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Mendeleev Commun., 2005, 15(6), 256–259
Mendeleev Communications

Determination of ampicillin using the Belousov–Zhabotinskii oscillating system

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DOI: 10.1070/MC2005v015n06ABEH002172

A new analytical method was developed for the determination of ampicillin by the perturbation of ampicillin to a Belousov–Zhabotinskii oscillating chemical system, which involves the Ce^{IV}-catalysed reaction between potassium bromate and malonic acid.

A study in nonlinear dynamics has been well developed. One of the important applications is an oscillating chemical system.[1–3] The kinetics of this oscillating chemical system is of both theoretical and experimental interest,[4–6] since the concentrations of reaction intermediates vary sensitively with time.

A typical oscillating chemical reaction is the Belousov–Zhabotinskii (BZ) reaction.[6] This reaction involves the oxidation of an organic species such as malonic acid by an acidified bromate solution in the presence of a metal ion catalyst. The Ce^{IV}–Ce^{III} and $[Fe^{III}(phen)]^{3+}$–$[Fe^{II}(phen)]^{2+}$ couples are the two most widely used catalysts. In a closed system, the BZ reaction exhibits a short induction period followed by an oscillating phase. The colour of the solution alternates between yellow and colourless for the Ce^{IV}–Ce^{III} couple. The oscillations may last over 2 h.

Ultimately, with decreasing concentrations of the major reactants such as potassium bromate and malonic acid, the system proceeds in the direction of decreasing Gibbs energy. Consequently, the oscillation dies out and the system drifts slowly towards its chemical equilibrium.

The mechanism of the BZ reaction has been investigated extensively. The famous FKN mechanism[7] is generally accepted. Two major processes (A and B) control the BZ reaction alternately and result in concentration oscillations of the intermediate species. A third process (C) is a link between processes A and B. The overall reactions are as follows:

Process A:

$$BrO_3^- + 2Br^- + 3CH_2(COOH)_2 + 3H^+ \rightarrow 3BrCH(COOH)_2 + 3H_2O \quad (1)$$

Process B:

$$BrO_3^- + 4Ce^{3+} + 5H^+ \rightarrow HOBr + 4Ce^{4+} + 2H_2O \quad (2)$$

Process C:

$$HOBr + 4Ce^{4+} + BrCH(COOH)_2 + H_2O \rightarrow 2Br^- + 4Ce^{3+} + 3CO_2\uparrow + 6H^+ \quad (3)$$

The mechanism is autocatalytic. The concentration of Br^- in the BZ system plays an important role.[8] It determines whether it is process A or B controlling at a particular time. The function of process A, however, is to remove Br^- from the system, while process B, also called autocatalytic oxidation, begins when process A has driven $[Br^-]$ to a sufficiently low value. The onset of process B is accompanied by a rapid production of Ce^{IV}, which becomes a reactant in process C to regenerate Br^-. In addition to supplying Br^- to suppress process B, process C resets

process B by reducing Ce^{IV} back to Ce^{III}. The reaction continues until the concentration of one of the reactants falls below a level necessary to sustain the cycling.

The BZ reaction is of interest for kinetic analysis.[9] Analytical applications of the BZ reaction have been focused on metal ions and inorganic anions.[10–12] A few studies have been carried out in organic analysis.[13–16]

We found that ampicillin can affect the amplitude of the BZ quinone (BQ) reaction. At 30 °C, the decrease in the amplitude $\Delta A = A_0 - A$ (where A_0 is the amplitude injection quinone, and A is the amplitude injection ampicillin and quinone mixture) is proportional to the concentration of ampicillin in the range 5.0×10^{-9}–1.0×10^{-7} mol dm^{-3}, $\Delta A = 2.42C - 10.30$, ($r = 0.9995$) (the unit of concentration is nmol dm^{-3}). Foreign ions did not interfere with the determination. Cyclic voltammetry (CV) was employed to study the mechanism.

The oscillating assembly comprised a 50 ml glass reaction vessel fitted with a Model CS-501 super thermostat and a Model ML-902 magnetic stirrer (Shanghai Pujiang Analytical Instrumental Factory) for homogenization. A KL-98 electrochemical analytical instrument (Tianjin Instrumental Stock Finitude Company) was used to record the potential change. A Type 213 platinum electrode was used as the working electrode, a Type 213 platinum electrode as a counter electrode and a Type saturated calomel electrode as a reference electrode.

High-purity deionized water was used for preparing 0.25 M potassium bromate, 0.4 M malonic acid and 0.04 M cerium sulfate [$Ce(SO_4)_2\cdot4H_2O$] solutions in 0.8 M H_2SO_4.

Potentiometric measurements were performed in a closed thermostatted glass container with a magnetic stirrer (stirring rate of 500 rpm). To obtain stable values of A_0 or A, all of the experiments were performed at 30 °C.

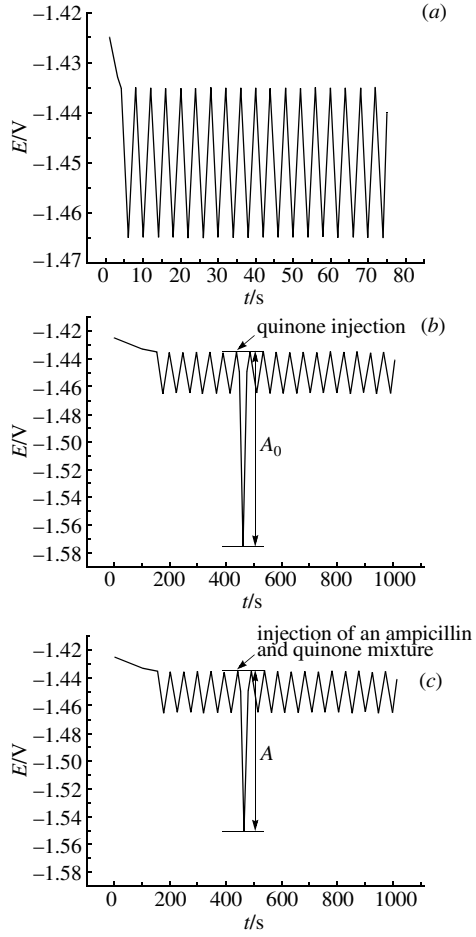


Figure 1 Typical oscillation profiles for the proposed oscillating system obtained in the presence of quinone and an ampicillin and quinone mixture perturbation using platinum electrodes: (*a*) [BQ] = 0, [AM] = 0; (*b*) [BQ] = = 1.0×10^{-6} mol dm^{-3}, [AM] = 0; (*c*) [BQ] = 1.0×10^{-6} mol dm^{-3}, [AM] = = 4.0×10^{-8} mol dm^{-3}. $KBrO_3$, 0.25 M, 7.0 ml; $CH_2(COOH)_2$, 0.4 M, 7.0 ml; Ce^{IV}, 0.04 M, 1.0 ml; H_2SO_4, 0.8 M, 5.0 ml.

Table 1 Effect of concentration of ampicillin *versus* ΔA ([BQ] = = 1.0×10^{-6} mol dm^{-3}).

Concentration of ampicillin/ nmol dm^{-3}	ΔA/mV
5	2.6
10	11.6
15	27.1
20	39.1
25	50.5
30	61.5
35	74.1
40	86.4
45	98.9

In order to understand the mechanism of the inhibitory effect of quinone on the BZ reaction, CV was applied to monitor the species in the BZ system, which reacted with quinone.

Figure 1(*a*) shows a typical oscillation profile for the BZ oscillating chemical system. When only quinone is added to the BZ medium, the first amplitude of oscillation decreases. Figure 1(*b*) shows a typical oscillation profile for the BZ system in the presence of quinone perturbation. When an ampicillin and quinone mixture is added to the BZ medium, Figure 1(*c*) shows an oscillation profile in the presence of ampicillin and quinone perturbation. When only ampicillin is added, the oscillation profile is similar to that in Figure 1(*a*).

In the range 5.0×10^{-9}–1.0×10^{-7} mol dm^{-3}, ΔA ($A_0 - A$) is proportional to the concentration of ampicillin (Table 1). The correlation between the ΔA of oscillation and the ampicillin concentration was linearly regressed as follows:

$$\Delta A = 2.42C - 10.30,$$

where unit of concentration is nmol dm^{-3}. According to $3\sigma/k$, the limit of detection is 3.3×10^{-11} mol dm^{-3} (σ is the standard deviation, k is the slope, $n = 11$). We carried out 11 determinations in a 20 nM ampicillin solution (standard deviation, 0.8%; regression parameters $R = 0.9995$).

More than 20 foreign ions were studied with respect to their effect on the determination of ampicillin. The results are shown in Table 2. Large amounts of alkali and alkaline earth metal ions do not interfere with the determination, neither do most common anions interfere except for chloride and iodide.

To obtain a constant and maximum value of ΔA in the determination of quinone, the effect of the concentrations of sulfuric acid, potassium bromate and cerium(IV) were examined.

The effect of potassium bromate concentration was studied over the range 0.1–0.4 M. Figure 2(*a*) shows that a maximum response to quinone perturbation was obtained at a potassium bromate concentration of 0.25 mol dm^{-3}. The concentrations of Ce^{IV} and sulfuric acid were also studied, and similar results were obtained [Figure 2(*b*),(*c*)]. The influence of malonic acid concentration was investigated over the range 0.3–0.6 mol dm^{-3}. A higher concentration of malonic acid caused a lower change of amplitude [Figure 2(*d*)]. When the concentration of malonic acid was decreased to under 0.3 mol dm^{-3}, the oscillation cannot last long times. Therefore, the following experiments were carried out at [$KBrO_3$] = 0.25 M, [Ce^{IV}] = 0.04 M, [H_2SO_4] = 0.8 M and [$CH_2(COOH)_2$] = 0.4 M.

To clarify which species in the BZ system reacted with quinone, the cyclic voltammograms of quinone were recorded in the following media: (I) H_2SO_4 + $KBrO_3$ + quinone; (II) H_2SO_4 + + $CH_2(COOH)_2$ + quinone; (III) H_2SO_4 + Ce^{IV} + quinone. The

Table 2 Effect of foreign ions on the determination of 10 nM ampicillin ([BQ] = 1.0×10^{-6} mol dm–3).

Foreign ions	Maximum tolerated molar ratio
K^+, Na^+, Li^+, Mg^{2+}, HPO_4^{2-}, $H_2PO_4^-$, NO_3^-, SO_4^{2-}	5500
Ca^{2+}, Ba^{2+}, Cu^{2+}, Zn^{2+}, Al^{3+}	3800
Co^{2+}, Ni^{2+}, Mn^{2+}	900
Ac^-, Ag^+	500
Fe^{3+}, Fe^{2+}	200
Cl^-, I^-	50

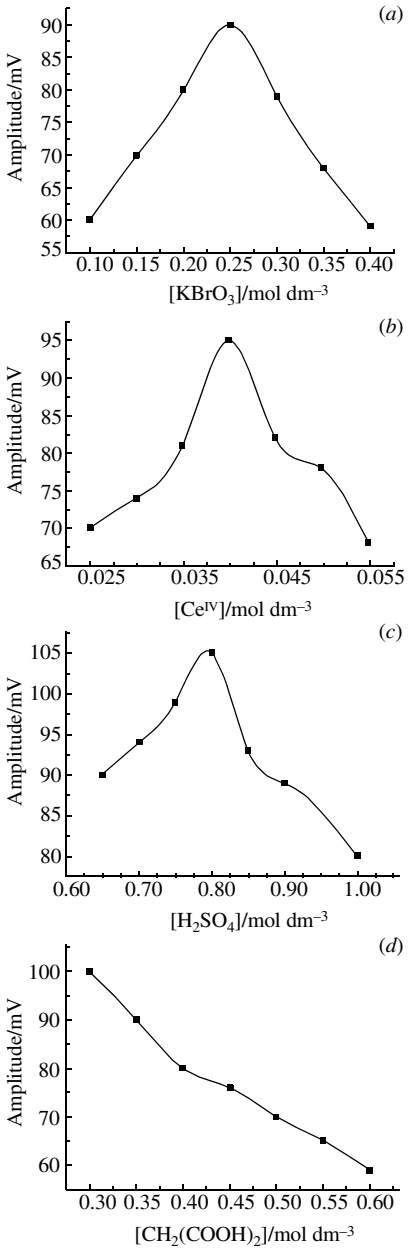
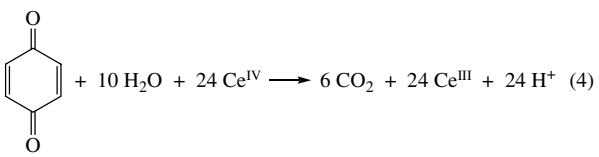


Figure 2 Influence of the concentrations of (*a*) potassium bromate; (*b*) cerium(IV); (*c*) sulfuric acid and (*d*) malonic acid on the quinone perturbed oscillating reaction. (*a*) 0.04 M Ce^{IV} + 0.4 M $CH_2(COOH)_2$ + + 0.8 M H_2SO_4; (*b*) 0.25 M $KBrO_3$ + 0.4 M $CH_2(COOH)_2$ + 0.8 M H_2SO_4; (*c*) 0.25 M $KBrO_3$ + 0.04 M Ce^{IV} + 0.4 M $CH_2(COOH)_2$ + 0.8 M H_2SO_4; (*d*) 0.25 M $KBrO_3$ + 0.04 M Ce^{IV} + 0.8 M H_2SO_4. [BQ] = 4.0×10^{-6} mol dm^{-3}.

results indicate that only Ce^{IV} can react with quinone, as shown in Figure 3.

We considered a possible mechanism for this system. When quinone is introduced into the system, it can be oxidised by Ce^{IV}, so that the concentration of Ce^{IV} decreases while that of Ce^{III} increases. The value of ln([Ce^{IV}]/[Ce^{III}]) decreases extraordinarily and the potentiometric oscillations are finally damping down. The reaction is as follows:



$$+ 10\,H_2O + 24\,Ce^{IV} \longrightarrow 6\,CO_2 + 24\,Ce^{III} + 24\,H^+ \quad (4)$$

As the concentration of Ce^{III} increases, it can react with free radicals $BrO_2^{\cdot}$,[13]

$$BrO_2^{\cdot} + Ce^{III} + H^+ \rightarrow HBrO_2 + Ce^{IV} \quad (5)$$

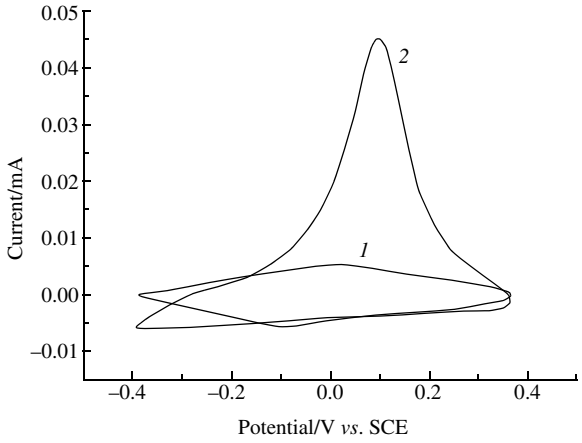
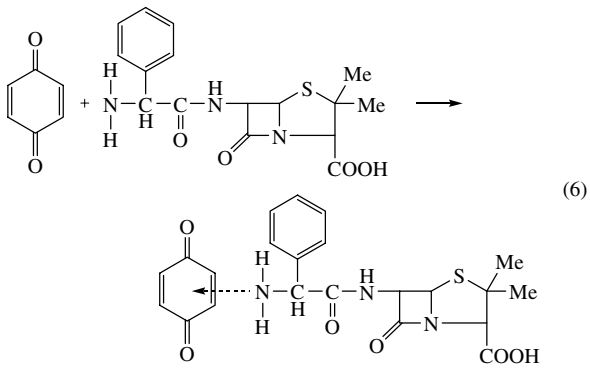


Figure 3 Cyclic voltammograms of reactions between quinone and Ce^{IV} obtained in the absence and in the presence of quinone: (*1*) [BQ] = 0; (*2*) [Q] = 4.0×10^{-6} mol dm^{-3}. [Ce^{IV}] = 0.04 mol dm^{-3}, [H_2SO_4] = 0.8 mol dm^{-3}.

Reaction (5) occurs very quickly, and Ce^{IV} can be regenerated in a very short time. Therefore, the system can reconvert to the same regular oscillation state as it initially does.

When ampicillin is added to the BZ quinone system, the ampicillin reacts with quinone to make an ampicillin and quinone complex,[17] another quinone may react with Ce^{IV} to form a quinone radical (BQ·) and its oxidation product (P), the results to decrease the concentration of quinone. Thus, the amplitude of oscillation in the BZ system decreases. The reaction is as follows:



(6)

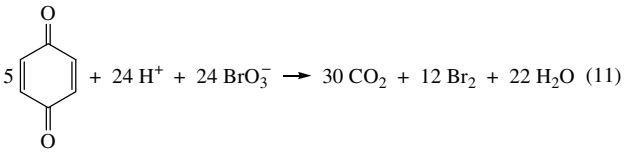
$$Ce^{IV} + BQ \rightarrow Ce^{III} + H^+ + BQ\cdot \quad (7)$$

$$HBrO_2 + BQ\cdot \rightarrow HOBr + P \quad (8)$$

$$Br_2 + 2BQ\cdot + 2H_2O \rightarrow 2Br^- + 2H^+ + 2P \quad (9)$$

$$HOBr + Br^- + H^+ \rightarrow Br_2 + H_2O \quad (10)$$

Once a large amount of quinone is added to the BZ system, a quinone molecule reacts with Ce^{IV}, the rest of the quinone can be oxidised by BrO_3^-, thus the solution gradually becomes yellow. When this solution is extracted with carbon tetrachloride, the organic layer appears to be yellow. This extracted substance is bromine, as indicated using potassium iodide and sodium thiosulfate.



$$5 + 24\,H^+ + 24\,BrO_3^- \longrightarrow 30\,CO_2 + 12\,Br_2 + 22\,H_2O \quad (11)$$

Although BrO_3^- can also react with Br^- to generate bromine, the amount of bromine produced by this reaction is very limited because of the low concentration of Br^- in the system. Therefore, reaction (11) is supposed to be another source of bromine.

In reaction (11), BrO_3^- is consumed, hence reaction (2) cannot take place as fast as in the previous situation; furthermore, the regeneration of Ce^{IV} is inhibited. On the other hand, since the

concentration of malonic acid does not change in the system, the amount of bromine is therefore cumulated.

This work was supported by the Natural Science Foundation of LongDong University.

References

1 K. D. Arum, *J. Phys. Chem*., 2000, **104**, 3257.
2 G. Rabai, M. Orban and I. R. Epstein, *J. Phys. Chem*., 1992, **96**, 5414.
3 S. K. Scott, *Oscillations, Waves and Chaos in Chemical Kinetics*, Oxford University Press, Oxford, UK, 1994.
4 R. J. Field, M. Burger, *Oscillations and Travelling Waves in Chemical Systems*, Wiley, New York, 1985.
5 K. Zhang, W. Ma, R. Cai, Z. Lin and N. Gan, *Anal. Chim. Acta*, 2000, **413**, 115.
6 S. Shen, H. Sun, J. Shan and J. Liu, *Indian J. Chem*. 2002, **41A**, 532.
7 R. J. Field, E. Koros and R. M. Noyes, *J. Am. Chem. Soc*., 1972, **94**, 8649.
8 R. M. Noyes, *J. Am. Chem. Soc*., 1980, **102**, 4644.
9 A. M. Zhabotinskii, *Zh. Anal. Khim*., 1972, **27**, 437 [*J. Anal. Chem. USSR* (*Engl. Transl.*), 1972, **27**, 382].
10 L. P. Tichonova, L. N. Zakrevskaya and K. B. Yatsimirskii, *Zh. Anal. Khim.*, 1978, **33**, 1991 [*J. Anal. Chem. USSR* (*Engl. Transl.*), 1978, **33**, 1529].
11 J. Gao, H. Yang, X. Liu, J. Ren, Q. Li and J. Wang, *Talanta*, 2002, **57**, 105.
12 K. Zhang, R. Cai, W. Ma, Z. Liu and N. Fan, *Anal. Sci*., 2000, **16**, 967.
13 J. Gao, J. Ren, W. Yang, X. Liu, H. Yang, Q. Li and H. Deng, *J. Electroanal. Chem*., 2002, **520**, 157.
14 J. Gao, H. Yang, J. Ren, X. Liu, X. Lu, J. Hou and J. Kang, *Talanta*, 2001, **55**, 99.
15 Y. Dong, K. Gai and X. Gong, *Chem. Anal. (Warsaw)*, 2004, **49**, 739.
16 Y. Dong, K. Gai and X. Gong, *J. Chinese Chem. Soc.*, 2004, **51**, 7.
17 L. Song, Y. Wang, S. Xuan and C. Zhang, *J. Taiyuan University of Technology*, 1999, **30**, 3.

Received: 15th April 2005; Com. 05/2496