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Design of pH-Regulated Oscillators[1]

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Received March 15, 1990 (Revised Manuscript Received May 14, 1990)

The hydrogen ion concentration is one of the most important and most easily measured quantities in nearly all reactions in aqueous solution, from inorganic systems to complex processes in living organisms. One might expect then that efforts to measure and understand pH changes would have played a major role in the study of oscillatory chemical reactions, nearly all of which occur in aqueous solution. Surprisingly, the role of H^+ as a major species in chemical oscillators has been largely ignored until quite recently.

In this Account, we discuss a new family of oscillating reactions consisting of systems that display large-amplitude (several pH units) pH oscillations in unbuffered solution, but only monotonic behavior in the presence of acid–base buffers. Such systems can be designed using procedures based on simple mathematical models. They bear strong analogies to both thermokinetic and neural oscillators.

In the early stages of the experimental investigation of chemical oscillations, systems were monitored either spectrophotometrically or potentiometrically, with redox or halogen ion specific electrodes. The redox potential measurements that dominated these studies are considerably less informative than the pH, since the former give a mixed potential, while the latter is species specific. Few publications before 1985 mention pH changes in an oscillatory reaction. Several extrema in $[H^+]$ as a function of time were reported in a study of the thermal decomposition of sodium dithionite in aqueous solution.[3] Despite the acidic media of the Bray–Liebhafsky[4] (H_2O_2–IO_3^-, $[H^+] \approx 0.01$–0.1 M) and the Belousov–Zhabotinskii[5] (BZ: bromate oxidation of an organic reductant, $[H^+] \approx 0.1$–1 M) reactions, which create unfavorable conditions for pH measurement, small-amplitude periodic changes in pH have been found[6,7] in these well-known oscillatory systems.

The variation of pH in such systems is not intimately involved in the oscillatory phenomenon, but rather serves as a consequence or indicator of the oscillation. Oscillations in redox potential or in other parameters occur even if the pH change is suppressed by addition

Table I
pH-Regulated Oscillators

reactn system	year	ref
$S^{2-} + H_2O_2$	1985	14
$IO_3^- + HSO_3^- + Fe(CN)_6^{4-}$	1986	23
$S_2O_3^{2-} + H_2O_2 + Cu^{2+}$	1987	13
$IO_3^- + HSO_3^- + thiourea$	1987	28
$IO_3^- + HSO_3^- + S_2O_3^{2-}$	1988	19, 39
$BrO_3^- + HSO_3^- + Fe(CN)_6^{4-}$	1989	30
$H_2O_2 + HSO_3^- + Fe(CN)_6^{4-}$	1989	16
$H_2O_2 + Fe(CN)_6^{4-}$	1989	33
$IO_4^- + S_2O_3^{2-}$	1989	20
$IO_4^- + NH_2OH$	1989	34
$IO_3^- + NH_2OH$	1990	1

of an appropriate acid–base buffer. For example, the redox potential of the chlorite–thiosulfate reaction buffered at pH's between 2 and 5 in a flow reactor shows periodic oscillation.[8] Without the buffer, oscillations are found not only in the redox potential but also in $[H^+]$.[9] We can conclude that hydrogen ion is not a key species; its kinetic role is not essential in these reactions, and the oscillation is governed by species other than H^+.

There is a strong analogy between the role of pH in chemical oscillators and the role of temperature. Chemical oscillation is necessarily accompanied by periodic changes in the rate of heat production and hence by temperature variations. With the exception of some early microcalorimetric measurements on the BZ reaction,[10] little attention has been paid to the temperature in aqueous oscillatory reactions.[11] Vidal and Noyau[12] distinguish between oscillations that are thermokinetic in origin, i.e., temperature controlled, and those in which the temperature merely follows the chemistry. Thermokinetic oscillations tend to be of larger amplitude, and the accompanying concentration variations are extinguished if the system is thermostated.

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(3) Rinker, R. G.; Lynn, S.; Mason, D. M.; Corcoran, W. H. *Ind. Eng. Chem. Fundam.* 1965, *4*(3), 282–288.

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(10) Körös, E.; Orbán, M.; Nagy, Z. *Nature (London), Phys. Sci.* 1973, *242*, 30–31.

(11) In contrast, thermokinetic oscillations in catalytic and gas-phase systems have received a great deal of attention. See, for example: Sheintuch, M.; Schmitz, R. A. *Catal. Rev.—Sci. Eng.* 1977, *15*, 107–172. Griffiths, J. F. *Annu. Rev. Phys. Chem.* 1985, *36*, 77–104.

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pH-Regulated Oscillators

In pH-regulated oscillators, the concentration of hydrogen ion, or that of its counterpart hydroxide ion, plays a critical kinetic governing role in the dynamical behavior of the system.[13] The initial concentration of hydrogen ion is usually significantly lower than and never exceeds those of the reactants. Since the amplitude of the pH change is always large, the relative change in [H+] is dramatic, and its effect on the rate can be extremely high. The role of hydrogen ion is kinetic rather than thermodynamic. The thermodynamic driving force is the free energy change of the redox reaction between the reagents. In the presence of buffer, the reaction still occurs, but with nonoscillatory kinetics.

The first pH-regulated oscillator discovered, in 1985, was the oxidation of unbuffered sodium sulfide solution by excess hydrogen peroxide in a flow reactor (CSTR).[14] Since that time the number of such systems has grown rapidly. Table I lists the known pH-regulated oscillators.

We see that all of these systems are composed of one oxidant and either one or two reductants, yielding a two- or a three-component system.[15] Although the repertoire of oxidants employed in other oscillatory reactions (ClO_2^-, BrO_3^-, IO_3^-, IO_4^-, H_2O_2, $S_2O_8^{2-}$, MnO_4^-, O_2) is wide ranging, only IO_3^-, IO_4^-, BrO_3^-, and H_2O_2 participate in the reported pH oscillators. There is no a priori reason to exclude other oxidants in pH-regulated oscillators. The reductants used successfully to date are sulfur- or nitrogen-containing species and ferrocyanide ion.

In the two-component systems the reductant can be oxidized in two different manners. For instance, in the sulfide–hydrogen peroxide system the following two routes are possible:

$$H_2O_2 + HS^- + H^+ \rightarrow \frac{1}{8}S_8 + 2H_2O \qquad (1)$$

$$4H_2O_2 + HS^- \rightarrow SO_4^{2-} + 4H_2O + H^+ \qquad (2)$$
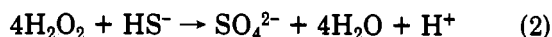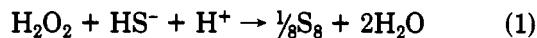
The partial oxidation (1), which requires acid in order to proceed, leads to a temporally stable intermediate, S_8 in the present example, $S_4O_6^{2-}$ or NO_2^- in other cases. If the reactants are available in high concentration, but [H+] is limited, the system exhausts its supply of hydrogen ion, and the pH rises. The increased pH favors the total oxidation of the reductant (2), which is accompanied by formation of acid, generating favorable conditions for the acid-consuming reaction (1) to revive. Under appropriate conditions, such a system may give rise to periodic changes in the acidity as shown, for example, in Figure 1.

In three-component pH-regulated oscillators, neither reductant can be oxidized in two different ways. On oxidation, one reductant produces, while the other consumes, H+. An example of such an oscillator is the hydrogen peroxide–sulfite–ferrocyanide system.[16] Both HSO_3^- and $Fe(CN)_6^{4-}$ have only one stable oxidation product (SO_4^{2-} and $Fe(CN)_6^{3-}$, respectively). The oxidation of hydrogen sulfite (3) serves as the source of

(13) Orbán, M.; Epstein, I. R. *J. Am. Chem. Soc.* **1987**, *109*, 101–106.
(14) Orbán, M.; Epstein, I. R. *J. Am. Chem. Soc.* **1985**, *107*, 2302–2305.
(15) We do not count as a "component" the free acid introduced to compensate for the basic character of the substrate (e.g., S^{2-}, SO_3^{2-}) or to adjust the initial pH to the proper value (e.g., $S_2O_3^{2-}$).
(16) Rábai, Gy.; Kustin, K.; Epstein, I. R. *J. Am. Chem. Soc.* **1989**, *111*, 3870–3874.
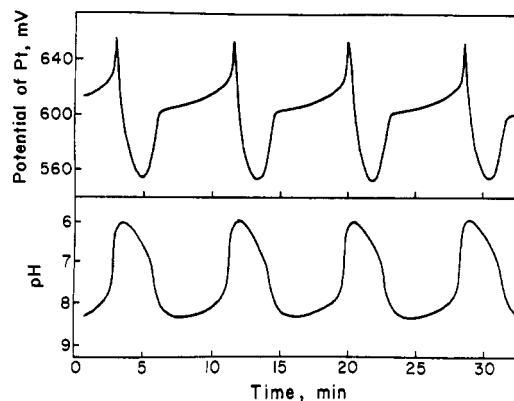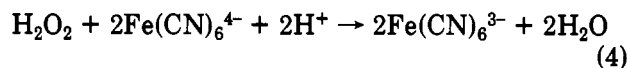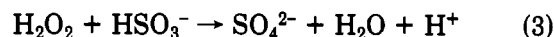

Figure 1. Oscillation in the potential of a Pt electrode (top) and in pH (bottom) in the reaction of $[H_2O_2]_0 = 0.4$ M, $[Na_2S]_0 = 0.0167$ M, and $[H_2SO_4]_0 = 0.001$ M in a flow reactor with reciprocal residence time $k_0 = 6 \times 10^{-4}$ s^{-1}.

hydrogen ions, while the oxidation of ferrocyanide (4) consumes them:

$$H_2O_2 + HSO_3^- \rightarrow SO_4^{2-} + H_2O + H^+ \qquad (3)$$

$$H_2O_2 + 2Fe(CN)_6^{4-} + 2H^+ \rightarrow 2Fe(CN)_6^{3-} + 2H_2O \qquad (4)$$
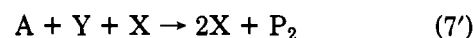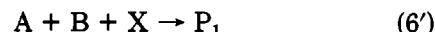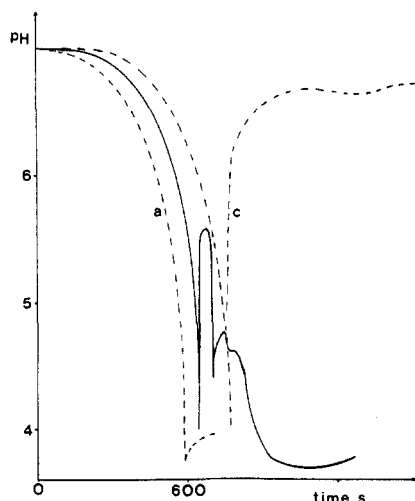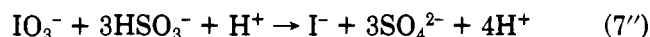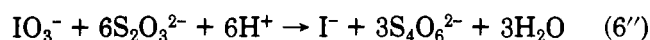
Systematic Design of pH-Regulated Oscillators

Table I shows that the number of pH-regulated oscillators doubled in 1989. The rapid growth in the number of these reactions has resulted from a systematic procedure for their design, which we now discuss briefly.

Higgins[17] was one of the first to argue that autocatalytic steps are ideal building blocks for systems that produce oscillations in the concentrations of intermediates. Many autocatalytic models and mechanisms have been proposed for chemical oscillators. The oldest, eqs 5–7, was formulated by Lotka in 1910[18] and serves as the basis for our design procedure for pH-regulated oscillators.

$$A \rightarrow Y \qquad (5)$$

$$X \rightarrow P \qquad (6)$$

$$X + Y \rightarrow 2X \qquad (7)$$

Lotka's model shows damped oscillations in the concentrations of X and Y under certain initial conditions. To construct a real oscillatory system on the basis of this model, one has to find chemical reactions that follow the kinetics of eqs 5–7. There are, however, several obstacles. First, the model contains elementary steps. A chemist cannot choose pure elementary reactions for experimental work, because they are always accompanied by other elementary steps. In nature, elementary reactions are not available independently from one another. Fortunately, Lotka's model can be extended in a more realistic fashion without losing its oscillatory character. For instance, the first-order steps can be replaced by higher order steps representing complex component processes:

$$A + B \rightarrow Y \qquad (5')$$

$$A + B + X \rightarrow P_1 \qquad (6')$$

$$A + Y + X \rightarrow 2X + P_2 \qquad (7')$$

(17) Higgins, J. *Ind. Eng. Chem.* **1967**, *59*(5), 19–62.
(18) Lotka, A. J. *J. Phys. Chem.* **1910**, *14*, 271–274.

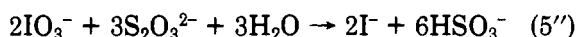260 *Acc. Chem. Res., Vol. 23, No. 8, 1990*

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Figure 2. Solid line shows an oscillatory pH vs time curve in the iodate–sulfite–thiosulfate[19] system under batch conditions: $[IO_3^-]_0 = 0.010$ M, $[SO_3^{2-}]_0 = 0.020$ M, $[S_2O_3^{2-}]_0 = 0.010$ M, and $[H^+]_0 = 0.0092$ M. Dashed lines indicate the narrow range of $[H^+]$ that is favorable for oscillation. The oscillation disappears when $[H^+]_0$ is either slightly higher ($[H^+]_0 = 0.0098$ M (a)) or lower ($[H^+]_0 = 0.0088$ M (c)) than the optimum value.

A second difficulty in constructing a real oscillator that corresponds to the Lotka scheme is that X is involved in two reactions. It is not easy to find two chemical reactions, one of which is autocatalytic, with a common species unless this common species is H^+ (or OH^-). Hydrogen ion takes part in most chemical reactions in aqueous solution.

Model equations 5′–7′ were developed in a study of the oscillatory iodate–sulfite–thiosulfate system.[19] Iodate and thiosulfate can react with each other in two different ways. At relatively low hydrogen ion concentrations, transient formation of bisulfite takes place (eq 5″). The final product of the oxidation is sulfate (eq 7″), which produces hydrogen ions.

$$2IO_3^- + 3S_2O_3^{2-} + 3H_2O \rightarrow 2I^- + 6HSO_3^- \quad (5'')$$

$$IO_3^- + 6S_2O_3^{2-} + 6H^+ \rightarrow I^- + 3S_4O_6^{2-} + 3H_2O \quad (6'')$$

$$IO_3^- + 3HSO_3^- + H^+ \rightarrow I^- + 3SO_4^{2-} + 4H^+ \quad (7'')$$

When $[H^+]$ is relatively high, thiosulfate is oxidized to tetrathionate (reaction 6″), a relatively inert product, which cannot be oxidized further by iodate. Hydrogen ions are consumed in reaction 6″. Hydrogen ion accelerates the oxidation of bisulfite ion, because the protonated form H_2SO_3 is oxidized more rapidly than HSO_3^-. For this reason, the formation of H^+ in reaction 7″ is an autocatalytic process. In the absence of any additional acid–base buffer (the sulfite–bisulfite couple acts as an internal buffer), the iodate–sulfite–thiosulfate system is found to be oscillatory in a narrow range of initial concentrations. Figure 2 shows the experimentally measured damped pH oscillations in a closed reactor. Calculations reveal that a model consisting of the separately determined empirical rate laws of the component reactions (5″–7″) also gives damped oscillation. There is an interesting kinetic cross effect, namely, the catalytic effect of thiosulfate ion on the iodate oxidation of sulfite ion and the inhibition of the iodate oxidation of thiosulfate ion by sulfite ion. These

effects, however, are not essential for the oscillation, although they do modify the detailed dynamical behavior.

Despite the rich variety of hydrogen ion consuming and producing reactions at our disposal, we have not yet been able to generate further batch oscillators of this type. The difficulty lies in the requirement, in addition to the hydrogen ion consuming (6″) and the autocatalytic hydrogen ion producing (7″) reactions, of a third process, which continuously produces the species (in this case HSO_3^-) from which hydrogen ion forms (reaction 5″). This further condition makes oscillatory reactions of this kind exceedingly rare. What can be done to overcome this difficulty? The answer lies in using a CSTR to replace the chemical reaction (5′ or 5″) by a continuous inflow of the species from which hydrogen ion is formed.

Designing pH-Regulated Oscillators in a CSTR

In a CSTR, only two model reactions are necessary for oscillation:

$$X \rightarrow P \quad (8)$$

$$Y + X \rightarrow 2X \quad (9)$$

A model[20] consisting of elementary steps 8 and 9 reaches a stable steady state in a CSTR. If this steady state is perturbed by the flow rate (or other parameters) being changed, the reacting system shows damped oscillations. For the oscillations to be sustained, the rate laws of reactions 8 and 9 must be more complex; they cannot be elementary reactions. This simple model suggests how to design a pH oscillator (at least a damped one) in a CSTR. Choose a reaction that produces H^+ (i.e., X) autocatalytically, and couple it with a hydrogen ion consuming reaction. If there is no disturbing cross talk between the two component processes, the system may show oscillatory behavior. It is important that the rates of the component reactions be comparable.

One may well ask if the above procedure constitutes a design or a search. It is clear that designing any chemical system must include some element of search for appropriate reactions. Devising chemical oscillators cannot be totally analogous to designing a house, because the building blocks for a house can be ordered, within reason, with precisely specified attributes, while the elements of the oscillatory reaction, are both imperfectly characterized and restricted in their properties. We must find the appropriate reactions in nature, and this part of the design is necessarily a search.

The first pH-regulated oscillatory system, the hydrogen peroxide–sulfide reaction (eqs 1 and 2), was discussed above. We now summarize the other pH-regulated oscillators discovered to date.

Thiosulfate Ion–Oxidant Oscillators

Thiosulfate would seem to be a promising reductant for use in pH-regulated oscillators, because it can be oxidized either to sulfate, which produces hydrogen ion, often autocatalytically, or to tetrathionate in a hydrogen ion consuming reaction by the same oxidants. As shown in Table I, pH-regulated oscillation has been reported in the reactions of thiosulfate with hydrogen peroxide[13]

(19) Rábai, Gy.; Beck, M. T. *J. Phys. Chem.* **1988**, *92*, 4831–4835.

(20) Rábai, Gy.; Beck, M. T.; Kustin, K.; Epstein, I. R. *J. Phys. Chem.* **1989**, *93*, 2853–2858.

and with periodate.[20] An empirical rate law model, which accounts for the oscillation, has been proposed for the latter system.

$$4IO_4^- + S_2O_3^{2-} + H_2O \rightarrow 2SO_4^{2-} + 4IO_3^- + 2H^+ \quad (10)$$
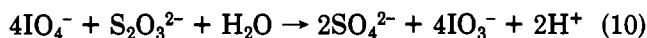
The rate of reaction 10 increases with $[H^+]$, i.e., the reaction is autocatalytic in hydrogen ion. The rate equation is

$$v_{10} = (k_{10}[H^+]^2 + k_{10}'[H^+]^3)[IO_4^-][S_2O_3^{2-}] \quad (10')$$

Iodate ion formed in reaction (10) can oxidize excess thiosulfate ions to tetrathionate in a hydrogen ion consuming reaction (11).

$$IO_3^- + 6S_2O_3^{2-} + 6H^+ \rightarrow 3S_4O_6^{2-} + 3H_2O + I^- \quad (11)$$
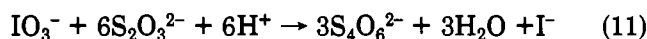
$$v_{11} = k_{11}[IO_3^-][S_2O_3^{2-}]^2[H^+]^2 \quad (11')$$

Reactions 10 and 11 occur under the conditions of the oscillation in a CSTR and during the early part of the batch reaction. No other reactions need be invoked in order to describe the main qualitative features of the complex dynamical behavior of this system.

The hydrogen peroxide–thiosulfate–copper(II) oscillatory system[13] also shows bistability and oscillation. The oscillations in pH are as large as 3–4 pH units, so that the effect of hydrogen ion on the rates of the component reactions is considerable. Copper(II) is present at catalytic levels and is essential for the oscillation. Apparently, the catalyst accelerates one or more of the component processes, most likely the hydrogen ion forming total oxidation of thiosulfate to sulfate. If bisulfite, however, is introduced into the CSTR along with the thiosulfate and hydrogen peroxide, copper ions are not required for oscillation.[16] The HSO_3^- can react with hydrogen peroxide, quickly forming H^+, and no catalyst is needed to accelerate the formation of hydrogen ion.

Mixed Landolt Systems

The Landolt-type reactions[21,22]—the iodate oxidation of reductants such as SO_3^{2-}, $Fe(CN)_6^{4-}$, AsO_3^{3-}, and NH_2OH—are another set of promising candidates for pH oscillators. All of these reactions are autocatalytic, and some composite reactions and/or the overall process itself produces or consumes H^+. For pH oscillations, the proper combination of two reductants is required. Other parameters (rate constants, ratios of reactant concentrations, initial pH) must also be appropriately matched.

The iodate–sulfite–ferrocyanide reaction[23] represents a three-component pH-regulated oscillator derived from two Landolt reactions. Both an empirical rate law model[24] and elementary-step mechanisms[25,26] have been proposed for this system. The oscillatory cycle starts with the autocatalytic reaction between IO_3^- and HSO_3^-. The autocatalysis arises in two ways: a direct route, indicated in reaction 7", and an indirect pathway in-

volving reaction 12 and the fast reaction between iodine and sulfite.

In excess iodate the oxidation of HSO_3^- takes place at an ever-increasing rate until it terminates when all the HSO_3^- is consumed. This oxidation process, in which a weak acid, HSO_3^-, is transformed to a strong acid, HSO_4^-, is marked by a spectacular pH drop. After the sulfite is consumed, a moderate pH rise results from the reaction between the excess IO_3^- and the product I^-.

$$IO_3^- + 5I^- + 6H^+ \rightarrow 3I_2 + 3H_2O \quad (12)$$
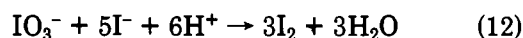
In order to restore the original high-pH state, we need a second reductant to consume the reactive I_2 without forming H^+. In this way, we obtain an indirect consumption of H^+. The reagent $Fe(CN)_6^{4-}$ meets this requirement by reducing the I_2 in reaction 13.

$$I_2 + 2Fe(CN)_6^{4-} \rightarrow 2I^- + 2Fe(CN)_6^{3-} \quad (13)$$
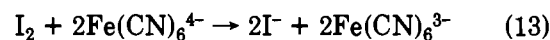
A direct hydrogen ion consuming process between ferrocyanide and iodate is possible as well.[26]

$$IO_3^- + 6Fe(CN)_6^{4-} + 6H^+ \rightarrow$$
$$I^- + 6Fe(CN)_6^{3-} + 3H_2O \quad (14)$$
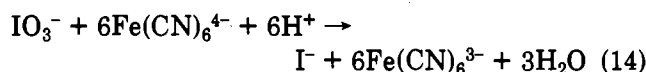
As the pH increases, all the reactions slow down, and the inflow can return the system to its initial state. A simple, four-variable (HSO_3^-, SO_3^{2-}, H^+, I_2) model proposed by Gáspár and Showalter[27] puts the above picture into quantitative terms and accounts for essentially all of the observed dynamics.

The dynamical behavior of the iodate–sulfite–thiourea oscillatory reaction can be explained in much the same way.[28] Thiourea plays the role of the hydrogen ion consuming reagent, because it can react with I_2 formed in the H^+-consuming reaction (12) without regenerating H^+.

$$2(NH_2)_2CS + I_2 \rightarrow (NH_2)_2CSSC(NH_2)_2^{2+} + 2I^- \quad (15)$$
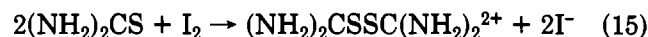
The further oxidation of dithiobisformamidine to sulfonic acid or to sulfate by iodine is possible,[29] but it probably does not take place under the conditions of the oscillation.

In spite of some significant differences in their behavior, the bromate–sulfite–ferrocyanide oscillatory system[30] seems to be closely related to its iodate analogue. The amplitude and frequency of the pH oscillations in the two systems are similar, and wherever possible, analogous component reactions have been proposed to account for the oscillation. It is clear that the H^+-producing process is reaction 16.

$$BrO_3^- + 3HSO_3^- + H^+ \rightarrow Br^- + 3SO_4^{2-} + 4H^+ \quad (16)$$
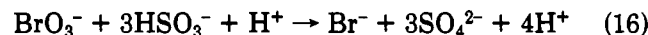
The indirect H^+-consuming reaction, however, cannot be copied from the equivalent IO_3^- process (12), because the reaction between BrO_3^- and Br^- is too slow to produce enough Br_2 in the pH range within which the system oscillates. The direct reaction (17) between bromate and ferrocyanide has been shown to be fast

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(22) Eggert, J.; Scharnow, B. *Z. Elektrochem. Angew. Phys. Chem.* **1921**, *27*, 455–470.
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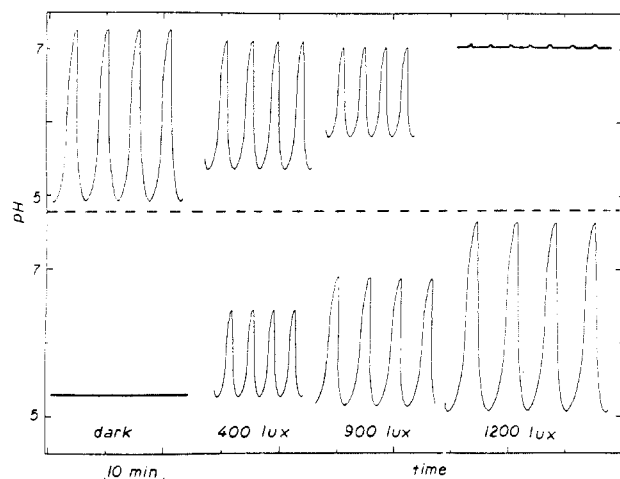
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Figure 3. Effect of illumination on oscillatory behavior in the hydrogen peroxide–ferrocyanide reaction in a CSTR. When the input concentrations (top) are $[H_2O_2]_0 = 5 \times 10^{-2}$ M, $[Fe(CN)_6^{4-}]_0 = 3.3 \times 10^{-3}$ M, and $[H^+]_0 = 1.8 \times 10^{-3}$ M at $k_0 = 1.9 \times 10^{-3}$ s^{-1}, the amplitude decreases with increasing light intensity. At $[H_2O_2]_0 = 5.0 \times 10^{-2}$ M, $[Fe(CN)_6^{4-}]_0 = 3.3 \times 10^{-3}$ M, $[H^+]_0 = 2.33 \times 10^{-3}$ M, and $k_0 = 3.0 \times 10^{-3}$ s^{-1}, illumination induces oscillations (bottom).

enough[31,32] to serve as the negative feedback for H^+ in this system.

$$BrO_3^- + 6Fe(CN)_6^{4-} + 6H^+ \rightarrow$$
$$Br^- + 6Fe(CN)_6^{3-} + 3H_2O \quad (17)$$
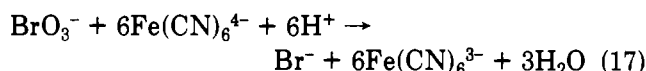
The halogenate oxidant in the mixed Landolt oscillators can be replaced by hydrogen peroxide to yield the hydrogen peroxide–sulfite–ferrocyanide oscillatory system discussed earlier (eqs 3 and 4). Under appropriate initial conditions in a CSTR, the system shows large-amplitude pH oscillation, which can be described by an empirical rate law model.[16]

When the excess of hydrogen peroxide is increased, the contribution of the H^+-producing reaction (18) between hydrogen peroxide and ferricyanide increases. If

$$2Fe(CN)_6^{3-} + H_2O_2 \rightarrow 2Fe(CN)_6^{4-} + O_2 + 2H^+ \quad (18)$$

the ratio of $[H_2O_2]$ to $[Fe(CN)_6^{3-}]$ exceeds 10-fold, no HSO_3^- is needed to generate oscillation. Reaction 18 can replace the fundamental process (3). The two-component oscillating reaction between H_2O_2 and ferrocyanide ion is regulated by pH and is extremely sensitive to light[33] as illustrated in Figure 3. The key step in the proposed mechanism,[33] and the one responsible for the photosensitivity, is the light-induced formation of monoaquapentacyanoferrate(II). The overall process in this case is the decomposition of H_2O_2 catalyzed by the monoaquapentacyano iron complex.

Periodate and Iodate Oxidation of Hydroxylamine

Both periodate[34] and iodate[1] can oxidize hydroxylamine in an oscillatory reaction in a CSTR. In the case of periodate, two different modes of oscillation have been found, one, in relatively low hydroxylamine excess, with a period of a few minutes, and the other, when NH_2OH is in greater excess, with a period of several
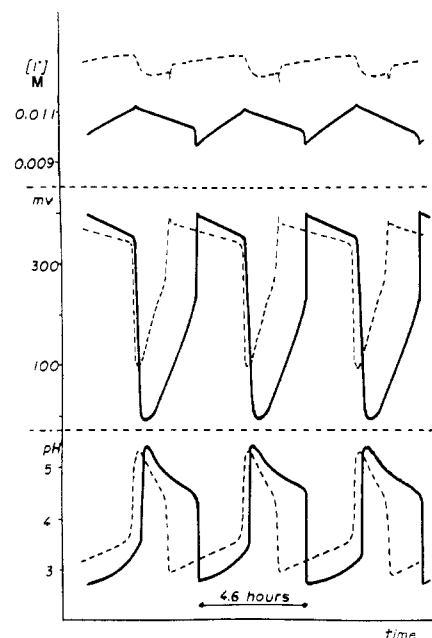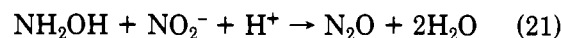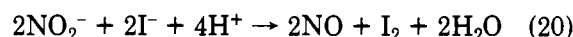
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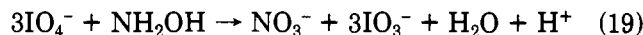(34) Rábai, Gy.; Epstein, I. R. *J. Phys. Chem.* **1989**, *93*, 7556–7559.

Figure 4. Measured (solid lines) and calculated (dashed lines) oscillatory traces in the iodate–hydroxylamine reaction in a CSTR. Input concentrations: $[NH_3OH^+]_0 = 0.050$ M, $[NaOH]_0 = 0.040$ M, and $[IO_3^-]_0 = 0.0130$ M (0.0136 M in the calculations); $k_0 = 1.51 \times 10^{-4}$ s^{-1}. The ratio $[I^-]/[I_2]$ was used to calculate the redox potential.

hours. Only the long-period oscillation is found in the reaction with iodate (Figure 4).

If hydroxylamine is not in large excess, it is oxidized to nitrate by periodate, producing H^+ in an autocatalytic pathway whose stoichiometry is given by reaction 19. Nitrite formed as an intermediate in this process can consume hydrogen ions in reactions with iodide (20) and excess hydroxylamine (21).

$$3IO_4^- + NH_2OH \rightarrow NO_3^- + 3IO_3^- + H_2O + H^+ \quad (19)$$

$$2NO_2^- + 2I^- + 4H^+ \rightarrow 2NO + I_2 + 2H_2O \quad (20)$$

$$NH_2OH + NO_2^- + H^+ \rightarrow N_2O + 2H_2O \quad (21)$$

Several additional reactions must be added to describe the details of the short-period oscillations in the periodate–hydroxylamine reaction.[34]

In a larger excess of hydroxylamine, the main product of the oxidation is N_2O, and no nitrite accumulation is observed.[1] Consequently, NO_2^- cannot play the role of the hydrogen ion consumer. It is known, however, that the reaction between hydroxylamine and iodine is not very fast and is strongly inhibited by hydrogen ion.[35] Iodine can form in the Dushman reaction (12) and accumulates in the mixture while hydroxylamine is still present. A portion of the accumulated I_2 can leave the solution by evaporation during the very long time required for an oscillation, and this first-order removal of iodine finally consumes hydrogen ion. Inclusion of I_2 evaporation is essential for an accurate simulation of the long-period oscillations. The dashed lines in Figure 4 show the simulated oscillatory traces.

Future Prospects

Measurement of pH gives the experimentalist a simple and powerful tool for the study of oscillatory reac-

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tions. With this approach, one may obtain additional information about known oscillatory reactions to make possible the refinement of mechanisms for those systems in which the periodic change in pH serves either as an indicator or as the governing force behind the oscillation. As studies turn increasingly toward more complex systems, particularly coupled systems, the ability to measure and control a single well-defined variable that affects multiple steps in a process will become even more crucial.

We may expect a continuing growth in the number of pH-regulated oscillators. The design approach described above is simple to apply. We note also the recent work of Nagypál and collaborators,[36] who use the acceleratory effect of H^+ on a number of redox reactions to design systems capable of generating spatially propagating chemical reaction fronts.

The pH-regulated oscillators discovered thus far (and in fact, the vast majority of chemical oscillators) have been confined to redox reactions. There is no reason, however, to exclude other types of reactions from being oscillatory. For instance, preliminary calculations[37] show that the substitution reaction between a copper–triglycine complex and ethylenediaminetetraacetate ion, which is autocatalytic in hydroxide ion,[38] can serve as the starting point for a hydroxide ion oscillator in a CSTR. If we add a hypothetical OH^-- and/or triglycine-consuming reaction to the published[38] mecha-

nism of this autocatalytic (nonredox) reaction, the concentration of OH^- undergoes oscillation.[37] A search for appropriate OH^-- or triglycine-consuming steps is now under way.

Another potential application of the ideas presented here is to biological systems. Many biological processes involve coupled oscillatory reactions, and often the reactions are extremely sensitive to pH. Whether pH regulation is used as a control mechanism remains to be established. We pointed out the analogy between pH-regulated and temperature-controlled oscillations earlier. Another suggestive analogy is between the role of pH in the systems discussed here and the role of the membrane potential in neural oscillators. In the neuron, the role of an individual chemical reaction or process is played by an ion-specific conductance. The membrane potential, which is affected by all the conductances, influences the values of many of these conductances by affecting the probability of opening of the ion channels associated with a given conductance. The overall cell oscillation results from the interaction of all the channels. Thus, like the pH in a chemical system, the membrane potential affects and is affected by the activity of nearly all the "reactions" in the system. It will be interesting to see if analogies like these ultimately prove useful in transferring some of our understanding of chemical oscillators to more complex biological systems.

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Organochromium(III) Chemistry: A Neglected Oxidation State

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Received April 2, 1990 (Revised Manuscript Received May 2, 1990)

Chromium, the lightest and most abundant of the group 6 transition metals, has played a prominent role in the history of organometallic chemistry. While the Danish pharmacist W. C. Zeise is generally credited with the discovery of the first compound featuring a transition metal–carbon bond ("Zeise's salt", $K^+[Pt(C_2H_4)Cl_3]^-\cdot H_2O$, reported in 1827),[1] F. Hein's early investigation of the reaction of $CrCl_3$ with PhMgBr (published from 1919 on)[2] yielded ill-understood "Chromorganoverbindungen", which remained mys-

terious until the dawn of modern organometallic chemistry in the early 1950s. Bis(benzene)chromium (1955),[3] (phenylmethoxycarbene)pentacarbonylchromium, the first structurally characterized carbene complex (1965),[4] and *trans*-iodo(phenylcarbyne)tetracarbonylchromium, the first carbyne complex (1973, all prepared in E. O. Fischer's laboratory),[5] are other historical landmarks on the path toward understanding the metal–carbon bond.

Chromium compounds also find use as catalysts, adding a utilitarian dimension to the study of its or-

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