CONTROL OF MOISTURE CONTENT IN FLUIDIZED BED GRANULATION BY NEURAL NETWORK

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This paper describes a practical method for moisture control in fluidized bed granulation by means of a neural network. Wet granulation of pharmaceutical powder was conducted using an agitation fluidized bed, and moisture content was continuously measured by IR (infrared) moisture sensor. A neural network system for moisture control was developed using moisture content and its changing rate as input variables, and the moisture control characteristics were investigated by the neural network system with a back propagation learning. Good response and stability without overshoot were achieved by adopting the developed systems. This system also maintained favorable stability under various operating conditions.

Introduction

Granulation in a fluidized bed progresses along with complex interactions of several elementary processes, and the mechanism of granulation or the effects of operational variables on granule properties have not been well understood yet. Davis and Gloor (1971, 1972), Rankell *et al.* (1964) and Shinoda *et al.* (1972) have studied the effects of some variables experimentally, while Schoefer and Wörts (1977a, 1977b, 1978) have systematically and quantitatively investigated the effects of process variables in fluidized bed granulation. In these studies, it has commonly been reported that the main factor determining granule properties is the moisture content of granules, thus the granule growth and the product yield are very sensitive to the operational moisture content. Therefore, the effective production of granules with excellent reproducibility requires accurate moisture control. However, the water transfer mechanism and changes in physical properties of the starting powder materials were so complex as to make it difficult to construct a dynamic model for the moisture control system. Most of the operations in the manufacturing process have been controlled by experts' decisions, depending on empirical knowledge gained from past experience.

In this paper, a moisture control system comprised of an IR moisture sensor and a neural network system was developed and its application to a fluidized bed granulation process was described. Moisture control characteristics were investigated using the neural network system with back propagation learning, and the optimum structure was

determined. Performance of the system was investigated in fluidized bed granulation of pharmaceutical powder under various operating conditions.

1. Experimental

1.1 Experimental apparatus

Figure 1 shows a schematic diagram of the experimental apparatus employed. An agitation fluidized bed (NQ-125, Fuji Paudal Co., Ltd.) was used for granulation (Watano *et al.*, 1994, 1995a). This fluidized bed was equipped with an agitator blade

Fig. 1 Schematic diagram of experimental apparatus employed 1: blower, 2: bag filter, 3: spray nozzle, 4: pump, 5: binder liquid, 6: neural network system, 7: IR moisture sensor, 8: motor, 9: agitator blade, 10: air distributor, 11: heater, 12: orifice flow meter

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Table 2 List of powder samples used

Formulation	Lactose	Cornstarch	Crystallinecellulose	Acetaminophen
No. 1	0.210 kg	0.090 kg	—	—
No. 2	0.090 kg	0.210 kg	—	—
No. 3	0.162 kg	0.069 kg	0.069 kg	—
No. 4	0.129 kg	0.042 kg	—	0.129 kg

Table 1 Operating conditions

Fluidizing air velocity	0.6 m·s ⁻¹
Agitator rotational speed	10.0 s ⁻¹
Air temperature	313 K
Binder (water) feed rate	1.5×10 ⁻⁴ kg·s ⁻¹
Spray air pressure	1.5×10 ⁵ Pa

which turned on a center axis at the bottom of the vessel to create a tumbling and compacting motion on the granules. Under the blade, an air distributor composed of three circular plates of different diameters was provided. Heated air for particle fluidization was blown from slits between each plate, creating a circulating flow. Fine powders lifted by the fluidizing air were entrapped by bag filters and brushed down by pulsating jets of air.

Granule moisture content was continuously monitored by an IR moisture sensor (Watano *et al.*, 1994, 1996). This sensor had an optical fiber linking the main body of the sensor with the granulator to improve operating flexibility. A device to prevent powder adhesion by blowing a heated air was also attached to the extremity of the fiber. Based on the correlation between granule surface IR absorption and granule moisture content measured by a drying method, wet basis moisture content was continuously measured during fluidized bed granulation (Watano *et al.*, 1996).

The experimental conditions are summarized in Table 1.

1.2 Powder samples

Table 2 gives the list of powder samples used. Starting materials for granulation were 0.300 kg in weight, consisting of lactose, cornstarch, crystallinecellulose, and acetaminophen, of which the charge weight were shown in the table. Lactose, cornstarch and crystallinecellulose were used as excipient, and acetaminophen was used as an antipyretic analgesic drug which showed sparingly soluble characteristics. 0.015 kg of hydroxypropylcellulose was adopted as a binder, which was mixed as a dry powder into the starting materials before granulation. Purified water was used for the binder liquid, which was sprayed by a binary nozzle located 100 mm above the powder bed (median size of the spray mist was around 40 μm). In this study, formulation No. 1 shown in Table 2 was used in the granulation experiments, except for the

tests which investigated validity of the neural network system.

2. Theory of neural network with back-propagation learning

An artificial neural network is a data processing method which models the data transmission mechanism of neurons (Rumelhart *et al.*, 1986). Generally, the operation of a neuron (neuron unit) is modeled as follows:

$$y = f\left(\sum_{i=1}^n \omega_i x_i - \theta\right) \quad (1)$$

where x_i is an input data into the unit, y is an output from the unit and θ is a threshold value. Here, ω_i is a synaptic weight which shows the strength of the unit connection, and f indicates an activation function. Sigmoid function (Eq. (2)) is used for the activity function, since it is a differentiable algebraic function, of which the differential equation is described as Eq. (3).

$$f(y) = \frac{1}{1 + \exp(-y)} \quad (2)$$

$$f'(y) = f(y)[1 - f(y)] \quad (3)$$

In this study, a hierarchy neural network with a back-propagation learning proposed by Rumelhart *et al.* (1986) was used.

Figure 2 illustrates a hierarchy M-layer neural network. The circles are neurons which are variables taking values ranging from 0 to 1. The data are inputted to the input layer and are outputted from the output layer defined as follows: if $x_i^{(m)}$ is an input data to the i th unit in the m th layer ($m=1, \dots, M$), $y_j^{(m-1)}$ is an output from the j th unit in the $(m-1)$ th layer and $\omega_{ij}^{(m)}$ is a weight between the unit connection, the following relations are valid:

$$x_i^{(m)} = \sum_j \omega_{ij}^{(m)} y_j^{(m-1)} \quad (4)$$

$$y_i^{(m)} = f(x_i^{(m)}) \quad (5)$$

Here, in Fig. 2, a particular unit of $y_0^{(m-1)}$ of which the output was always 1 was used to express the threshold value of i th unit in the m th layer as $-\omega_{i0}^{(m)}$.

Fig. 2 Hierarchy M-layer neural network

Back-propagation is a learning algorithm to update the weight and the threshold value by making the error function (Eq. (6)) minimum.

$$E = \frac{1}{2} \sum_{i=1}^{N_M} (y_i^{(M)} - d_i)^2 \quad (6)$$

In this case, learning is conducted using the following correcting equation to update the weight in steps,

$$\omega_{ij}^{(m)}(s+1) = \omega_{ij}^{(m)}(s) - \eta \frac{\partial E}{\partial \omega_{ij}^{(m)}} \quad (7)$$

where, η is a learning rate determining the speed of learning convergence and s is a learning cycle. In general, convergence speed increases with η , however, too large a η has a tendency to make the learning results unstable.

3. Results and Discussion

3.1 Moisture control by PID control method

Figure 3 shows the performance of moisture control by means of a PID controller, and Fig. 4 illustrates the temporal change in the manipulated variable (output of liquid feed pump). In this experiment, $0 \leq t \leq 900$ s showed the damping process, which was programmed to increase moisture content 1% per minute. The process during $900 \leq t \leq 1800$ s indicated granulation with moisture content maintained at $W=15\%$ for 900 s (fixed command control). This control process aimed to make particle size

Fig. 3 Performance of moisture control by PID controller (Formulation No. 1)

Fig. 4 Temporal change in PID control output (Formulation No. 1)

distribution narrower and to increase product yield. The drying process began from $t=1800$ s. Here, tuning of the PID parameter was based on the method proposed by Ziegler and Nichols (1942) with some correction on the basis of experience, and the control example shown in Fig. 3 was the best tuning result among the investigations ($P=4\%$, $I=75$ s, $D=13$ s). Also, the granulated product, which had about $220\text{ }\mu\text{m}$ of mass median diameter and more than 90% of the yield between 75 and $500\text{ }\mu\text{m}$, was obtained when the granulation was conducted under this conditions.

As can be seen from Fig. 3, an overshoot was observed at the beginning of the fixed command control at $W=15\%$ ($t=900$ s), and moisture change showing fluctuation with a long setting time. The output of the pump shown in Fig. 4 involved repetition of maximum and zero outputs, showing that the system experienced extensive dead time element and time constant, and that the PID control system was not fit to control moisture content in a fluidized bed granulation process, where the controlled variable did not reflect the manipulated variable immediately, due to the lag element. It was also found that the tuning of PID parameters was difficult because the dynamic characteristics of moisture control were very complex.

As previously reported (Shinoda *et al.*, 1972; Watano *et al.*, 1995b), the relation between moisture content and granule median diameter was linear, and granule growth was very sensitive to moisture content during fluidized bed granulation. For example, if moisture control overshoot, granule diameter was finally determined by the overshoot moisture content. In addition, if the control result differed from batch to batch, reproducibility of the granulated product could not be guaranteed. To maintain product quality and guarantee reproducibility, elimination of overshoot and achievement of control stability are very important.

However, it is difficult to obtain sufficient control results because of the complex dynamic characteristics of the moisture control. Especially, in the fixed command control process in which moisture content was kept constant, damping and drying were repeated periodically to maintain constant moisture content, and each process showed different dynamic characteristics; in the damping during moisture fixed command control process, surface moisture content increased rapidly when the binder liquid was sprayed. By contrast, in drying during the control process, surface moisture content did not decrease for a time despite drying, because of the constant drying region, where surface moisture content was maintained due to equilibrium between surface water evaporation speed and water transfer rate from interior to surface. Once the surface moisture content decreased, it was difficult to increase surface moisture content rapidly,

because the interior moisture content was considerably decreased at that time. Due to the different dynamic characteristic, moisture control was very difficult. In addition, dynamic characteristics showed unpredictable changes owing to external conditions such as operating variables and to variations in the physical properties of the starting materials.

Therefore, in constructing a moisture control system, these different dynamic characteristics must be taken into consideration. Conventional techniques, however, cannot adjust to this complicated process. We concluded therefore that it was difficult to expect much more progress in response and stability, whatever tuning was conducted in the PID control system.

3.2 Development of a moisture control system by neural network

Moisture change during granulation has a lag element, and its dynamic characteristics are so complex that it is difficult to construct a model-based system for moisture control. However, if the process characteristics are understood from past experience, application of a neural network (Rumelhart *et al.*, 1986) to the control system is very effective. In this experiment, we tried to remove overshoot and improve control stability and response using a neural network with a back propagation learning.

Figure 5 shows a block diagram of a moisture control system. Deviation $W(t)$, the difference between desired ($W_d(t)$) and measured values ($W_m(t)$) of moisture content, and changing rate of the measured values $\Delta W_m(t)$ were adopted as input variables; they were defined as follows

$$\begin{aligned} W(t) &= W_d(t) - W_m(t) \\ \Delta W_m(t) &= W_m(t) - W_m(t-1) \end{aligned} \quad (8)$$

The result of computing by the neural network system ($V(t)$) was used to control the output power of the liquid feed pump.

Table 3 indicates the normalized learning data, which corresponded to d in Eq. (6). $\pm 1\%$ of moisture deviation from the desired value was divided into five sections, and $\pm 0.05\% \cdot \text{s}^{-1}$ of the moisture changing rate was also divided into five sections to make the learning data normalized. By combining $W(t)$ and $\Delta W_m(t)$, the learning data could be changed in 36 different values (the number in the table showed the optimum pump output used for the learning data). In these learning data, the following procedures were considered.

i) if the measured moisture content approached the desired value very fast ($W(t)$ small and $\Delta W_m(t)$ large), the pump output was regulated in advance to make the damping speed small. This was the means to prevent overshoot considering the lag element.

Fig. 5 Block diagram of moisture control system by neural network

Table 3 Learning data for back propagation learning

	$W(t)$						
	0	0.2	0.4	0.6	0.8	1	
$\Delta W_m(t)$	0	0	0.3	0.4	0.6	0.7	
	0.2	0	0	0.2	0.3	0.5	0.6
	0.4	0	0	0.1	0.2	0.4	0.5
	0.6	0	0	0	0.1	0.3	0.4
	0.8	0	0	0	0	0.2	0.3
	1	0	0	0	0	0.1	0.2

ii) if the moisture deviation ($W(t)$) was large, the pump output was made large regardless of the changing rate of the measured values to promote the control response.

Figure 6 shows a four-layer neural network applied in this study. For the input-layer, two units composed of moisture deviation $W(t)$ and moisture changing rate $\Delta W_m(t)$ were used to describe the lag element in the granulation process as particularly shown in Table 3. The two input variables were processed in parallel in each unit in accordance with Eq. (2). The output-layer had only one unit, which generated the optimum output power of the liquid feed pump, V . Therefore, the input variables $W(t)$ and $\Delta W_m(t)$ corresponded to the input variable x in Eq. (4), and the output power of pump V matched the output valuable y in Eq. (5).

The optimum number of middle-layers and middle-layer units were determined to be two and five, respectively, based on the pre-experimental results; comparing the results obtained by the one middle-layer and the those by the two middle-layers, the errors of the latter were much smaller than the former. In the case of three middle-layers, however, errors over 10,000 learnings were prone to fluctuate. As to the number of middle-layer units, the errors in five middle-layer units were the smallest among the errors obtained by middle-layer units from one to five, and no difference if the number of the units increased over five units was found.

Figure 7 shows an example of error convergence

Fig. 6 Four-layer neural network applied in this study

Fig. 7 Error convergence characteristics

behavior under various learning rates and learning cycles. Seen from the figure, errors were decreased with an increase in the learning rate and each final error after 20,000 learnings was prone to convergence in a constant value. Therefore the optimum learning rate was determined to be $\eta=0.8$ and the learning cycle was 20,000.

3.3 Application of neural network to moisture control

Figures 8 and 9 illustrate the temporal change in

Fig. 8 Performance of moisture control by neural network (Formulation No. 1)

Fig. 9 Temporal change in control output using neural network system (Formulation No. 1)

Fig. 10 Performance of developed neural network system under various powder samples

Fig. 11 Performance of the developed neural network system under various inlet air temperatures

moisture content and the results of neural network computing, respectively. Unlike the PID control experiments, the overshoot at the beginning of the fixed command control near $t=900$ s was fully removed and excellent control stability was achieved

throughout the granulation (Fig. 8). These results were due to the neural network's excellent learning ability of the moisture control characteristics.

It can also be seen from Fig. 9 that the output fluctuations of neural network computing were

considerably smaller than those of PID control. In the PID control, the output fluctuations were large because the controlled variable did not reflect the manipulated variable immediately when the process involved a large lag element. By contrast, the neural network showed small output fluctuation because it generated output taking lag element into consideration as described in Table 3.

3.4 Stability to the change in powder samples and operating conditions

In the manufacturing processes, various granules are produced using various powder samples under various operating conditions. In these cases, tuning of the control parameters is sometimes very difficult because the properties of powder samples and dynamic characteristics in the moisture control markedly vary.

In this contribution, performances of the moisture control by the developed neural network system were investigated under various powder samples and operating conditions.

Figures 10 and 11 indicate performances of the moisture control under various powder samples and inlet air temperatures, respectively. Unlike the PID control method, each experiment of different powder samples and inlet air temperatures has small overshoot and excellent stability. This was due to the excellent learning ability of the moisture control characteristics. It could thus be concluded that the moisture content during fluidized bed granulation could be well controlled by using the developed neural network system with the back propagation learning.

Conclusion

Based on the hierarchy neural network, a system was established for controlling moisture content in fluidized bed granulation. The control characteristics were investigated using a neural network with a back propagation learning, and the optimum structure of the neural network was determined based on the error convergence behavior. Good response and stability without overshoot, impossible to attain with conventional techniques, were achieved by using the control system developed. The validity of the system was confirmed under various powder samples and operating conditions.

Nomenclature

d	= learning data	[—]
E	= error function	[—]
f	= activation function defined by Eq. (6)	[—]
K	= gain of output	[—]

t	= time	[s]
T_{in}	= inlet air temperature	[K]
u	= fluidizing air velocity	[m/s]
$V(t)$	= out put of liquid feed pump	[—]
$W(t)$	= deviation defined by Eq. (8)	[%]
W_d	= desired value of moisture content	[%]
$W_m(t)$	= measured moisture content	[%]
$\Delta W_m(t)$	= moisture changing rate	[%/s]
x	= input data to neuron	[—]
y	= output data to neuron	[—]
ω	= synaptic weight	[—]
η	= learning rate	[—]

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