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RESEARCH PAPER

An On-line Adaptive Glucose Feeding System Incorporating Patterns Recognition for Glucose Concentration Control in Glutamate Fermentations

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Abstract In glutamate fermentation, intermittent feeding is the most widely used glucose feed strategy. This feeding strategy causes severe fluctuations of glucose concentration and osmotic pressure in fermentation broth, which deteriorates the viability of the cell and reduces glutamate production in turn. In order to maintain glucose concentration at stable and constant levels, an on-line prediction and feedback control system based an empiric mass balance model was developed. However, the control system did not work properly and sometimes glucose concentration could even decline to 0 level (glucose exhaustion), as the model parameter varies in different runs. As a result, a novel model-based adaptive feedback control system incoporating with an artificial neural network (ANN) based pattern reconition unit for on-line diagnosizing the fault of glucose exhaustion was proposed and applied for glutamate fermentation. This adaptive control system could accurately detect glucose exhaustion when it occurs, and then immediately updates the control parameter based on some pre-defined rule. With the proposed control system, glucose was automatically fed, and its concentration could be maintained at desired levels constantly. As a result, glutamate concentration was 17 ~ 30% higher than that of the traditional fermentations using the intermittent glucose feed strategy.

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1. Introduction

Corynebacterium glutamicum is a typical and common used strain for nucleotides and amino acids production, particularly for L-glutamate. Glutamate is widely used in food, pharmaceutical, and other industries with a production scale of more than 2.2 million tons per year [1]. In glutamate fermentation, glucose is fed as the carbon source, glucose concentration in broth is a crucial state variable which significantly affects glutamate production performance. In glutamate fermentation, either industrial or bench scales, glucose concentration is generally controlled by manual and intermittent feeding according to the manpower based off-line measurements [2]. This feeding strategy generally leads to large fluctuations in glucose concentration and variations in osmotic pressure in fermentation broth, which decreases the cell viability and finally reduces glutamate production [3]. Therefore, it is essential to develop an automatic glucose feeding strategy for the objectives of stabilizing glucose concentration and saving operation/labor costs.

An electrode for on-line detection of glucose concentration has been exploited [4], but it is very difficult to use it in industrial production due to the high cost and operation complexity of the detection unit. In many cases, some important but un-measurable process variables could be on-line predicted by certain kind of model based soft sensor techniques [5-7]. If the method is effective in

glutamate fermentation, then fermentation performance improvements would be largely expected.

In our previous studies, we found that glucose concentration could be predicted by on-line measurable oxygen uptake rate (OUR) and correlating the glucose production amounts with the oxygen consumption amounts by an empiric mass balance model. Therefore, glucose feed rate could be regulated automatically by a feedback controller to maintain (predicted) glucose concentration at desired set-points. However, due to the time-varying nature of the glutamate fermentation, the relationship coefficient in between the amounts of glucose and oxygen consumptions in the empiric mass balance model was subject to variations batch to batch. The inaccuracy of the model spoils the performance of the model-based feedback control system. The parameter of the feedback control system must be on-line adaptively self-tuned to deal with the varied model parameters, to ensure a better control performance.

Artificial neural network (ANN) is a digitized model of the human brain, computer programs designed for simulating the way in which human brain processes information. ANN learns (or is trained) through experience with appropriate learning exemplars just as human do, not from programming. ANN gathers its knowledge by detecting the patterns and relationships in data [8]. With the strong capability of character extraction, it is considered as an excellent pattern recognition tool and has been widely used in recent years [9-11]. In glutamate fermentation, maintaining glucose concentration at relatively low and stable level is beneficial to its production. However, due to the above mentioned parameter variations in the empiric mass balance model, glucose exhaustion occurred which severely deteriorated the fermentation performance. If the "exhaustion" happened, the dynamic characteristics/ pattern changes could be reflected by the on-line measurable parameters such as dissolved oxygen (DO), pH, OUR and CO_2 evolution rate (CER). In this study, a novel model-based adaptive feedback control system incoporating with an artificial neural network (ANN) based pattern reconition unit for on-line diagnosizing the fault of glucose exhaustion was proposed and applied for glutamate fermentation. In this case, the ANN was trained by normal fermentation data and several intently created "glucose exhaustion" data, thus an on-line fault diagnosis unit was created. Based on the on-line diagnosis results, the feedback control system automatically/ adaptively regulates its parameter to avoid glucose exhaustion and to keep glucose concentration at low/stable levels, aiming to achieving a high and stable glutamate production.

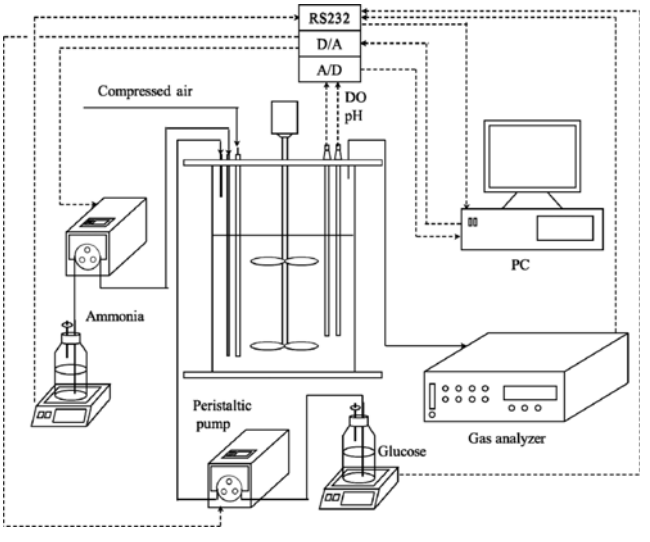

Fig. 1. Glutamate fermentation monitoring and control system.

2. Materials and Methods

2.1. Strain

C. glutamicum S9114 was used throughout the study. Seed medium and seed culture conditions were same as described before [12].

2.2. Fermentation medium

Ingredients of the fermentation medium were as follows: glucose 140 or 80 g/L, K_2HPO_4 1.5 g/L, $MgSO_4$ 0.4 g/L, urea 5.5 g/L, $FeSO_4$ 2×10^{-3} g/L, $MnSO_4$ 2×10^{-3} g/L, thiamine 5×10^{-5} g/L, corn slurry 5 g/L, biotin 3×10^{-6} g/L. Glucose feed medium contained: glucose 500 g/L.

2.3. Glutamate fermentation in 5 L bioreactor

Glutamate fermentation was carried out in a 10 L bioreactor, with the initial medium volume of 5 L and, inoculum size of 8% (v/v). Aeration rate was 1.3 vvm during the entire fermentation period, and dissolved oxygen concentration (DO) was maintained in a range of 20 ~ 30% by manually adjusting the agitation rate. pH was automatically controlled in the range of 7.0 ~ 7.2 by feeding 25% (v/v) ammonia water. Electronic balances connected to an industrial PC *via* RS232 communication cable was used to on-line monitor and calculate ammonia and glucose consumption rates by weighing the weight losses of ammonia and glucose feeding reservoirs.

O_2 and CO_2 concentrations in the exhaust gas were measured on-line by a gas analyzer (LKM2000, Lokas Co., Korea). CER and OUR were calculated accordingly. Temperature was stabilized at 32ºC throughout the fermentation. Glucose feed rate was regulated by the strategies described in section of "Process model and the feedback control system". Diagram of the fermentation monitoring and control system is shown in Fig. 1.

2.4. Analytical methods

Cell concentration was determined by measuring the optical density at 620 nm (OD_{620}). Glutamate and glucose concentrations were determined with SBA-40C biosensor (Shandong Academy of Science, China). The osmolality of broth was determined with OSMOMAT-030 osmometer (Gonotec, Germany).

2.5. Process model and the feedback control system

2.5.1. Empiric process model – correlations between the amounts of oxygen and glucose consumed

Oxygen and glucose are the two essential substrates in glutamate production. Eq. (1) could be used to calculate the total oxygen consumption amount M_{O_2} in the unit of "gram" between during a certain time interval (t_1~t_2). Here, OUR was the oxygen uptake rate in the unit of "mmol/L/h", MW_{O_2} indicated O_2 molecular weight, and V represented the working volume of fermentation broth, which was 5 L in the work. Therefore, the oxygen consumption amount (gram) M_{O_2} could be determined by

$$M_{O_2} = 10^{-3} \times V \times MW_{O_2} \int_{t_1}^{t_2} OUR(t)dt = 0.032V \int_{t_1}^{t_2} OUR(t)dt \quad (1)$$

On the other hand, glucose consumption amount M_G (gram) during the period (t_1~t_2) could also be calculated by counting its feeding amount and concentration variation, as described by Eq. (2).

$$M_g = S(t_2)V - S(t_1)V + S_F \int_{t_1}^{t_2} F(t)dt = (S(t_2) - S(t_1))V + S_F L(t)$$
$$L(t) = \int_{t_1}^{t_2} F(t)dt \quad (2)$$

Here, $S(t_1)$ and $S(t_2)$ were glucose concentrations (g/L) at time instant t_1 and t_2 (t_1<t_2), S_F (g/L) was glucose feeding concentration, and $L(t)$ was the glucose feeding amount during the period (t_1~t_2). In aerobic fermentations, the two substrates consumption amounts could be generally correlated in a linear form throughout the fermentation period, that is,

$$M_g = K \times M_{O_2} \quad (3)$$

Where K was the linear correlation coefficient and it was generally subject to variation batch by batch.

2.5.2. Determination of glucose feeding amount (rate) with the feedback control system based on oxygen consumption on-line measurement

Eq. (3) could be used to determine glucose feeding amount ($L(k)$) in control interval k in between time instant k and k+1, using on-line measured oxygen consumption amount data, that is,

$$(S(k+1) - S(k))V + S_F L(k) = K(0.032V \int_k^{k+1} OUR(t)dt) \quad (4)$$

In general, high concentrated glucose solution (*e.g.* S_F > 500 g/L) was used for glucose feeding, so that volume variation of the broth could be ignored (V = constant). In Eq. (4), $S(k)$ and $S(k$+1) represented glucose concentration at time instant of k and k+1, respectively. Assuming that glucose concentration is to be maintained at a set-point of S^* at the time instant of k+1 ($S(k$+1) = S^*), the glucose feeding amount in control interval k in between time instant k and k+1 ($L(k)$) could be determined by automatically regulating the feeding rate $F^*(k)$ by the PC, relevant communication interface and the peristaltic pump. Here, ΔT represented the length of control interval.

$$L^*(k) = \frac{[S^* - S(k)]V + 0.032KV \int_k^{k+1} OUR(t)dt}{S_F}$$
$$F^*(k) = \frac{[S^* - S(k)]V + 0.032KV \int_k^{k+1} OUR(t)dt}{S_F \times \Delta T} \quad (5)$$

The glucose concentration ($S(0)$) when initiating the control system could be actually off-line measured. Then, on-line glucose concentration prediction could be iteratively calculated by Eq. (6).

$$\hat{S}(k+1) = \frac{\hat{S}(k)V + S_F F^*(k)\Delta T - 0.032KV \int_k^{k+1} OUR(t)dt}{V}$$
$$\hat{S}(0) = S(0) = S_0 \quad (6)$$

2.5.3. Adaptive control system with an ANN based fault diagnosis unit

The proposed feedback glucose feeding system used on-line measured oxygen consumption amount to predict glucose concentration and to determine its feeding rate. Therefore, its control performance strongly relied on the accuracy of the linear correlation coefficient in between the consumed amounts of glucose and oxygen, K. As mentioned above, K may vary in different batches. A lowly set K may lead to glucose exhaustion, and a highly set K would cause glucose over-feeding leading to a glucose extra-accumulation. Accurately identifying K is very important in achieving good (glucose concentration) control performance. Among the two faults, the occurrence of glucose exhaustion would be fatal to the glutamate fermentation since it would irreversibly damage cells metabolic activities and eventually lead to a fermentation failure. The occurrence of "glucose

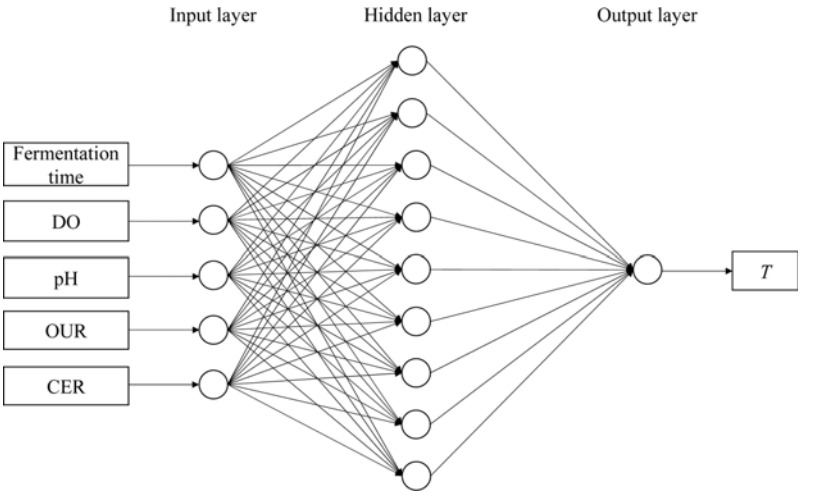

Fig. 2. Topology of the ANN based fault diagnosis unit.

exhaustion" could be reflected by patterns changes in on-line measurable variables such as DO, pH, OUR, CER, etc. When the "glucose exhaustion" fault occurred and was detected on time, failure like-hood fermentation could be rescued by immediately taking certain action *via* enhancing glucose feeding rate.

As a result, an ANN based fault diagnosis unit was developed to on-line detect the "glucose exhaustion" fault. As shown in Fig. 2, this ANN unit consisted of 5 inputs neurons (Fermentation time, DO, pH, OUR and CER), 9 hidden neurons, and 1 output neuron defined as *T*. To develop the ANN model, existing data pairs reflecting "glucose exhaustion" fault and "glucose sufficiency" were firstly used to train the ANN fault diagnosis unit. Here, the neuron outputs in output layer were categorized as "1" and "0", corresponding to the status of "glucose exhaustion" fault and "glucose sufficiency", respectively. The intently created training set including 200 pairs of input-output data was used for training the fault diagnosis unit. 50% of the data represented "glucose exhaustion" fault, and the rest of 50% represented "glucose sufficiency" status. The most widely used back-propagation (BP) algorithm was applied in this study, with the learning rate of 0.05 and the momentum coefficient of 0.9 [8]. Beside the training data pairs, another 34 unused input-output data pairs were selected as the test set. According to the real output of the test set, an optimal threshold was determined to ensure that the data in the test set was accurately divided into "glucose sufficiency" and "glucose exhaustion" categories.

The adaptive glucose feeding control system incorporating with the ANN based fault diagnosis unit was thus proposed. The operation procedure for the adaptive control system was illustrated in Fig. 3. The ANN pattern recognition unit was activated at an interval of 3 min, with the inputs data of fermentation time, DO, pH, OUR and CER collected/renewed in every 3 min. When *T* value (output of the ANN) was higher than the predetermined threshold in a pattern recognition cycle, then "glucose exhaustion" status was judged. In this case, *T* was valued as 1 ($T = 1$). Otherwise, *T* was valued as 0 ($T = 0$). Once the status of "glucose exhaustion" was detected, the following two actions were taken: (1) predicted glucose concentration was set to 0 g/L to delete the error between the actual and the predicted glucose concentrations; (2) the linear correlation coefficient of the process model *K* in Eq. (3) was updated by adding an increment (δ) to its initial value to increase glucose feeding rate. On the other hand, if the status of

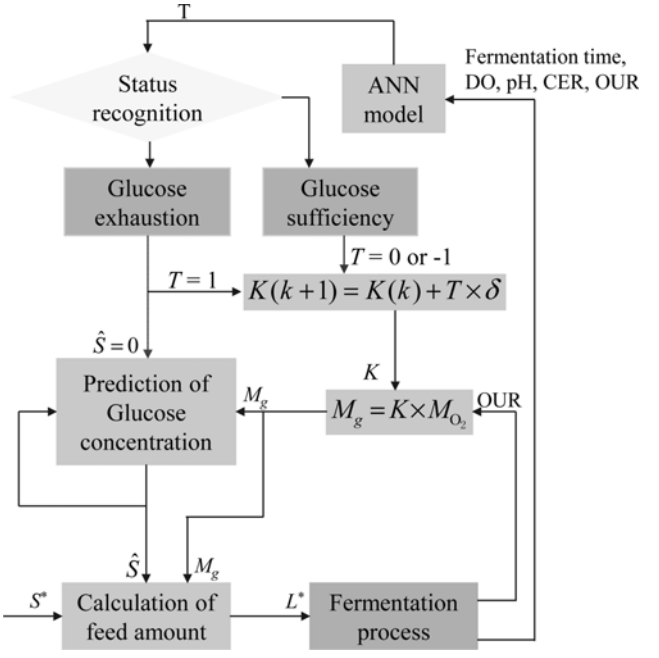

Fig. 3. Diagram of the proposed adaptive control strategy.

"glucose sufficiency" was detected for 10 consecutive recognition cycles, T was then forced to be valued as "-1" (T = -1) to avoid the possible glucose over-feeding and high residual glucose concentration. In glutamate fermentation, maintaining glucose concentration at lower levels is extremely important, in the terms of increasing glucose conversion yield, reducing osmotic pressure in fermentation broth, as well as reducing purification cost. Iterative renewing K was implemented in the following ways, with the initial K valued at the minimum level $K_{\min}$.

$$K(k+1)=K(k)+T\times\delta$$
$$K(0)=K_{\min}\quad \delta=0.2\quad T=+1,\ \ or\ \ 0\ or-1 \tag{7}$$

$$F(k)=\frac{[S^{*}-S(k)]V+0.032K(k)V\int_{k}^{k+1}OUR(t)dt}{S_F\times\Delta T}$$
$$0\le F(k)\le F_{Max} \tag{8}$$

Here, T could be considered a symbol factor, indicating the increase/unchanged/decrease directions in glucose feeding rate, δ was step-wise parameter and δ was set 0.2 in this case. In this way, glucose feeding rate F could be adaptively regulated.

3. Results and Discussion

3.1. Correlations between the amounts of oxygen and glucose consumed

Fig. 4 showed that the linear correlation coefficient of the process model K in different fermentation runs. The slope M_g versus M_{O_2} (K) was in strict linear correlation but with different K values in different runs. The run depicted by the filled circles had the smallest slope (K = 2.52), while the run represented by open squares showed the largest slope (K = 4.11). As K largely varied in the ranges of 2.5 ~ 4.0,

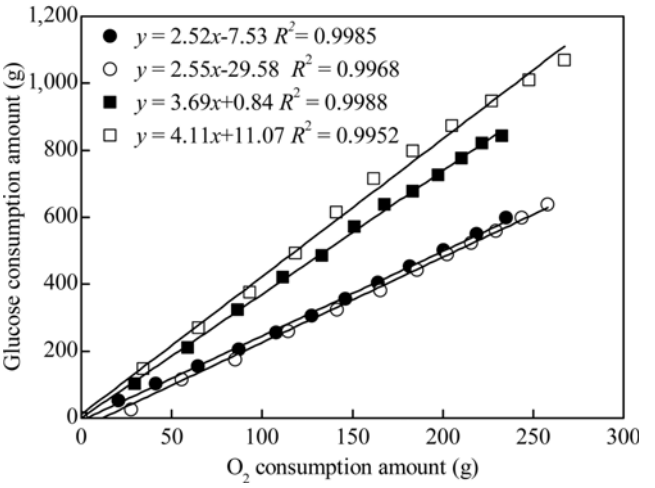

Fig. 4. The functional relationship between the accumulated consumption amounts of oxygen and glucose.

adaptive glucose feeding control incorporating with pattern recognition unit and iteratively renewing K for developing an adaptive glucose feeding control system was absolutely necessary.

3.2. Glutamate fermentations with intermittent glucose feeding strategies

The intermittent feed is the most widely used glucose feed strategy in industrial glutamate production, and it was also employed in the current study for comparison purpose. The intermittent feeding strategy was initiated when glucose concentration in broth decreased to 10 g/L. Three runs were conducted using the intermittent feeding strategy and the fermentation performances were listed in Table 1 (run #1~3). The fermentation curves of the fermentation (run #1) with the intermittent feeding strategy were depicted in Fig. 5 (Figs. 5A and 5C). As shown in Fig. 5, with the intermittent feeding strategy, glucose concentration varied from 10 g/L to about 30 ~ 50 g/L within short period, leading to a large change in osmotic pressure of the fermentation broth. This largely deteriorated the overall

Table 1. Fermentation performance of the runs with intermittent and adaptive glucose feeding strategies

Run #	Glucose feeding strategy	Initial glucose concentration (g/L)	Glucose concentration control levels (g/L)	Numbers of Feeding	Concentration of glutamate (g/L)
1	Intermittent feed	124	N/A	Low (2)	52
2	Intermittent feed	128	N/A	Medium (4)	50
3	Intermittent feed	125	N/A	High (6)	53
4	Intermittent feed	74	N/A	Medium (4)	43
5	Intermittent feed	75	N/A	Medium (4)	44
6	Feedback control	72	10 ~ 20	>100	62
7	Adaptive control	71	5	>100	62
8	Adaptive control	72	10	>100	64
9	Adaptive control	74	15	>100	65

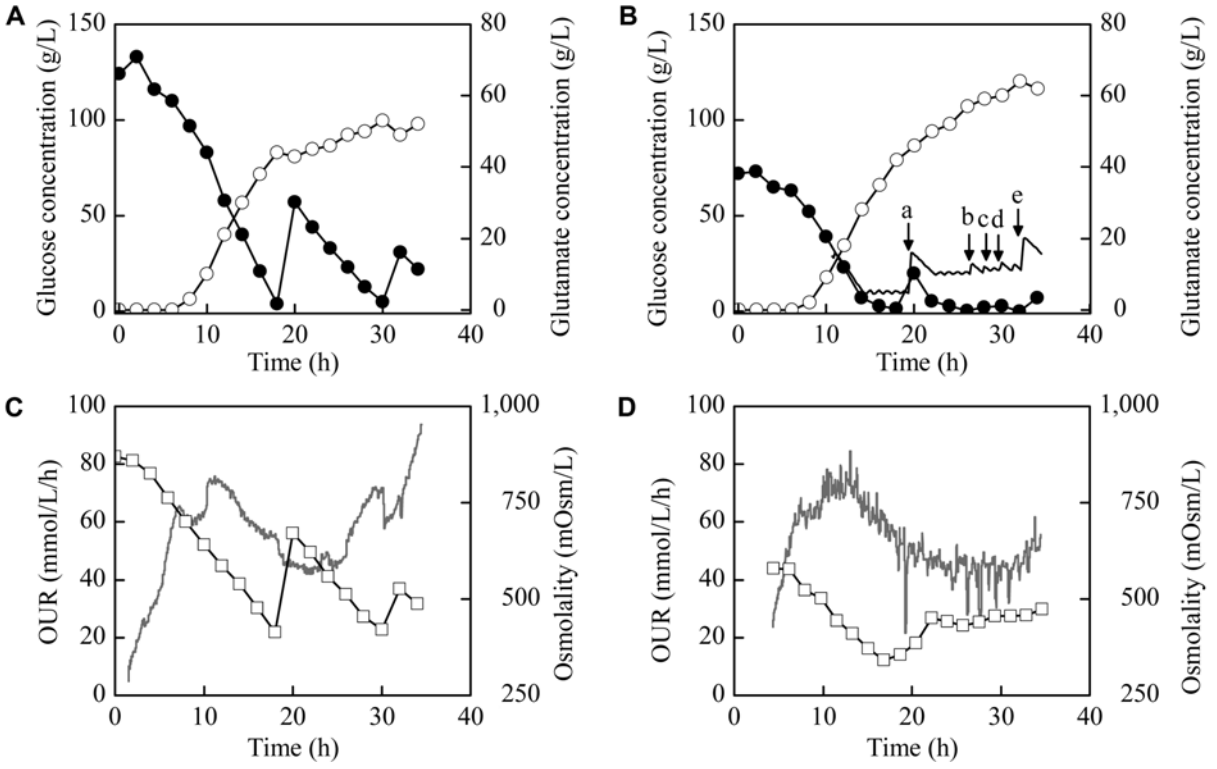

Fig. 5. Variations of concentrations of glucose and glutamate, OUR and osmolality. A: variations of glucose and glutamate concentrations with the intermittent glucose feed strategy. Filled circles: actual glucose concentrations; open circles: glutamate concentrations. B: variations of the glucose and glutamate concentrations with the feedback glucose concentration control strategy. Filled circles: actual glucose concentrations; solid line: predicted glucose concentrations; open circles: glutamate concentrations. C: variations of the OUR and osmolality with the intermittent glucose feed strategy. Open squares: osmolality; solid red line: OUR. D: variations of OUR and osmolality with the feedback glucose concentration control strategy. Open squares: osmolality; solid red line: OUR.

glutamate fermentation performance, and the final glucose concentration ended at lower levels of 52 g/L.

In glutamate fermentation, OUR actually reflects cell metabolic viability. In run #1, when concentrated glucose solution was fed at 18 and 30 h, osmotic pressure of the fermentation broth (osmolality) increased accordingly and quickly (Fig. 5C). As a result, OUR suddenly decreased at 18 and 30 h, and could not return to the original level in a short period (Fig. 5C). It was reported that, for the strain *C. glutamicum* ATCC17965, severe fluctuations in osmotic pressure decreases cell viability [3]. The results shown in Figs. 5A and 5C showed that the strain used in this work (*C. glutamicum* S9114) also had the similar effect (cell viability change in response to osmotic shock).

Higher initial glucose concentrations (120 ~ 130 g/L) were applied in run #1~ #3 and relatively lower initial glucose concentration (70 ~ 80 g/L) was adopted in run #4 and #5 to investigate the influence of initial glucose concentration on glutamate production. The glutamate yields of run #4 and #5 were lower than those with a high initial glucose concentration (Table 1). The higher initial glucose concentration may repress cell growth and deteriorate cell viability at the early fermentation stage. However, it could reduce the numbers of intermittent glucose feeding, that is why most of industrial glutamate fermentations start with high glucose concentration.

3.3. Glutamate fermentations with the feedback control system based on oxygen consumption on-line measurement

The proposed feedback glucose feeding control system based on oxygen consumption on-line measurement was adopted in this study, by setting the value of K at the lowest level of 2.52. The fermentation performance was shown in Fig. 5B. In this case, the set-point of glucose concentration was set at 10 g/L. Although the predicted glucose concentration was stably controlled at the set point during the period of 14 ~ 18 h, the off-line measured glucose concentration gradually decreased and reached to 0 g/L at about 19.5 h. To increase the real glucose concentration, the set point was manually raised up to 20 g/L at the point "a" as in Fig. 5B. In this way, the predicted glucose concentration was stably controlled at 20 g/L after 22 h, but the corresponding real glucose concentration was much lower than 20 g/L, and continued to decrease. At the time

points of "b", "c", "d" and "e" points (Fig. 5B), glucose was exhausted once again, and the set-point of glucose concentration was manually/consecutively raised up from 20 to 22 g/L, 23 g, 24 and 30 g/L, respectively. Although glucose was repeatedly exhausted in this run, its concentration was stably kept at low level and the severe fluctuations in osmolality was prevented (Fig. 5D). The sudden OUR decreases were caused by glucose depletion. Immediately after the glucose addition, OUR returned to its original level (Fig. 5D). As the large fluctuations in glucose concentration was relieved and glucose was basically maintained at low level, the final glutamate concentration reached 62 g/L (Fig. 5B), which was much higher than those of using the intermittent feed strategy (either high – 120 ~ 130 g/L or low – 70 ~ 80 g/L initial glucose concentration). However, this control system required frequent glucose off-line measurements and glucose concentration set-points changes; it was actually not an automatic control in real meaning.

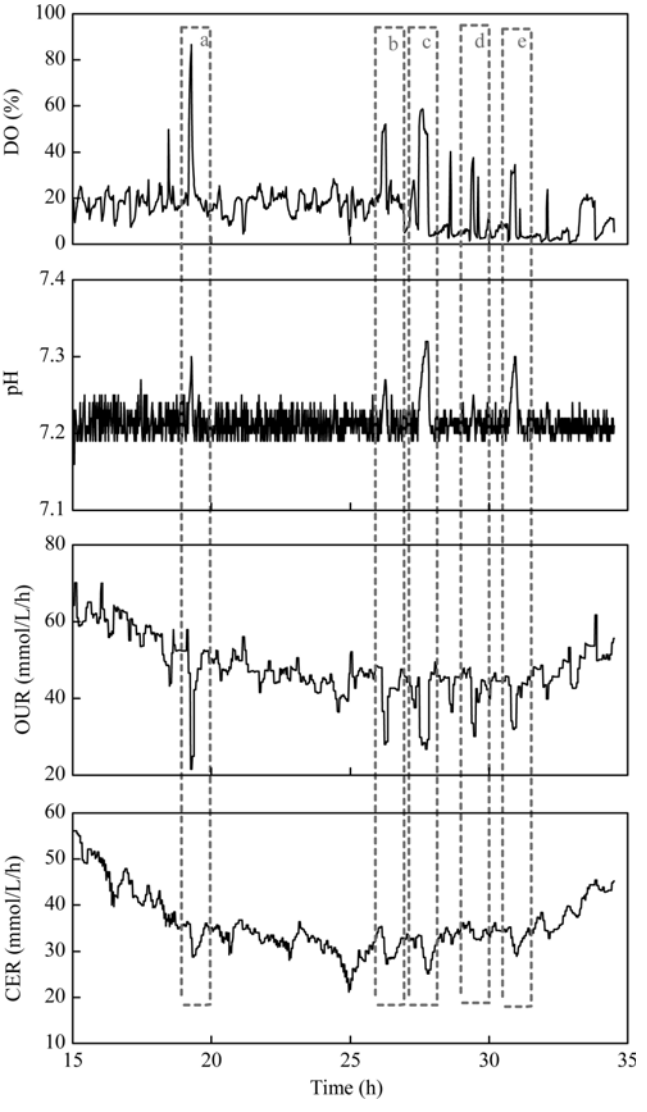

Fig. 6. Variation patterns of the on-line measurable variables including DO, pH, OUR, and CER under the conditions of "glucose sufficient" and "glucose exhaustion" .

3.4. Glutamate fermentations with the on-line adaptive glucose feeding system incorporating patterns recognition

As mentioned above, the proposed feedback glucose feeding strategy was not a real automatic control system, a full automatic control must be considered. In Fig. 6, glucose depletion at points of "a" ~ "e" and the corresponding variation patterns of the on-line variables of DO, pH, OUR and CER were depicted and marked by red rectangles. Fig. 6 indicated that glucose exhaustion was closely associated with increases in DO and pH, and decreases in OUR and CER. As a result, the proposed ANN model based patterns recognition units were applied to categorize the glucose concentration status using the on-line variables.

The performance of the ANN model based patterns recognition unit was tested using 34 input-output testing

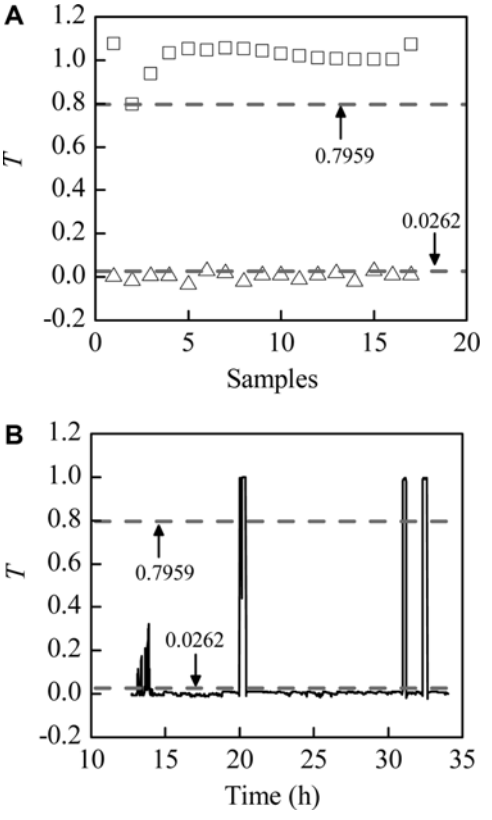

Fig. 7. The performance of the ANN model based patterns recognition unit. A: off-line recognition results. Open squares: outputs for "glucose exhaustion"; open triangles: outputs for "glucose sufficiency". Dashed lines: the thresholds classifying the two categories. B: on-line patterns recognition results for "glucose exhaustion" data. Solid line: on-line recognition results/outputs; dashed lines: the thresholds classifying the two categories.

data pairs, which consisted 17 pairs data representing "glucose sufficiency" and "glucose exhaustion" respectively. Fig. 7A showed the off-line patterns recognition results. An optimal threshold should be determined to divide the sample data into "glucose sufficiency" and "glucose depletion" categories. In this case, the minimum outputs threshold representing "glucose exhaustion" was 0.7959 whereas the maximum outputs threshold representing "glucose sufficiency" was 0.0262. Theoretically, "T = +1" should be returned when the recognition unit detecting the status as "glucose exhaustion", while "T = 0" should be returned when the recognition unit detecting the status as "glucose sufficiency". However, in real calculations, the ANN outputs could not reach the "theoretical" values. As a result, we categorized any outputs above 0.7959 as "glucose exhaustion" (T = +1) and any outputs below 0.0262 as "glucose sufficiency" (T = 0). The outputs in the range of 0.0262 ~ 0.7959 were actually the fuzzy results, and in these cases T was valued as "0" (T = 0) to maintain the current glucose feeding rate without change. The above mentioned thresholds were selected empirically. Fig. 7B indicated the on-line patterns recognition results, when "glucose exhaustion" status was intently created at 20, 31, and 32.5 h. The recognition unit detected the status quickly and accurately.

3.5. Glutamate fermentations with the ANN fault diagnosis unit based adaptive control system

The ANN fault diagnosis unit based adaptive control system was implemented in three glutamate fermentation runs by setting glucose concentration control levels at 5, 10, and 15 g/L, respectively (Table 1, run #7~ #9). Fig. 8 showed the results of patterns recognition results, performance of fermentation and process control, using run #8 as the example. As shown in Fig. 8A, glucose exhaustion occurred at time points of "a" ~ "f", and the faults were quickly detected by the patterns recognition unit. Once "glucose exhaustion" (T = +1) was detected, the predicted glucose concentration was set to 0 g/L, and the slope K was renewed/increased according to Eq. (7). A total of 6 "glucose exhaustion" faults were during the fermentation. With the proposed feedback control system with patterns recognition unit, the predicted glucose concentration returned to the set point, while the actual glucose concentration increased to the set-point level (10 g/L, Fig. 8B). The glucose concentration could be roughly/stably maintained in the range of 0 ~ 10 g/L throughout the fermentation. Osmolality did not suffer from severe fluctuation, and OUR was stable except in the instant when glucose was depleted (Fig. 8C). Final glutamate concentration reached a level of 64 g/L. Final glutamate concentrations of run #7 and run #9 also reached 62 and 65 g/L, respectively.

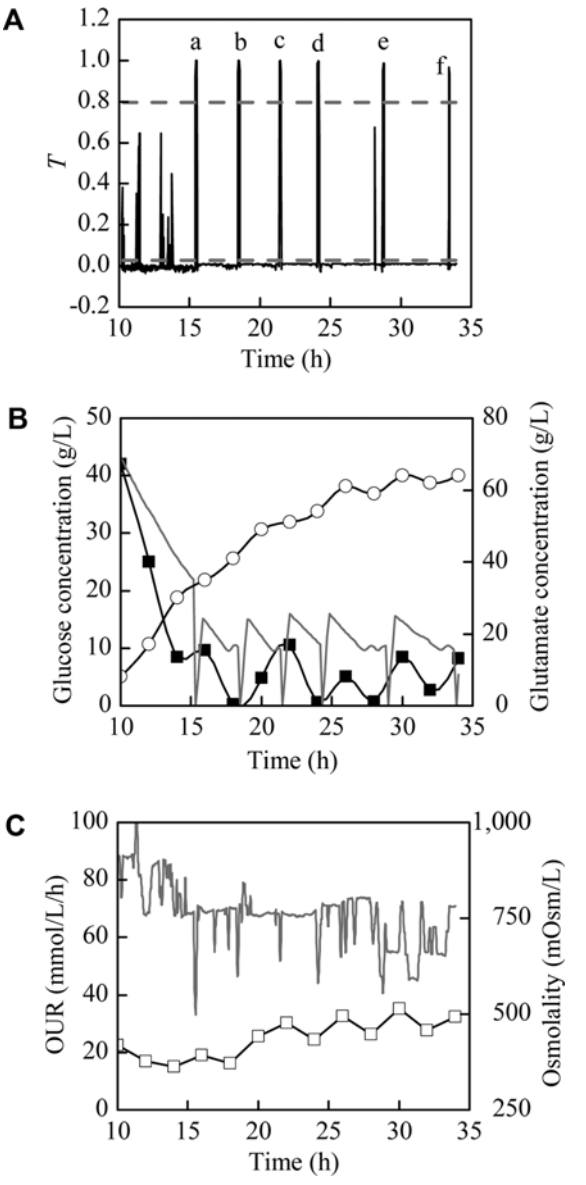

Fig. 8. The result of the pattern recognition system and fermentation performance. A: the result of the pattern recognition system. a ~ f: the points where glucose was depleted. B: variations of the glucose and glutamate concentrations with the adaptive glucose concentration control strategy. Open circles: glutamate concentrations; filled squares: actual glucose concentrations; solid red line: predicted glucose concentration. C: variations of the OUR and osmolality with the adaptive glucose concentration control strategy. Open squares: osmolality; solid red line: OUR.

In glutamate fermentations, process disturbances are unavoidable. For example, addition of antifoam causes DO to fluctuate, *etc*. The three fermentation runs using the proposed control system and setting glucose concentration at different set-points could deal with process perturbations and indicate the robustness of the control system. Although the final glutamate concentration was only equivalent with that of the fermentation run (run #6) using the traditional

feedback control system, the complicated/frequent off-line glucose measurements could be avoided and the automatic glucose feeding in real meaning could be realized.

4. Discussion

Maintaining glucose concentrations at low/stable levels is extremely important for glutamate fermentation. The manually-operated intermittent feed has been the most widely used method for glucose feeding in industrial glutamate fermentation up to date, and the automatic feedback glucose feeding control strategies are seldom applied, because of the unavailability of on-line glucose concentration measurements. On-line predictions of glucose concentration by measuring oxygen or ammonia consumption are the two effective methods, but both of them suffer with the chemical stoichiometric coefficients variations leading to the deteriorated control performance. In the case of glucose concentration prediction based on on-line ammonia consumption amounts measurements but without OUR/CER detections, the faults of "glucose exhaustion" is not easy to recognize, which deteriorate the control performance in turn. In this study, the proposed feedback control system incorporating with ANN model based patterns recognition unit could deal with the state status of "glucose exhaustion" or "glucose over-feeding" by evaluating the ANN output T and then regulate glucose feeding rate adaptively. As a result, glutamate fermentation performance could be significantly improved. We must admit that the final glutamate concentration was only about 60 g/L which is far below the industrial fermentation case (12%, 120 g/L). This is because that we could only use old generation of *C. glutamicum* strain (we hold) instead of the industrially used one. However, as the strains basically have dynamic features, we believe that the proposed control system could be extended/applied in real industrial glutamate fermentations.

5. Conclusion

In this study, a novel adaptive feedback control system incoporating with an ANN based pattern reconition unit was proposed and implemented in glutamate fermentations. This control system could handle the fault status of "glucose exhaustion" and "glucose over-feeding", so that glucose concentrations could be automatically maintained at low/stable levels. As a result, glutamate concentration was 17 ~ 30% higher than that of the traditional fermentations using the intermittent glucose feeding strategy.

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