulation of cell 1 begins.

A. Experiment

The chlorine dioxide–iodide reaction in a single CSTR possesses two different stable steady states [one with low iodide (LI) and one with high iodide (HI) concentration] and also shows sustained oscillatory behavior. In narrow ranges of parameters, bistability of two steady states, or bistability of the HI steady state and the oscillatory state are found. The HI state shows excitable responses when stimulated by chlorine dioxide or by chlorite ion. The LI state is not excitable either by these species or by iodide ion. The response of the chlorine dioxide–iodide reaction differs from that observed in most excitable chemical systems. Superthreshold stimulations generate transient oscillations before the system returns to a steady state. The number of oscillations depends on the distance of the system from the oscillatory region of the parameter space and on the strength of the stimulation. By varying flow rate and input concentrations of chlorine dioxide and iodide at constant H2SO4 input (pH = 2), excitatory and/or oscillatory conditions were determined in the uncoupled reactor cells.

The experimental arrangement consisted of two thermostatted (25 ±0.2 °C) plexiglass CSTRs, each of volume 16 mL. The solutions of chlorine dioxide, sulfuric acid, and potassium iodide were delivered separately into the cells by peristaltic pumps. Chlorine dioxide was prepared as described by Lengyel et al., and the other chemicals were the highest purity commercially available. The sodium chlorite used for stimulation was twice recrystallized. The concentration of chlorine dioxide was determined spectrophotometrically (ε = 1263 cm⁻¹ M⁻¹ at 360 nm), and solution concentration was checked just before each experiment was started. The stock solutions were kept at 0 °C to avoid evaporation of ClO₂.

A schematic diagram of the computer-controlled apparatus is shown in Fig. 2. Iodide-selective electrodes with calomel reference electrodes were used to monitor each reactor. Low electrode potential corresponds to high [I⁻]. Signals from the electrodes were collected with the PC-Mate Lab Master data acquisition system. About 10–20 min after both reactors were filled, one of the cells was stimulated by an additional flow of 0.01 M NaClO₂. This stimulation was controlled as follows. One output channel from the computer was used to set the path of the solenoid valve SV, the other to control the speed of rotation of the peristaltic pump PP3. At the start of stimulation, the peristaltic pump was set to its highest speed of rotation. The flow rate k₀ was then decreased exponentially according to

$$k(t) = k_0 e^{-kt}$$

where k₀ is the initial rate of the additional flow, k is a positive number characterizing the rate at which the additional flow decreases, and t₀ is the time at which the potential of the iodide electrode in the triggering (“presynaptic”) cell drops below the trigger value Eᵣ.

1. Results: Two identical cells

We studied the dynamical behavior of two cells with identical parameters (±2%) in the excitable range. In Fig. 3 we show examples of dynamical behavior for three different trigger values. Regular alternation of quiescent periods and periods of oscillation is observed until the trigger value exceeds a critical level beyond which only simple oscillation occurs in both reactors. The phases in the two reactors are shifted by half the bursting period Tᵣ/2. When reactor 1 is oscillating, reactor 2 is in the period of quiescence and vice versa.

Simple oscillation [Fig. 3(c)] occurs when the trigger value is reached in one reactor before a period of oscillations (burst) is established in the other reactor. Stimulation then causes consumption of iodide ions, and the qui-
Experiments in a single CSTR show that the chlorine dioxide-iodide reaction possesses five distinct regions of dynamical behavior.21 There is thus a wide range of possibilities for coupling combinations of nonidentical cells. However, with reciprocally triggered, exponentially decreasing stimulation, the dynamical behavior of the coupled system is primarily determined by the transient response to stimulation. Previous experiments reveal that stimulation of the reaction by chlorite ion results in three types of response: (a) transient oscillation followed by return to the steady state; (b) sustained oscillations; and (c) return to the steady state without any oscillation. We expect qualitatively different dynamical behavior only by coupling cells with distinct combinations of these responses. We exclude conditions under which a single stimulation results only in simple return to the steady state and periodic stimulation is unable to generate bursting behavior. Thus we study the case in which excitable conditions are established in one reactor while in the other the reaction is maintained in the oscillatory mode. The excitable conditions in cell 2 were kept constant. The parameters for cell 1 were the same as in cell 2, except for the input concentration of iodide ion. By varying \([I^-]_1\), we could scan a range of oscillatory conditions in cell 1. Two examples of bursting behavior are shown in Fig. 5.

The period decreases significantly as \(k\) increases. Smaller \(k\) values correspond to stronger stimulation and lead to a longer period of quiescence, because the concentration of added chlorite ions decreases only slowly and more iodide ion is consumed by the added chlorite, so it takes longer for the system to return to the oscillatory mode.

2. Results: Two different cells

Experiments in a single CSTR show that the chlorine dioxide-iodide reaction possesses five distinct regions of dynamical behavior.21 There is thus a wide range of possibilities for coupling combinations of nonidentical cells. However, with reciprocally triggered, exponentially decreasing stimulation, the dynamical behavior of the coupled system is primarily determined by the transient response to stimulation. Previous experiments reveal that pulse stimulation of the reaction by chlorite ion results in three types of response: (a) transient oscillation followed by return to the steady state; (b) sustained oscillations; and (c) return to the steady state without any oscillation. We expect qualitatively different dynamical behavior only by coupling cells with distinct combinations of these responses. We exclude conditions under which a single stimulation results only in simple return to the steady state and periodic stimulation is unable to generate bursting behavior. Thus we study the case in which excitable conditions are established in one reactor while in the other the reaction is maintained in the oscillatory mode. The excitable conditions in cell 2 were kept constant. The parameters for cell 1 were the same as in cell 2, except for the input concentration of iodide ion. By varying \([I^-]_0\), we could scan a range of oscillatory conditions in cell 1. Two examples of bursting behavior are shown in Fig. 5.

B. Modeling

Lengyel et al. have proposed a model that accurately describes the kinetics of the chlorine dioxide-iodide reaction based on two overall stoichiometric processes

\[
\begin{align*}
2\text{ClO}_2 + 2I^- &\rightarrow I_2 + 2\text{ClO}_2^- , \\
\text{ClO}_2^- + 4I^- + 4H^+ &\rightarrow \text{Cl}^- + 2I_2 + 2H_2O .
\end{align*}
\]

The rate laws for the two processes are

\[
R_1 = k_1 [\text{ClO}_2] [I^-] , \\
R_2 = k_2a [\text{ClO}_2^-] [I^-][H^+] + k_2b [\text{ClO}_2^-][I_2][I^-]/(u + [I^-]^2) ,
\]

where \(u\) is a phenomenological parameter that determines the level of \([I^-]\) below which substrate inhibition by iodide ion becomes negligible.

Under the conditions of these experiments, the system is well characterized by the concentrations of three chemical species in the model—\(\text{ClO}_2, \text{ClO}_2^-,\) and \(I^-\). The model has been analyzed in a single CSTR and with pulse stimulation which gives rise to excitability and bursting. With
two coupled CSTRs, there are six variables, and the differential rate equations are

\[
\begin{align*}
\frac{dX}{dt} &= -R_1 + k_0 \left[ X_0 - X \right] - k_1 X, \\
\frac{dY}{dt} &= -R_2 + k_0 \left[ Y_0 - Y \right] - k_1 Y, \\
\frac{dZ}{dt} &= R_1 = R_2 - k_0 Z + k_1 [Z_f - Z_i],
\end{align*}
\]

where \(X = [\text{ClO}_2^+]\), \(Y = [\text{I}^-]\) and \(Z = [\text{ClO}_2^-]\), and \(i=1,2\) specifies the reactor cell. The concentration of \(I_2\) in the rate expressions (3) is given by \([I^-] + [I_2] = [I^-]_0\). The coupling between cells is represented by the term \(k_{f,i}^j\), the flow rate of the stimulation, which is determined as follows. If \(Y_f^i\) crosses its trigger value, \(Y_f^j\), from below at time \(\tau\) while \(k_{f,j}^i = 0\), then \(k_{f,j}^i\) is set to 0 and the supplemental flow into cell \(j\) is initiated by setting

\[
k_{f,j}^i = k_{f,j}^{00} e^{-k_{f,j}^{0} \tau}.
\]

This algorithm corresponds to the experiments where a new stimulation is initiated when the potential of the iodide electrode in the stimulated cell drops below \(E_r\).

Examples of numerical simulations of Eqs. (4)-(5) are shown in Fig. 6 for some examples of coupling identical cells. The qualitative agreement with the experiments is quite good. The numerically obtained dependence of the period on the trigger value and on the rate of decrease of stimulation \(k\) also resembles the experimental observations (cf. Figs. 4 and 7). When \(Y_r > 5 \times 10^{-5}\) M, the period of bursting \(T_b\) is almost constant. For smaller values the period varies significantly with the trigger value. This dependence is not smooth, but has many plateaus, because the sensitivity to stimulation varies with the phase of the oscillatory reaction. As observed experimentally, \(T_b\) decreases with increasing \(k\) as a result of the weaker stimulation.

In Fig. 8 we show the results of simulating the dynamical behavior of two different cells. The results are in qualitative agreement with the experimental results shown in Fig. 5.

III. ALTERNATING MASS EXCHANGE COUPLING

The other form of coupling that we investigated as a possible source of bursting behavior involved mass exchange between the two reactors. The usual coupling of this type utilizes bidirectional convection or diffusive flow, but such coupling is not conducive to bursting behavior in the chlorine dioxide–iodide reaction system. In the scheme we employ, mass exchange occurs only in one direction at a time, and the direction of this flow is governed by the concentrations in the cells.

A. Experiments

The experimental realization of the coupling is shown in Fig. 9. The arrangement is similar to that employed in
the reciprocal stimulation experiments. Now, however, instead of controlling a solenoid valve and a peristaltic pump, the computer regulates the switching of two solenoid valves. At any given time, only one valve is open, allowing exchange only in one direction. The mass exchange is governed by the speed of the peristaltic pump between the reactors, PP3. To avoid changes in the volume of solution in the reactors, the maximum flow rate between reactors must be less than or equal to the smaller of the two input flow rates to the CSTRs.

Such coupling inevitably introduces a time delay, just as does the time required for molecules of neurotransmitter to traverse a synaptic gap. We attempted to minimize this lag by shortening the tubes between the reactors and by using tubes with small diameters at high pump speeds. Under these conditions, mass transport between reactors required about 3 s, a time much less than a typical period of oscillation or bursting.

The conditions correspond to excitability in cell 1 and to stationary or oscillatory behavior in cell 2 for the uncoupled system. To elicit a superthreshold response in one CSTR, the inflow from the other reactor must contain a high level of $[\text{ClO}_2^-]$ (or $[\text{ClO}_3^-]$) and a low level of $[\text{I}^-]$. Since the excitable steady state is characterized by high $[\text{I}^-]$ and low levels of the other two species, coupling two CSTR's in this state by mass exchange does not lead to bursting. To obtain a superthreshold response, which can then lead to bursting, it is necessary to couple a CSTR with excitable conditions with one in either the low iodide steady state or the oscillatory state. For simplicity, we chose the former alternative.

The direction of mass exchange is controlled by the potential of the iodide electrode in the excitable cell 1. When the potential in cell 1, $E_1$, drops below $E_{\text{down}}$, mass exchange is initiated from cell 2 to cell 1. This direction of coupling is maintained until $E_1$ begins to increase and exceeds the more positive value $E_{\text{up}}$. At that moment, the
direction of flow is switched, and the output from cell 1 is delivered to cell 2. Some representative examples of the dynamical behavior in this configuration are shown in Fig. 10.

B. Simulations

Simulating this type of coupling is more complex than the case described earlier. Two new effects are present. First, because the intercellular flow contains time-varying concentrations of iodide ion and iodine, the number of iodine atoms is no longer constant in each reactor. Therefore, the system can no longer be accurately described by \( X = [\text{ClO}_2] \), \( Z = [\text{ClO}_2^-] \) and the concentration of a single iodine-containing species \( Y = [\text{I}^-] \). It is necessary to introduce two additional differential equations for \( P_i \), the concentration of \( \text{I}_2 \) in each reactor. A second consideration is the time delay caused by mass transport between the cells.

A rigorous treatment of this effect would require the solution of a set of coupled integrodifferential delay equations, treating the tubes between the cells as tubular reactors. Because the delay in our experiments is relatively short as noted above, we have neglected any reaction occurring in the tubes during the transfer. We take the time lag explicitly into account and obtain the following set of eight differential delay equations for the system of two coupled CSTRs with alternating mass exchange,

\[
\begin{align*}
\frac{dX_i}{dt} &= -R_1^{(i)} + k_0^{(i)} [X_0^{(i)} - X_i^{(i)}] + k_{ji} [X_{(i-r)}^{(j)} - X_i^{(i)}], \\
\frac{dY_i}{dt} &= -R_1^{(i)} - 4R_2^{(i)} + k_0^{(i)} [Y_0^{(i)} - Y_i^{(i)}] \\
&+ k_{ji} [Y_{(i-r)}^{(j)} - Y_i^{(i)}], \\
\frac{dZ_i}{dt} &= R_1^{(i)} - R_2^{(i)} - k_0^{(i)} Z_i^{(i)} + k_{ji} [Z_{(i-r)}^{(j)} - Z_i^{(i)}], \\
\frac{dP_i}{dt} &= 0.5R_1^{(i)} + 2R_2^{(i)} - k_0^{(i)} P_i^{(i)} + k_{ji} [P_{(i-r)}^{(j)} - P_i^{(i)}],
\end{align*}
\]

where \( i,j = 1,2 \) and \( \tau \) is the delay time, i.e., the concentrations in the input to cell \( j \) at time \( t \) correspond to the concentrations in cell \( i \) at time \( t - \tau \). Linear interpolation was used in the simulations to obtain these values at the required previous times.

The simulations were initiated as in the case of reciprocally triggered exponentially decaying stimulation. As in the experiments, parameters were chosen to yield excitability in cell 1 and steady state or oscillation in cell 2 for the uncoupled system. The direction of mass exchange was controlled by the variable \( Y^{[\text{I}^-]} \) in the excitable cell with parameters \( Y_{\text{up}} \) and \( Y_{\text{down}} \) corresponding to the experimental \( E_{\text{up}} \) and \( E_{\text{down}} \), respectively. Some numerical simulations are shown in Fig. 10. Several different time delays were employed in the simulations, but the results appear insensitive to the value chosen for \( \tau \) so long as \( \tau \) is of the order of the actual experimental delay time.

IV. DISCUSSION AND CONCLUSION

We have examined two approaches to coupling the chlorine dioxide–iodine reaction in a pair of CSTRs. Coupling by reciprocally triggered stimulation does not belong either to the category of physical coupling or of chemical coupling, it is more analogous to reciprocal synaptic coupling between neurons. Information about the state of one reactor is used to control external stimulation of the other. The behavior of the reaction in the individual CSTRs is qualitatively similar to the behavior of a periodically stimulated reaction in a single reactor, but in the coupled
appropriate stimulation and/or coupling. Response to a superthreshold stimulation, will show only sim-
ple oscillation when coupled by reciprocally triggered stim-
ulation. An oscillatory mode in which stimulation can
give rise to bursting behavior with appro-
riate number of the neuron pair in order to produce sustained burst-
ing behavior.20

The simulations with our simple models are in good
qualitative agreement with the results of our experiments.
It is difficult to achieve quantitative agreement (e.g., the
same number of oscillations per burst for the same param-
eter values), especially when the oscillation is very rapid.
One reason for this difficulty is that the concentration may
change faster than the response time of the iodide-selective
electrode. Another difficulty in making direct quantitative
comparisons between the numerical and experimental re-
sults is that at very low iodide concentrations the electrode
responds to species other than I⁻.23 In general, our simu-
lations display a higher frequency of oscillation during the
burst period than do the experiments.

The results presented here suggest that relatively sim-
ples inorganic reactions, many of which are well understood
at a mechanistic level, may provide useful models for un-
derstanding the dynamics of bursting behavior in much
more complex arrays of coupled neurons.

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system the frequency of stimulation is controlled internally
by the system itself.

We find that, with this form of coupling, bursting oc-
curs over a wide range of parameters when the uncoupled
systems are in the excitable or the oscillatory mode. It is,
however, necessary to administer a stimulus to initiate the
bursting behavior when excitable steady states have first
been established in the reactor cells. If the cells are in the
oscillatory parameter range, no initial stimulus is required
so long as the trigger value is in the range of the amplitude
of oscillations. This feature has an analog in neural sys-
tems. The behavior of two model neurons with postinhib-
itory rebound linked by reciprocal inhibitory synapses de-
pends on whether the cells are pacemakers or are silent
without synaptic input. Pacemaker neurons will fire alter-
nating bursts over a wide range of parametric values, while
non-pacemakers require triggering by synaptic input or by
an inhibitory postsynaptic potential delivered to one mem-
ber of the neuron pair in order to produce sustained burst-
ing behavior.20

Our investigations suggest that bursting in a chemical
system can be obtained when a reaction exhibits a transient
oscillation after stimulation of an excitable state. On the
other hand, systems that show the more common form of ex-
citability, with a single large amplitude excursion in re-
sponse to a superthreshold stimulation, will show only sim-
ple oscillation when coupled by reciprocally triggered stim-
ulation. An oscillatory mode in which stimulation can
cause a large phase shift by transient extinction of the os-
cillation can also give rise to bursting behavior with appro-
riate stimulation and/or coupling.

Bursting is more difficult to achieve when cells are
coupled by alternating mass exchange. The amount of
chlorite exchanged between reactors in this approach is
significantly lower and produces a smaller effect than sim-
ple stimulation by a pure solution of chlorite. Only two
transient peaks were observed in an experiment in which
an excitable state in one reactor was linked to a CSTR in
the I⁻ steady state.

The simulations with our simple models are in good
qualitative agreement with the results of our experiments.
It is difficult to achieve quantitative agreement (e.g., the
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The results presented here suggest that relatively sim-
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more complex arrays of coupled neurons.

FIG. 11. Dynamical behavior in two cells coupled by alternating mass exchange simulations. $k_{d1}=5\times10^{-3}$ s⁻¹, $X_0=1\times10^{-4}$ M in both cells. $k_{d2}=k_{d1}=5\times10^{-3}$ s⁻¹, $Y_{up}=5.13\times10^{-3}$ M, $Y_{down}=1\times10^{-4}$ M, time delay $\tau_d=3$ s. Cell 1: $Y_0=4.7\times10^{-4}$ M, cell 2: $Y_0=1\times10^{-4}$ M (a), $Y_0=2\times10^{-4}$ M (b).