Special Issue: Novel Analytical Approaches towards SDGs

Notes

Integrated continuous flow method with dual feedback-based controls for online analysis and process control

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Abstract

The concept of an integrated automated continuous flow method with dual feedback controls is presented for diluting a stock solution to provide a solution of a given concentration. The one control is used for the online process monitoring by a feedback-based flow ratiometry, where the product (the diluted liquid) is titrated through the rapid bidirectional scan of the product/reagent flow ratio. The feedback control limits the scanning to the necessary range to increase the analytical throughput. The other control is used for the process control to output the product with a preset concentration. The merging ratio of the stock solution and a solvent (diluent) is changed based on the information from the online analysis. The concept was verified by applying it to producing 0.1 mol dm^{-3} CH_3COOH. When the stock concentration was changed from 0.1 (reference concentration) to 0.3 and then 0.2 mol dm^{-3}, the system searched for the suitable merging ratio and converged the output concentration to the reference value within 7.43 min with a relative error below 1.05 %. The mean throughput rate of the process analysis was 11.2 titrations min^{-1}. Successful results were also obtained for the 0.1 mol dm^{-3} HCl production. The present concept could be the basis for process control with reduced wasteful output and effluent treatment with eco-friendly treated water discharge, resulting in the contribution to SDGs' goals of 6 (Clean water and sanitation), 9 (Industry, innovation and infrastructure), and 14 (Life below water).

Keywords Feedback control, feedback-based flow ratiometry, flow titration, process control, online analysis, SDGs

Statements and Declarations

The authors have no competing interests to declare relevant to this article's content.

Introduction

Feedback-based flow ratiometry is a continuous flow titration method developed by Tanaka and Dasgupta *et al*. [1,2], where the equivalence point is efficiently determined by repeating upward and downward scans of the titrand/titrant flow ratio. The scanning is limited to the range of interest through a feedback-based control. They extended the concept to determine electrolytic dissociation constants based on the half equivalence point detection [3,4]. Tanaka *et al*. [5-8] realized unprecedented high throughput titration (maximally 46.9 titrations min^{-1} [8]) by combining the feedback-based control and a subsequent fixed triangular wave control, the latter of which had a higher scan rate and narrower scan range than the former.

Producing uniform products that meet quality standards is highly important in manufacturing pharmaceutical products [9,10], food [11], and so on. Online monitoring of a product's quality and feeding the analytical information back to the process control are useful for efficient production with less waste [12,13]. Fais *et al.* [14] developed a sensor-controlled flow apparatus for fast online titrations based on Tanaka and Dasgupta's concept [1,2]. They evaluated the performance of the apparatus by applying it to an acrylic acid miniplant.

In the present paper, we present a concept of an automated method with dual feedback controls for supplying a solution of a given concentration by diluting a stock solution. One control is used for online quality analysis, where the product (the diluted solution) is continuously titrated by a feedback-based flow ratiometry [1,2]. The other control is employed for process control, where the analytical results are fed back to the control of the stock solution/diluent confluence ratio for outputting a target concentration. The concept was successfully verified by applying it to the production of 0.1 mol dm^{-3} CH_3COOH and HCl. When the stock solution's concentration was changed, the system converged the confluence ratio to an optimal value within 7.43 min while repeating the high throughput titration at 11.2 titrations min^{-1}.

Experimental

Reagents

Aqueous CH_3COOH, HCl, and NaOH solutions were prepared by diluting commercial standard solutions for volumetric analysis (1, 5, and 5 mol dm^{-3}, respectively) purchased from Kanto Chemicals Co. with water. Analytical reagent grade bromothymol blue (BTB) was purchased from the same manufacturer. Sartorius Arium 611DI grade deionized water was used throughout.

Flow system

Figure 1 shows the flow system constructed in the present study. The system comprises quality analysis (A) and process control (B) components. Gilson Minipuls 3 MP-2 peristaltic pumps ($P_{1\text{-}4}$) were used for delivering solutions. In the quality analysis component (A), the product is online-sampled and titrated with 0.1 mol dm^{-3} NaOH containing 0.8 mmol dm^{-3} BTB by a feedback-based flow ratiometry [1,2]. The titrant flow rate is varied by P_1, controlled with the control signal V_{c1} from a laptop computer PC (Toshiba Dynabook Stellite 1850 SA120C/4) *via* an A/D-D/A converter (Measurement Computing, PC-Card DAS16/12-AO). A photodetector fabricated in-house with a yellow LED (rated current, 25 mA; manufacturer unknown), a photodiode (Hamamatsu Photonics S2281), *etc.* [7] was used for measuring the titrated liquid's relative transmittance. The photocurrent from D was converted into a voltage with a Hamamatsu C2719 current-voltage conversion amplifier (Amp) and acquired as the detection signal V_d in PC *via* the converter. In the process control component (B), a stock acid solution is aspirated and diluted with a solvent (H_2O) while the total flow rate F_{T1} is held constant. The diluent flow is varied by P_2, controlled with the control voltage V_{c2} from PC *via* the converter. PTFE tubing (1.59 mm outer diameter (o.d.), 0.5 mm inner diameter (i.d.)) was used as a conduit except for pump tubing (Pharmed tubing of 3.68 mm i.d. and 0.5 mm i.d.). The effective conduit length from the

confluence point C_1 to C_2 and that from C_2 to the detector D, estimated from the data shown in Fig. 3 (shown later), were 68.3 and 59.2 cm, respectively. The estimation process is described in detail in "Estimation of effective conduit length" in Supporting information. An in-house Excel VBA program was used to control the system, acquire the signals, and analyze and display the data. The program contained source code for the automatic removal of air signals [15] caused by air bubbles accidentally coming into the optical flow cell.

Principle

Figure 2 shows the present principle of the feedback-based process control using real data for 0.1 mol dm^{-3} CH_3COOH preparation. Initially, while the diluent (H_2O) flow is stemmed (*i.e.*, V_{c2} = 0 V), reference 0.1 mol dm^{-3} CH_3COOH is introduced. The solution is titrated with 0.1 mol dm^{-3} NaOH by the feedback-based flow ratiometry [1,2]. The principle of feedback-based flow ratiometry is described in Figs. S1 and S2 (Supporting information). The V_{c1} that gives the equivalence point (2.563 V: the mean value of the first nine V_{c1E} in this figure) is set as the reference value ($V_{c1E,Ref}$) for evaluating the product quality. When a stock CH_3COOH solution with a higher concentration (0.3 mol dm^{-3} in this case) is delivered, the V_{c1} that gives the equivalence point (V_{c1E}) shifts upwards from $V_{c1E,Ref}$ (2.563 V) because more titrant is required to neutralize the CH_3COOH. When V_{c1E} changes by 10 % or more from $V_{c1E,Ref}$ (A), V_{c2} increases to dilute the CH_3COOH, resulting in the V_{c1E} decrease after some delay. This delay corresponds to the time difference between the upstream operation and the downstream sensing.

This lag time causes over-dilution; hence V_{c1E} becomes lower than $V_{c1E,Ref}$. At this overshoot (B) instant, V_{c2} decreased to recover from the overshoot. When V_{c1E} becomes higher again than $V_{c1E,Ref}$. (C), the V_{c2} ramp direction is changed upward again. Such the reverse is repeated further three times. The average of adjacent V_{c2} maximum and minimum ($V_{c2,H1}$ and $V_{c2,L1}$, $V_{c2.L1}$ and $V_{c2,H2}$, $V_{c2,H2}$ and $V_{c2,L2}$) in this further repeating process are calculated. The V_{c2} is set at this average ($V_{c2,Set}$) to offset the lag time

effect and thus produce the desired output.

When V_{c1E} changes more than 10% from $V_{c1E,Ref}$ again due to the change in the stock solution concentration, V_{c2} resumes its scanning to find a new $V_{c2,Set}$ similarly to the procedure described above.

Results and Discussion

Optimization of analytical parameters

In the present method, the throughput rate of the feedback-based flow ratiometry is important to quickly determine the optimal control signal ($V_{c2,Set}$) to produce the desired output and, consequently, reduce the sample waste. Photometry using an acid-base indicator [1,6-8] was employed for the equivalence point detection because it was expected to give a much higher throughput rate than potentiometry using a glass electrode [2,5]. For example, titrations were carried out at 8.2 s/titration (photometry) [6] and 21.9 s/titration (potentiometry) [5] with almost the same flow systems except for the detectors. This difference was due to the indicator's fast color transition and the photodiode's faster response than the glass electrode. Since yellow LED was used as the light source, BTB, which shows the complementary color (*i.e.*, blue) against yellow in alkaline media, was selected as the indicator. The concentration of BTB in the titrant (0.1 mol dm^{-3} NaOH) was set at 0.8 mmol dm^{-3} because it gave considerable V_d change (> 0.5 V) during the color transition. The V_{c1} scan rate was investigated in 100 – 500 mV s^{-1} by using 0.1 mol dm^{-3} HCl and 0.1 mol dm^{-3} NaOH as a titrand and a titrate, respectively. In this experiment, the H_2O channel in Fig. 1 was closed. As shown in Fig. S3 (Supporting information), the RSD of V_{c1E} increased significantly when the scan rate was higher than 350 mV s^{-1}. Although the throughput rate of the feedback-based flow ratiometry is virtually independent of the scan rate in principle [1], a higher scan rate is preferable to find the new equivalence point when the titrand concentration is considerably changed. The 200 mV s^{-1} was selected as the V_{c1} scan rate because it gave an acceptable RSD of 0.43 %.

The V_{c2} scan rate is investigated in 12 – 60 mV s^{-1}. The $V_{c2,Set}$ was obtained for producing 0.1 mol dm^{-3} HCl from the stock 0.2 mol dm^{-3} HCl. The V_{c2} was maintained at this $V_{c2,Set}$, and the product was titrated online by the feedback-based flow ratiometry. Although the obtained V_{c1E} was almost constant irrespective of the scan ratio (Fig. S4(A)), its RSD increased with the scan ratio (Fig. S4(B)) (Supporting information). Therefore, 12 mV s^{-1} was selected as the optimum V_{c2} scan rate.

Analytical Performance

Figure 3 shows the time courses of V_{c1}, V_{c2}, V_d, and V_{c1E}. The CH_3COOH concentration to be fed was changed from the reference concentration of 0.1 mol dm^{-3} (0 – 120 s) to 0.3 (120 – 825 s) and then 0.2 mol dm^{-3} (825 – 1800 s). The introduction of 0.3 mol dm^{-3} CH_3COOH caused the V_{c1E} (green) deviation from the reference value, $V_{c1E,Ref}$ (2.563 V in horizontal purple line). The detection of this deviation was fed back to V_{c2} (brown) for the P_2 operation at 144.6 s. After several oscillations, V_{c2} was set at 3.684 V ($V_{c2,Set}$) in 536.6 – 842.7 s. The V_{c1E} took 445.8 s after the CH_3COOH concentration change to recover to $V_{c1E,Ref}$. The V_{c1E} average in 565.8 – 814.1 s was 2.536 ± 0.037 V (n = 23), and the relative error against $V_{c1E,Ref}$ (2.563 V) was 1.05 %. Based on the calibration curve shown in Fig. S2 (Supporting information), this relative error corresponded to the absolute error of − 0.0021 mol dm^{-3} in the CH_3COOH concentration. Similarly, when the stock solution was changed from 0.3 to 0.2 mol dm^{-3}, the feedback operation was started at 826.0 s to recover V_{c1E} to $V_{c1E,Ref}$. Resulting V_{c1E} in 1233.5 – 1791.6 s was 2.561 ± 0.029 V (n = 56) with the relative error of 0.08 % (the absolute error: − 0.0002 mol dm^{-3}). The time needed for V_{c1E} to recover to $V_{c1E,Ref}$ after the concentration change was 408.5 s. This shorter recovery time compared to the previous one (445.8 s) is reasonable because the stock CH_3COOH concentration change was lower than that in the previous one. That is, it took a shorter time to locate the new $V_{c2,Set}$ for the lesser concentration change (0.3 to 0.2 mol dm^{-3}) than for the greater change (0.1 to 0.3 mol dm^{-3}). The overall throughput rate of the titration was sufficiently high at 11.2 titrations min^{-1}, corresponding to 5.36 s $titration^{-1}$. A similar experiment was carried out for HCl successfully; the

results are shown in Fig. S5 (Supporting information).

Due to the limitations inherent in the laboratory-level equipment, especially the low flow rates of the peristaltic pumps (P_2 and P_3) in the process control component (B in Fig 1), there would be various challenges in applying the present method to actual industrial processes. However, we believe the proposed concept can provide fundamental insight for process control, which reduces wasteful output and hence the consumption of raw materials, and for the effluent treatment that provides less environmental impact on treated water. Therefore, we conclude that the present study will contribute to the SDGs' goals of 6 (Clean water and sanitation), 9 (Industry, innovation and infrastructure), and 14 (Life below water).

Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Acknowledgments

The present study was partly supported by a Grant-in-Aid for Scientific Research (C) (15K07889) from the Japan Society for the Promotion of Sciences (JSPS).

Supporting Information

The effective conduit length estimation is described in detail on the first page. The principle of feedback-based flow ratiometry is shown in Fig. S1. The CH_3COOH calibration curve is shown in Fig. 2. Effect of the V_{c1} scan rate on the precision (RSD of V_{c1E}) of the feedback-based frow ratiometry is

shown in Fig. S3. Effect of the V_{c2} scan rate on V_{c1E} and its RSD for the 0.1 mol dm^{-1} HCl preparation from 0.2 mol dm^{-1} HCl is shown in Fig. S4. Results of the online analysis and process control for the 0.1 mol dm^{-1} HCl preparation are shown in Fig. S5.

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Figure Captions

Fig. 1 Flow system

A, online quality analysis component; B, process control component. $P_{1\text{-}4}$, peristaltic pumps. F_B, F_{T1}, and F_{T2}, flow rates of the P_1, P_3, and P_4 channels, respectively. $Acid_{stock}$, stock acid solution; $Acid_{product}$, acid solution produced; w, waste. V_{c1}, control voltage for process analysis by feedback-based flow ratiometry; V_{c2}, control voltage for process control; V_d, detector output voltage. C_1 and C_2, confluence points (polypropylene tee). D, LED-photodiode-based detector. Amp, current amplifier. PC, laptop computer.

Fig. 2 Principle of feedback-based process control

V_{c2}, control voltage for process control; V_{c1E}, V_{c1} (see Fig. 1) that gives equivalence composition between the sampled product and titrant; $V_{c1E,Ref}$, V_{c1E} for the reference sample with desired concentration; $V_{c2,Set}$, V_{c2} at which the desired output is expected. A−G, V_{c1E} at which its deviation or overshooting is sensed.

Fig. 3 Temporal profile of V_{c1}, V_{c2}, V_d, and V_{c1E} for 0.1 mol dm^{-3} CH_3COOH production

The sampling frequency was 10 Hz. The concentration of CH_3COOH to be delivered was changed from 0.1 (reference concentration) to 0.3 and then to 0.2 mol dm^{-3}. $V_{c1E,Ref}$, reference V_{c1E} that corresponds to 0.1 mol dm^{-3} CH_3COOH. $V_{d.Set}$, V_d that corresponds to the equivalence point (See. Fig. S1 in Supporting information). The scan rates of V_{c1} and V_{c2} were 200 and 12 mV s^{-1}, respectively. However, 75 mV s^{-1} (denoted by asterisks) was chosen for the initial V_{c2} scan to rapidly locate the new suitable mixing ratio when the concentration of the stock solution was changed.

Fig. 1

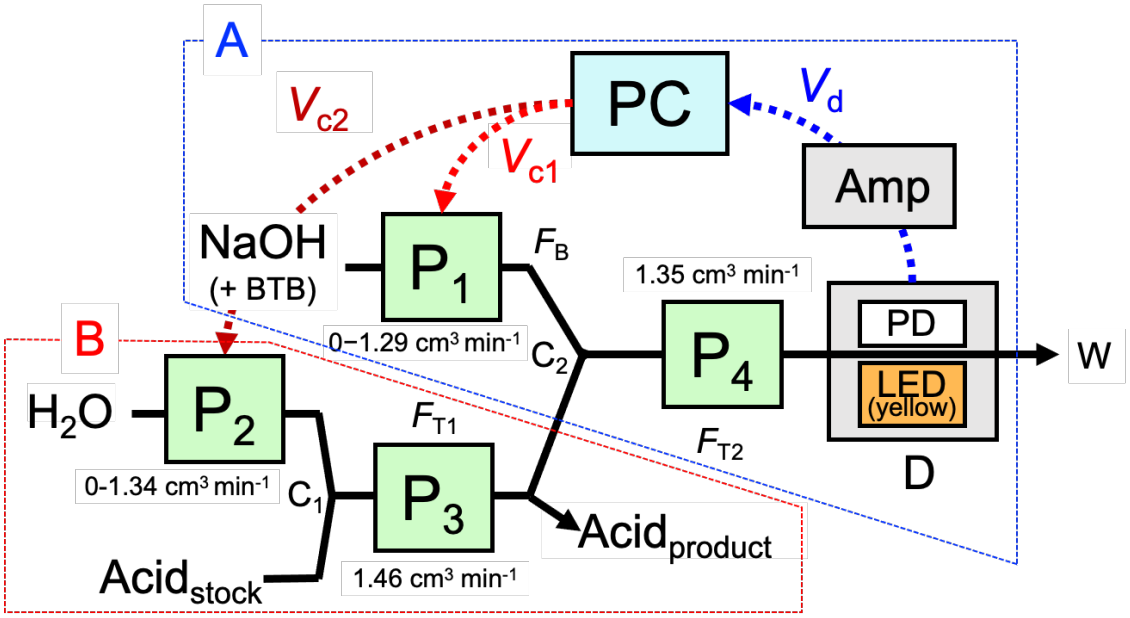
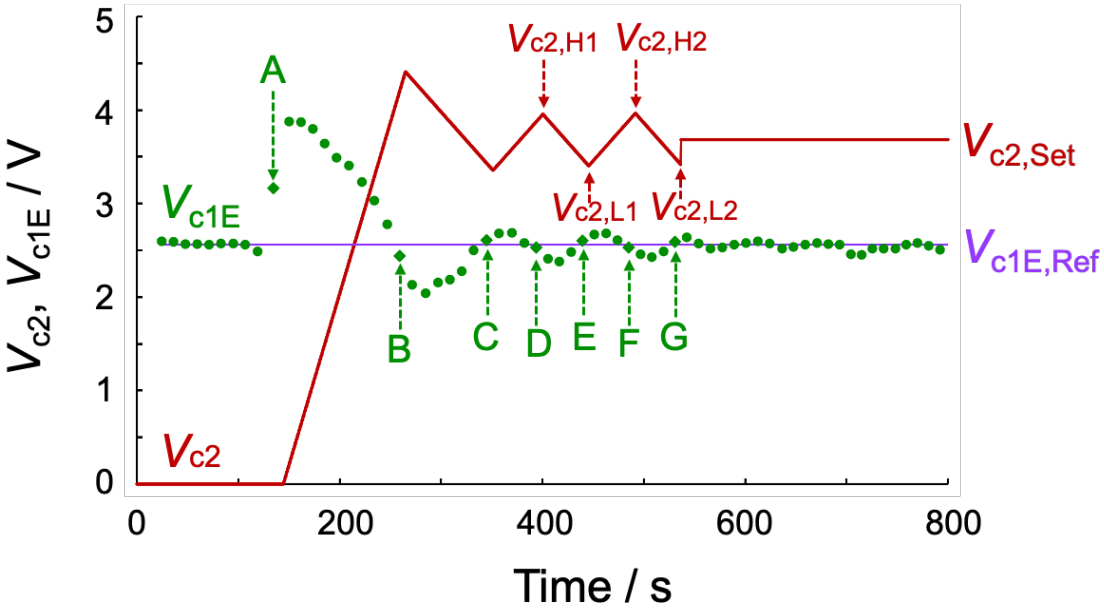

A
PC
V_{c2}
V_{c1}
V_d
Amp
NaOH
(+ BTB)
P_1
F_B
0–1.29 cm³ min⁻¹
1.35 cm³ min⁻¹
PD
LED
(yellow)
D
W
B
H_2O
P_2
0-1.34 cm³ min⁻¹
C_1
C_2
F_{T1}
F_{T2}
P_3
P_4
$Acid_{stock}$
1.46 cm³ min⁻¹
$Acid_{product}$

Fig. 2


V_{c2}, V_{c1E} / V
Time / s
$V_{c2,H1}$
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$V_{c2,L1}$
$V_{c2,L2}$
$V_{c2,Set}$
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B
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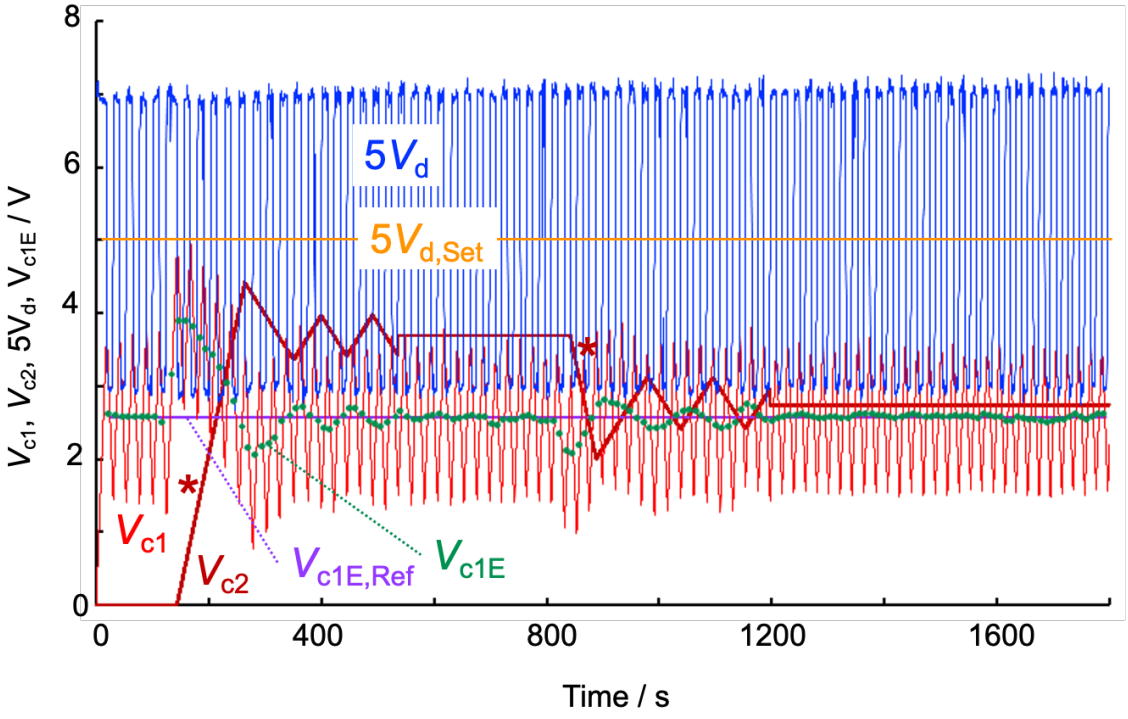
Fig. 3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6
4
2
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400
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Time / s
V_{c1}, V_{c2}, $5V_d$, V_{c1E} / V
$5V_d$
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