pH oscillations and bistability in the methylene glycol–sulfite–gluconolactone reaction

Klara Kovacs, Rachel E. McIlwaine, Stephen K. Scott and Annette F. Taylor*

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The Methylene Glycol–Sulfite–Gluconolactone (MGSG) reaction is the first example of an organic-based pH oscillator. This reaction is of particular interest as it displays large amplitude oscillations in hydroxide ion accompanied by small amplitude (10⁻³ V) oscillations in potential, indicating that it is not driven by redox processes. We investigate the reaction in a batch (closed) and flow (open) reactor and examine the role of the aging of the gluconolactone stock solution. The system is found to display oscillations and bistability for a wide range of flow rates and initial compositions. The experimental results are reproduced in numerical simulations in an extended model of the reaction in which the decay of the stock solution is incorporated. Finally, we analyse the features of the reaction that make it a suitable basis for the development of novel pH oscillators.

Introduction

The development of pH oscillating reactions is both of academic interest, as a means for investigating mechanism of reactions, and has potential applications, when coupled with pH sensitive polymers to create novel chemo-mechanical devices. For example, pH oscillators have been suggested as a source of fuel to drive synthetic muscles or periodic drug delivery. A pH oscillating reaction has been used to change the conformation of DNA from a folded to a random coil motif, thereby creating a pH-driven nano-switch. Coupling pH oscillators with complexation or precipitation equilibria has also been suggested as a means to probe the dynamics of certain biological processes.

It is well known that a chemical oscillator might be created by combining positive with negative feedback. Positive feedback involves autocatalysis and negative feedback is generated by a species, referred to as the inhibitor, that removes the autocatalyst. A key component of the negative feedback is that it must be delayed relative to the positive feedback, such that oscillations arise as a result of a kinetic instability. Typically, such systems display a cross-shaped phase diagram in a flow reactor, whereby for low concentrations of the inhibitor, bistability between a low and high autocatalyst concentration state is observed within a bounded range of flow rates. The region of bistability shrinks with increasing concentration of the inhibitor and a region of oscillations appears. This diagram has been used successfully to create a whole range of chemical oscillators without the need for a detailed knowledge of the chemical mechanism.

A design algorithm was proposed for pH oscillators involving acid/base autocatalysis combined with an acid/base removal reaction. Clock reactions, such as the bromate/sulfite reaction, which is autocatalytic in H⁺, display an induction period during which the pH decreases slowly followed by a rapid reaction event to the final pH. This reaction has been successfully coupled with an acid-consuming process, such as the ferrocyanide reaction in a flow reactor, to create a pH oscillator. To date, aside from the complex heterogeneous reaction of palladium-catalysed phenylacetylene oxidation, pH oscillators have been mainly developed using inorganic redox chemistry.

In order for pH oscillators to be used in conjunction with pH sensitive polymers or as probes of biological systems, less aggressive, biocompatible pH oscillators must be developed. The methylene glycol–sulfite reaction is a hydroxide ion clock reaction in batch and this reaction displays complex behaviour in a flow reactor. Recently, we demonstrated that the reaction may be coupled with the hydrolysis of gluconolactone to create the first organic-based pH oscillator. This reaction displays the unique feature of large amplitude oscillations in pH accompanied by small amplitude potential oscillations, thus demonstrating it is not based on redox processes. In this paper, we investigate this reaction in batch and in flow and compare these experiments to numerical simulations of the proposed mechanism of the reaction in which the decay of the gluconolactone stock solution is incorporated. The reaction is found to support both oscillations and bistability over a wide range of flow rates and displays a typical cross-shaped phase diagram. The experimental results are reproduced in simulations to good quantitative agreement. Finally, we discuss how this reaction may provide the basis for the development of novel pH oscillators.

Experimental and numerical procedures

Reactions were performed in a 50 ml water-jacketed cylindrical glass reactor. The pH was measured by a calibrated combination pH electrode (METTLER TOLEDO) and a HANNA pH meter connected to a computer. The electrode potential measurements were carried out with a combination redox electrode (Pt) and KEITHLEY 2000 multimeter also

Department of Chemistry, University of Leeds, UK LS2 9JT

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connected to a PC. The pH and potential measurements were performed in separate experiments. The temperature was kept constant at 20 °C with a HAAKE thermostat. The reactor was stirred by an IKA magnetic stirrer and the stirring rate was 400 rpm in all experiments.

The batch (closed) experiments were started upon addition of the gluconolactone and methylene glycol stock solutions ([X]₀) simultaneously to the sodium sulfite/bisulfite buffer solution. The concentrations, [X]₀, reported are the calculated initial concentrations in the reactor before the reaction takes place (i.e. [X]₀ = [X]₀/3). Stock solutions of methylene glycol were prepared by diluting 37% formalin solution (Aldrich) one day in advance to allow the complete de-polymerization. The buffer solution of sodium sulfite/bisulfite was freshly prepared daily from reagent grade Na₂SO₃ and Na₂S₂O₅ (Aldrich) with doubly distilled, deionised, water and bubbled with nitrogen to prevent aerial oxidation. The gluconolactone solution was prepared freshly from reagent grade D gluconic acid lactone (Aldrich) and used either immediately or at the recorded time, post dissolution of the solid.

In the open (flow) experiments, the three stock solutions were pumped into the reactor by a GILSON peristaltic pump. The flow rate was increased or decreased with the reactor filled initially with water, thus ensuring the low pH state was accessible from high flow rates when the system was bistable. The gluconolactone solution was used freshly prepared up to 1 hour old.

Simulations of the reaction were performed with the mechanism given in Table 1. The rate equations for the various species were constructed from the elementary rate laws. The rate constants were taken from the literature or adjusted in this work. Numerical integration of the resultant rate equations was performed using the package XPPAUT.14 The method of integration was CVODE with, typically, a time step of 0.01 and the tolerance set at tol = 1 × 10⁻⁷. For flow reactions, the rate equations were augmented with terms of the form k₀([X]₀ − [X]), where X is the species of interest and k₀ is the flow rate. The gluconolactone stock solution concentrations, [X]₀, were modelled by consideration of reactions (9) and (10) in Table 1 to give the following rate equations:

\[
\frac{d[GL]}{dt} = -(k_9 + k_{9OH}[OH^-])[GL] + k_{-9}[GA]_s
\]

\[
\frac{d[GA]}{dt} = (k_9 + k_{9OH}[OH^-])[GL] - k_{-9}[GA]_s - k_{10}[GA]_s + k_{-10}[G^-][H^+]
\]

\[
\frac{d[G^-]}{dt} = k_{10}[GA]_s - k_{-10}[G^-][H^+]
\]

\[
\frac{d[OH^-]}{dt} = k_5 - k_{-5}[OH^-][H^+]
\]

where GL = gluconolactone; GA = gluconic acid and G⁻ = gluconate anion.

**Results**

Typical pH–time curves are shown in Fig. 1 for the methylene glycol–sulfite reaction when coupled with GL hydrolysis in a closed batch reactor. The clock reaction profile develops into a single peak with increasing [GL]₀ (Fig. 1(a), curves 1–5). The time to maximum pH (t_clock) increases with increasing [GL]₀ and with increasing age, t_age, of the GL stock solution (Fig. 1(b)). This effect is more pronounced for solutions of higher initial concentration and the peak was completely suppressed for [GL]₀ = 0.017 M with t_age = 3000 s (Fig. 1(c)). These results were simulated using the mechanism in Table 1 and the theoretical curves (solid lines) are compared with the experimental data (triangles) in the second column of Fig. 1. For simulated reactions in batch, the initial concentrations ([X]₀) of GL, GA, G⁻ and acid were determined from the stock solution concentrations at 300 s with [X]₀ = [X]₀/3.

**Table 1** Mechanism for the methylene glycol–sulfite reaction with gluconolactone, where GL = gluconolactone; GA = gluconic acid and G⁻ = gluconate anion

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Rate constants</th>
<th>Ref. (* = adjusted in this work)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃(OH)H₂ → CH₃O + H₂O</td>
<td>(1)</td>
<td>k₁ = 5.5 × 10⁻³ s⁻¹</td>
</tr>
<tr>
<td>CH₃O + H₂O → CH₃(OH)H₂</td>
<td>(2)</td>
<td>k₂ = 5.0 M⁻¹ s⁻¹</td>
</tr>
<tr>
<td>CH₃O + H</td>
<td>(3)</td>
<td>k₃ = 3.1 × 10⁻¹ s⁻¹</td>
</tr>
<tr>
<td>CH₃(OH)H₂O → CH₃OH + H⁺</td>
<td>(4)</td>
<td>k₄ = 3.1 × 10⁻⁴ M⁻¹ s⁻¹</td>
</tr>
<tr>
<td>CH₃OH + H⁺ → CH₃(OH)H₂O</td>
<td>(5)</td>
<td>k₅ = 5.4 × 10⁻⁵ M⁻¹ s⁻¹</td>
</tr>
<tr>
<td>CH₃OH + H</td>
<td>(6)</td>
<td>k₆ = 1 × 10⁻⁹ M⁻¹ s⁻¹</td>
</tr>
<tr>
<td>CH₃(OH)H₂O → CH₃(OH)H₂O + H⁺</td>
<td>(7)</td>
<td>k₇ = 2 × 10⁻⁵ s⁻¹</td>
</tr>
<tr>
<td>CH₃OH + H₂O → CH₃OH + H⁺</td>
<td>(8)</td>
<td>k₈ = 1 × 10⁻⁵ M⁻¹ s⁻¹</td>
</tr>
<tr>
<td>GL + H₂O → GA</td>
<td>(9)</td>
<td>k₉ = 1 × 10⁻⁴ s⁻¹</td>
</tr>
<tr>
<td>GA → GL + H₂O</td>
<td>(10)</td>
<td>k₁₀ = 0.2 × 10⁻⁴ s⁻¹</td>
</tr>
<tr>
<td>GA → G⁻ + H⁺</td>
<td>(11)</td>
<td>k₁₁ = 2.5 × 10⁻⁷ s⁻¹</td>
</tr>
<tr>
<td>G⁻ + H⁺ → GA</td>
<td>(12)</td>
<td>k₁₂ = 1 × 10⁶ M⁻¹ s⁻¹</td>
</tr>
</tbody>
</table>
Oscillations are obtained when the reaction is performed in an open, flow, reactor. With the flow rate fixed, there is an induction period before the appearance of oscillations that depends on the concentrations of the reactants. The oscillations increase in amplitude and period with increasing flow rate. Typical examples of pH oscillations are shown in Fig. 2(a)–(c), where the flow rate is increased from $5.0 \times 10^{-3}$ s$^{-1}$ to $5.4 \times 10^{-3}$ s$^{-1}$ for $[\text{GL}]_0 = 0.0067$ M. The oscillatory amplitude reaches a maximum of three pH units, which can be sustained over $10^3$ s without dampening, despite the decay of the GL concentration in the stock solution (Fig. 2(d)).

Bifurcation diagrams of the pH as a function of flow rate were obtained by increasing the flow rate stepwise at regular time intervals. The minimum increment of the flow rate, $k_0$, was $1 \times 10^{-4}$ s$^{-1}$. Oscillations are observed for $k_0 \approx 4.5-5.4 \times 10^{-3}$ s$^{-1}$ with $[\text{GL}]_0 = 0.008$ M (Fig. 3(a)). The range of flow rates for which oscillatory behavior is observed is slightly shifted when the flow rate is decreased from a high value rather than increased from a low value. The oscillations grow in amplitude with increasing flow rate and disappear abruptly for a supercritical flow rate. The inset shows the small amplitude oscillations in potential for $k_0 = 5.4 \times 10^{-3}$ s$^{-1}$. (b) Bistability when $[\text{GL}]_0 = 0.003$ M, $\Delta = \text{steady state with increasing flow rate}, k_0$, $\nabla = \text{steady state with decreasing } k_0$.

Fig. 1 Batch (closed) MGSG reactions with initial concentrations of $[\text{CH}_2(\text{OH})_2]_0 = 0.1$ M, $[\text{SO}_3^{2-}]_0 = 0.005$ M, $[\text{HSO}_3^-]_0 = 0.05$ M. The first column shows the pH-time curves, and the second column compares experimental data (▲) with numerical simulations (solid lines). (a) Initial gluconolactone concentrations $[\text{GL}]_0$: 1 = 0.003 M, 2 = 0.004 M, 3 = 0.005 M, 4 = 0.017 M, 5 = 0.022 M. (b) $[\text{GL}]_0 = 0.0067$ M and age of the GL stock solution $t_{\text{age}}$: 1 = 300 s, 2 = 3600 s, 3 = 5400 s, 4 = 7200 s. (c) $[\text{GL}]_0 = 0.017$ M and age of the GL stock solution $t_{\text{age}}$: 1 = 300 s, 2 = 2000 s, 3 = 3600 s, 4 = 5400 s.

 Oscillations are obtained when the reaction is performed in an open, flow, reactor. With the flow rate fixed, there is an induction period before the appearance of oscillations that depends on the concentrations of the reactants. The oscillations increase in amplitude and period with increasing flow rate. Typical examples of pH oscillations are shown in Fig. 2(a)–(c), where the flow rate is increased from $5.0 \times 10^{-3}$ s$^{-1}$ to $5.4 \times 10^{-3}$ s$^{-1}$ for $[\text{GL}]_0 = 0.0067$ M. The oscillatory amplitude reaches a maximum of three pH units, which can be sustained over $10^3$ s without dampening, despite the decay of the GL concentration in the stock solution (Fig. 2(d)).

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The MGSG reaction displays a typical cross-shaped phase diagram as a function of the inflow concentration of the inhibitor species, $[GL_0]$, and the flow rate (Fig. 4(a)). With increasing $[GL_0]$, the higher and lower pH steady states are separated first by a large region of bistability, then by a region of oscillations. Oscillations are observed for a range of $[GL_0] = 0.005–0.023 \text{ M}$ and for a reasonable range of flow rates. A cross-shaped phase diagram is also observed for the variation of bisulfite/sulfite (b/c) with flow rate (Fig. 4(b)). This diagram is obtained by decreasing the inflow concentration of sulfite into the reactor with fixed $[HS_0]$. Oscillations are observed for values of b/c between 7 and 16.

The oscillations are reproduced in a model of the reaction with flow terms incorporated (Fig. 5). The inflow concentrations were determined from $[X]/3$, where $[GL_0]$, $[GA]$, and $[G]$, are calculated from reactions (9) and (10). There is an induction period before the appearance of oscillations, the length of which depends on the stock solution concentrations: in Fig. 5(a), the flow rate was fixed at $5.3 \times 10^{-3} \text{ s}^{-1}$ with $[GL_0] = 0.0067 \text{ M}$ and the emergence of oscillations is observed at 1000 s. The oscillations increase slowly in amplitude and period with increasing age of the stock solution. Small amplitude oscillations emerge when the flow rate was increased stepwise at 300 s intervals from $1.0 \times 10^{-3} \text{ s}^{-1}$ to $5.0 \times 10^{-3} \text{ s}^{-1}$ (Fig. 5(b)). The amplitude and period of the oscillations increases with increasing flow rate (Fig. 5(b)–(d)). The large amplitude oscillations do not change significantly in form over $10^3 \text{ s}$ (Fig. 5(e)).

The simulated bifurcation diagrams are shown in Fig. 6(a) and (b) for two different values of $[GL_0]$. These diagrams were produced by increasing/decreasing the flow rate stepwise at

![Fig. 4](image_url)  
**Fig. 4** Phase diagrams in the MGSG reaction in a flow reactor with inflow concentrations $[\text{CH}_2\text{(OH)}_2]_0 = 0.1 \text{ M}$, $[\text{HSO}_3^-]_0 = 0.05 \text{ M}$ where ● (light grey region) = oscillatory state, □ (dark grey region) = bistability △ = high pH steady state, ◀ = lower pH steady state. (a) Gluconolactone concentration–flow rate parameter plane, $[\text{SO}_3^{2-}]_0 = 0.005 \text{ M}$. (b) Bisulfite/sulfite (b/c)-flow rate parameter plane, $[GL_0] = 0.008 \text{ M}$.

![Fig. 5](image_url)  
**Fig. 5** Simulated pH oscillations (Table 1) in a flow reactor with $[\text{CH}_2\text{(OH)}_2]_0 = 0.1 \text{ M}$, $[\text{SO}_3^{2-}]_0 = 0.005 \text{ M}$, $[\text{HSO}_3^-]_0 = 0.05 \text{ M}$, $[\text{GL}_0] = 0.0067 \text{ M}$ and flow rate (a) fixed from $t = 0$ at $5.3 \times 10^{-3} \text{ s}^{-1}$; (b) increased from $k_0 = 0$ at $t = 0$ s to $k_0 = 5.0 \times 10^{-3} \text{ s}^{-1}$; (c) increased from $k_0 = 0$ at $t = 0$ s to $5.2 \times 10^{-3} \text{ s}^{-1}$; (d) and (e) increased from $k_0 = 0$ at $t = 0$ s to $k_0 = 5.4 \times 10^{-3} \text{ s}^{-1}$.

![Fig. 6](image_url)  
**Fig. 6** Simulations of the MGSG reaction (Table 1) in a flow reactor with inflow concentrations $[\text{CH}_2\text{(OH)}_2]_0 = 0.1 \text{ M}$, $[\text{HSO}_3^-]_0 = 0.05 \text{ M}$, $[\text{SO}_3^{2-}]_0 = 0.005 \text{ M}$. Upper row: bifurcation diagrams to show (a) oscillations for $[GL_0] = 0.008 \text{ M}$; (b) bistability for $[GL_0] = 0.003 \text{ M}$. Lower row: phase diagrams where B = bistability, SS1 = high pH steady state, SSII = lower pH steady state, ◇ = oscillations in the (c) gluconolactone concentration–flow rate parameter plane; (d) bisulfite/sulfite (b/c)-flow rate parameter plane.
300 s intervals. Oscillations emerge at $4.7 \times 10^{-3} \text{ s}^{-1}$ and grow in amplitude with increasing flow rate, disappearing at $6.0 \times 10^{-3} \text{ s}^{-1}$ for $[\text{GL}]_0 = 0.008 \text{ M}$. With $[\text{GL}]_0 = 0.003 \text{ M}$, bistability is observed between a high and low pH state. The phase diagrams in the GL--$k_0$ parameter plane and bisulfite/sulfite (b/c)--$k_0$ parameter plane are displayed in Fig. 6(c) and (d), respectively. These diagrams were reconstructed from the bifurcation diagrams with various $[\text{GL}]_0$ or b/c. Oscillations are observed for $[\text{GL}]_0 = 0.005$--0.012 M (Fig. 6(c)) and for b/c = 6--16.

**Discussion**

The reaction of methylene glycol with sulfite involves the consumption of the bisulfite/sulfite buffer present initially and displays clock-type behaviour in batch. The pH rises slowly during the induction period as the $\text{H}^+$ consumed by $\text{CH}_2\text{(O)}\text{SO}_3^-$ in reaction 4 is produced by dissociation of HSO$_3^-$ in reaction 2 (Table 1). The pH rises rapidly during the reaction event once all the HSO$_3^-$ has been consumed, and $\text{CH}_2\text{(O)}\text{SO}_3^-$ abstracts protons from H$_2$O, producing OH$^-$. However, while consumption of the buffer may explain the clock, it does not explain the complex behaviour observed in a flow reactor: this requires positive feedback, which is proposed to arise from the base-catalysis of the rate-determining step, reaction 1, and the production of OH$^-$ in the overall reaction:

$$2\text{CH}_2\text{(OH)}_2 + \text{SO}_3^2^- + \text{HSO}_3^- \rightarrow 2\text{CH}_2\text{(OH)}_3 + \text{H}_2\text{O} + \text{OH}^-$$

$$r = (k_1 + k_{1\text{OH}}[\text{OH}^-])\text{[CH}_2\text{(OH)}_2]$$

Positive feedback through autocatalysis arises when a product of a reaction catalyses its own production. The overall rate of production of OH$^-$ is catalysed by OH$^-$ (through $k_{1\text{OH}}[\text{OH}^-]$), as the rate-determining step is the dehydration of methylene glycol under our conditions, and the reaction is therefore, by definition, autocatalytic in OH$^-$. In a recent letter, we reported the first organic substrate-based pH oscillator by coupling the methylene glycol–sulfite reaction with the hydrolysis of GL. The MGS reaction displays a single peak indicative of positive feedback (OH$^-$ autocatalysis) coupled with delayed negative feedback (OH$^-$ removal) when performed in a batch reactor. The hydrolysis of GL produces acid and is also base-catalysed (reaction 9, Table 1):

$$\text{C}_6\text{H}_{10}\text{O}_6 + \text{H}_2\text{O} \rightarrow \text{C}_6\text{H}_{11}\text{O}_7 + \text{H}^+$$

$$r = (k_9 + k_{9\text{OH}}[\text{OH}^-])\text{[C}_6\text{H}_{10}\text{O}_6]$$

Thus, the concentration of OH$^-$ increases through process (A), which in turn increases the rate of production of acid through process (B). This provides the necessary delayed negative feedback for oscillations in an open system. The reaction produces a single peak in batch as the sulfite/bisulfite reactant is entirely consumed.

The gluconolactone hydrolysis in process (B) begins upon dissolution of the solid, and in the work presented here we investigated the effect of the decay of the stock solution on the clock time and oscillations. The clock time, $t_{\text{clock}}$, was found to increase with increasing $[\text{GL}]_0$, and with increasing age of the stock solution, $t_{\text{age}}$, such that the clock is completely suppressed for stock solutions greater than a critical age. The clock times are reproduced in the simulations of the model in Table 1. The change of $t_{\text{clock}}$ with $[\text{GL}]_0$ and $t_{\text{age}}$ can be explained by the initial decay of the stock solution before its addition to the other reactants. The rate of the decay of the stock solution clearly increases with increasing $[\text{GL}]_0$, and the additional acid produced in the GL stock solution maintains the buffer for longer in the batch MGS reaction. The clock time also depends sensitively on reactions (7) and (8), which contribute to the rate of consumption of the buffer. The rate constants $k_7$--$k_9$ were optimised in this work to best fit the clock times observed in experiments. The experimental clock times are reproduced in simulations for low values of $[\text{GL}]_0$ and $t_{\text{age}}$, but deviate at high values.

The existence of an induction time before the appearance of oscillations when the reaction is performed in a flow reactor is observed in both the experiments and simulations. Thus, the values of the flow rate for which oscillations are observed are shifted compared to those in simulations in which the stock solution concentration does not decay. However, the decay is very slow, particularly for low values of $[\text{GL}]_0$, such that the oscillations are maintained virtually without any change in form for over $10^3$ s. The experimental amplitude and period of the oscillations with increasing flow rate is reproduced to good quantitative agreement in the simulations. The form of the oscillations is different in the experiments, with the experimental oscillations displaying a broader peak. There is also some evidence of the emergence of a mixed mode (1 1) oscillation with increasing flow rate (Fig. 2(c)). The shape of the peak and the flow rate for which oscillations are observed depends sensitively on the rate constants of OH catalysis: $k_{1\text{OH}}$ and $k_{9\text{OH}}$. In particular, we note that $k_{1\text{OH}}$ is decreased relative to the previously reported value to best match the experimental data and $k_{1\text{OH}}/k_{9\text{OH}} = 1/8$. Further investigation of the influence of these two rate constants on the behaviour is merited.

The reaction displays bistability for low $[\text{GL}]_0$ and bisulfite/sulfite (b/c) and oscillations for higher values. The experimental bifurcation diagrams of pH with flow rate are reproduced with good quantitative agreement in the simulations of the mechanism in Table 1. The maximum values of pH in both the bistable region with $[\text{GL}]_0 = 0.003$ M and the oscillatory region with $[\text{GL}]_0 = 0.008$ M are slightly reduced in simulations compared to those observed in the experiments. The bistable region is also slightly shifted to higher flow rates in the experiments. The expected cross-shaped phase diagram is observed as a function of the inhibitor concentration, $[\text{GL}]_0$. The range of GL for which oscillations are observed is lower in the simulations by a factor of two. We also obtained a cross-shaped phase diagram in terms of the b/c ratio. Increasing b/c has the effect of increasing the clock time, as the rate of reaction (7) is reduced. Thus, the inhibitive process, i.e., the production of acid from GL, can dominate at higher b/c. The range of b/c for which oscillations are observed is reproduced in simulations with excellent agreement to the experiments.

This reaction is of particular interest as it displays large amplitude oscillations in pH with small amplitude oscillations in potential, and is therefore less aggressive than the known
inorganic-based (redox) pH oscillators. The bifurcation diagrams for this reaction were reproduced previously in simulations using the AUTO interface of XPP, considering the value of [X], fixed at some value. The oscillations emerged via a supercritical Hopf and disappeared via a saddle-node infinite period (SNIPER) bifurcation. The results reported here illustrate that little difference is observed on the behaviour with the decay of the GL incorporated into the model. Oscillations also appear via small amplitude oscillations and disappear abruptly with increasing flow rate. The cross-shaped phase diagram in [GL], was produced in both cases, but shifted slightly in terms of the range of [GL] and k_d for which oscillations are observed. The rate constants may be further optimised to obtain a better quantitative fit between the simulated phase diagram and the experiments.

In conclusion, the key features of the reaction that lead to pH oscillations are a base-producing reaction with a base-catalysed rate-determining step (dehydration of methylene glycol) coupled with a base-catalysed reaction that produces acid (hydrolysis of gluconolactone). The dehydration and the hydrolysis processes are also acid catalysed, but this channel is thought to be insignificant at the pH range in this work. However, as many such processes display similar acid/base catalysis, we expect that it will not be impossible to find an acid-catalysed, acid-producing reaction to couple with an acid-catalysed, base-producing reaction to generate acid-regulated pH oscillations. We note that the clock in the MGSG involves the consumption of the sulfate/bisulfite buffer, which plays an essential role in this particular system. However, in a minimal model we produced previously, we demonstrated that the presence of a buffer is not necessary for oscillations, provided the rate constant of the rate-determining step is small enough such that a clock reaction is observed in batch. Additionally, gluconolactone is the product of the glucose-oxidase enzyme catalysed reaction (a reaction widely exploited in biotechnology for the detection of glucose), presenting the potential for an enzymatic negative feedback step in the MGSG. This reaction therefore creates new possibilities for the development of pH oscillators to couple with pH-sensitive polymers.

Acknowledgements

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