Scientific Paper

EXPERIMENTAL DESIGN OF CRYSTALLIZATION PROCESSES USING TAGUCHI METHOD

Miran Hvalec, Andreja Goršek, and Peter Glavič

Faculty of Chemistry and Chemical Engineering, University of Maribor, Smetanova 17, Maribor, Slovenia

Received 14-05-2003

Abstract

Crystallization has become one of the most important unit operation in the chemical industries. The need to reduce the time from product discovery to market introduction is an inherent concern. In order to achieve the prescribed product quality characteristics, the process of engineering experimentation has to be optimized. Therefore, an experimental design method for crystallization processes is presented in this paper. Initially, the standardized Taguchi method was used to plan a minimum number of experiments. After identifying the working levels of the design factors and the main performance characteristics of the product under study, the method can be successfully applied to the crystallization processes. The simultaneous variations of the main crystallization parameters and their interactions were investigated using orthogonal array technique. A statistical analysis of 'signal-to-noise' ratio was followed by performing a variance analysis. After developing some special criteria, which depend on performance objectives, the optimal levels of the design factors were determined.

Crystallization of KNO_3 with desirable particle size as a performance characteristic was used to illustrate the design procedure. The effects of rotational frequency of the stirrer, linear cooling rate and added admixture on final particle size were studied. In order to keep the selected parameters constant during the experiment and to ensure reproduction of entire experiment the automated reaction calorimeter RC1 was used.

Key words: Taguchi method, crystallization, particle size

Introduction

Crystallization from solution is a widely used unit operation in the food, pharmaceutical and fine chemicals industries, where high purity crystals with prescribed size, shape and crystal size distribution (CSD) are required. The CSD and the crystal size affect the cost of down-stream unit operations such as filtration and drying. These are often limiting steps in chemical manufacturing processes; therefore, significant cost reduction can be realized by producing the crystal size having favorable filtration and drying properties.

Many papers have been published on crystal size control. Most of them deal with the investigation of temperature cooling profile,[1,2,3] seeding[2] and adding admixtures.[4,5] Usually, to find the influence of controlling parameter on crystal size a large number of experiments are needed. In order to avoid this, two statistical methods can be used to design the optimum number of experiments. Classical design of experiments (DOE) emphasizes prediction of future behavior of experiments from empirical model while running a fraction of full factorial design.[6] However, the classical DOE suffers the following limitations: two designs for the same experiment may yield different results and the designs normally do not permit determination of the contribution of each parameter. Taguchi DOE method, based on the classical one, is standardized design methodology that can easily be applied by investigators. Furthermore, designs for the same experiment by two different investigators will yield similar data and lead to similar conclusions.[7]

Once the crystal size is chosen as the main performance characteristic (the measure of quality), then the design factors, which will have an influence on it, have to be selected. There are no general guidelines for their selection. The choice should be based on the experiences from the previous experiments. Since most crystallization experiments usually involve a significant number of factors, according to the Taguchi method, the number of experiments can be reduced. Using a special orthogonal array only a small set from all the possible ones is selected. The sense of the orthogonal arrays method lies in choosing the level combinations of the design factors for each experiment. Depending upon the specified performance, the optimum will imply that the product has achieved the target value of the quality measure. Therefore, the aim is to attain quality by reducing the variation around the target. During the experiments, crystal size varies from the target value. Determination of the optimal levels of the design variables called factors is based on the assumption that these variations should be as narrow as possible. Thus, knowing the characteristic, i.e., whether a higher or lower value produces the preferred result, the levels of the factors, which are expected to produce the best result, can be predicted. Special criteria depending on the chosen performance characteristic have to be developed in order to identify individual contributions of factors and their interrelationships.

A practical definition of experimental design that can be applied to most crystallization processes is presented in this study. Batch crystallization of KNO_3 from its aqueous solution without seeding was performed on a liter scale under conditions approaching reality. Using the automated lab reactor all the important process variables are measured and controlled. The components of this flexible system are designed so that the results can be scaled up to the plant conditions. Out of different important crystallization parameters the effects of the rotational frequency of the stirrer, cooling rate and added admixture on the crystal size were investigated.

Taguchi approach to parameter design

Taguchi method provides a systematic and efficient approach for conducting experimentation to determine near optimum settings of design parameters for performance and cost. The method pushes quality back to the design stage, seeking to design a product/process, which is insensitive to quality problems. The Taguchi method utilizes orthogonal arrays to study a large number of variables with a small number of experiments.[7] It can reduce research and development cost by simultaneously studying a large number of parameters. Using orthogonal arrays the method can significantly reduce the number of experimental configurations. The conclusions drawn from small scale experiments are valid over the entire experimental region spanned by the control factors and their settings.

In order to analyze the results, the Taguchi method uses a statistical measure of performance called 'signal-to-noise' ratio, (*S*/*N*), where *S* is the standard deviation of the performance parameters for each array experiment and *N* is the total number of experiment in the orthogonal array.[9] After performing the statistical analysis of *S*/*N* ratio, an analysis of variance (ANOVA)[7] needs to be employed for estimating error variance and determining the relative importance of various factors. From their relative importance and from the *S*/*N* ratio, the optimum condition of factors is chosen. The result at this point is estimated using equation:

$$R = \overline{T} + \sum_i (\overline{A}_i - \overline{T}) \quad (1)$$

where $\overline{T}$ is grand average of results and $\overline{A}_i$ is average value of significant factors at level i.

Experimental

Crystallization of potassium nitrate

An automated double walled glass reaction calorimeter – RC1 (Mettler Toledo) with a 2 L working capacity and anchor stirrer was used (Figure 1).

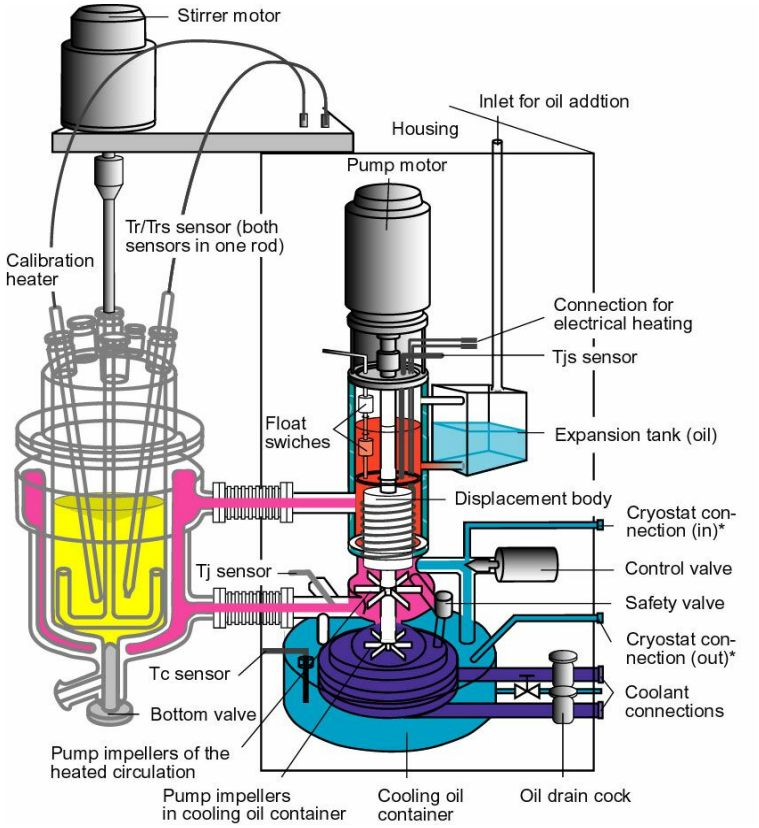

Figure 1. Reaction calorimeter with heat flow balancing.

It comprises a thermostated batch reactor, several peripheral universal controllers with final control elements and a PC. All experimental parameters such as rotational frequency of the stirrer, added amounts of liquid, etc. are measured, controlled and monitored. Thus the maximum flexibility is achieved and the processes can be programmed on the screen, exactly to the details. The determination of process parameters is not the only important feature of the RC1. It can be used to perform and repeat experiment once or several times in the same manner. Due to this reason RC1 was the most appropriate experimental reactor for our study.

A potassium nitrate aqueous solution, saturated at 65 °C, was used as a model solution. The solution was cooled using linear cooling profile from above the saturation temperature to 25 °C. After filtration, the drying process was carried out at 40 °C. The particle size of the dried potassium nitrate was examined by sieving.[8] The ISO 3310/1 standard was adopted with a twentieth root of ten, $\sqrt[20]{10}$, progressions in size of sieves.

Design of experiments

Design of experiments is an approach for systematically varying the controllable input factors and observing the effects of these factors on the output product parameters. The assumption used in our study was that the individual effects of the input factors on the output product parameters are separable. That means the effect of independent variable on the performance parameter does not depend on the different level settings of any other independent variable.

Before conducting the experiment, the knowledge of the product/process under investigation is of prime importance for identifying the factors likely to influence the outcome. In order to compile a comprehensive list of factors, the input to the experiment is generally obtained from the experts involved in the project. The objective of this research was to produce the product with the specific particle size. The linear cooling rate, rotational frequency of the stirrer and added admixture were chosen as the controllable input factors in our case, although other parameters exist having an influence on the desired particle size: seeding, start/seed temperature, end temperature, cooling curve etc. Therefore, an additional research in this area shall be carried out.

Once the independent variables (factors) are decided, the number of levels for each variable has to be selected. The selection of number of levels depends on how the outcome (particle size in our case) is affected due to different level settings. If the outcome is a linear function of the selected factor, then the number of level setting shall be 2. However, if the factor is not linearly related, then one could go for higher levels.

Rotational frequency of the stirrer and linear cooling rate were studied at five levels. Five admixtures, which influence the crystal size, crystal growth and nucleation, were chosen .[4, 5] Factors together with their levels are shown in Table 1. Normally, in the case of three factors with five levels, $5^3 = 125$ experiments should be conducted. In accordance with the Taguchi's method the standard orthogonal array L_{25}, with only 25

experiments (Table 2) could be used.[10] The second, the third and the fifth columns represent different levels of factors, the fourth one is for studying interaction between factors A and B. The sixth and the seventh columns could be used for two more factors, but they remained empty in our case.

Table 1. Factors and their levels.

Factors	Levels				
	1	2	3	4	5
A. Mixing speed/(r/min)	80	100	120	140	160
B. Linear cooling rate/(K/min)	0.1	0.4	0.8	1.5	2.0
C. Admixture added	Water	Methanol	Acetone	HNO_3	Heptane

Table 2. L_{25} orthogonal array.

Experiment No.	Factors [a]				Median particle size/mm	Uniformity grain coefficient
	A	B	A x B	C		
1	1	1	1	1	0.925	1.27
2	1	2	2	2	0.81	1.35
3	1	3	3	3	0.72	1.47
4	1	4	4	4	0.735	1.55
5	1	5	5	5	0.61	2.05
6	2	1	2	3	0.97	1.32
7	2	2	3	4	0.805	1.37
8	2	3	4	5	0.665	1.47
9	2	4	5	1	0.66	1.57
10	2	5	1	2	0.605	2.01
11	3	1	3	5	0.83	1.36
12	3	2	4	1	0.79	1.44
13	3	3	5	2	0.67	1.63
14	3	4	1	3	0.67	1.66
15	3	5	2	4	0.63	2.03
16	4	1	4	2	0.88	1.34
17	4	2	5	3	0.87	1.44
18	4	3	1	4	0.70	1.46
19	4	4	2	5	0.715	1.54
20	4	5	3	1	0.655	2.10
21	5	1	5	4	0.94	1.24
22	5	2	1	5	0.83	1.41
23	5	3	2	1	0.80	1.46
24	5	4	3	2	0.73	1.46
25	5	5	4	3	0.68	1.97

[a] For factors A, B and C, see Table 1.

Analysis of variance

The variance of the median particle size was calculated to identify the most important factors. Equations for conducting the variance are presented in this section. Sum of squares (S_i) of factor i at level k was calculated according to the equation:

$$S_i = \sum_k^L 1/N_k (\sum_j^N Y_j)^2 - (\sum_j^N Y_j)^2 / N \tag{2}$$

where N, is the total number of experiments (25 in our case), N_k the number of levels (5 in our case), and Y_j the median particle size.

The total sum of squares (ST) was calculated using equation:

$$S_T = \sum_j^N Y_j^2 - (\sum_j^N Y_j)^2 / N \tag{3}$$

Experimental error (S_e) was calculated:

$$S_e = S_T - \Sigma S_i \tag{4}$$

Mean square of factor i (V_i) was computed using the following equation:

$$V_i = S_i / f_i \tag{5}$$

where f_i is degree of freedom, which is one less than the number of levels. The total degree of freedom of the result (f_T) is one less than the total number of experiments. The degree of freedom for error variance (f_e) is the total degree of freedom minus sum of degree of freedom of factors. The next step was the calculatation of the variance ratio (F_i), which is the quotient of mean square of factor and error. The fraction of importance of each factor (in percents) was calculated according to the equation:

$$X_i = S_i - (f_i \times V_e \times 100) / S_T \tag{6}$$

The variance ratio, commonly called F statistic (named after Sir Ronal A. Fisher), is the ratio of variance due to the effect of a factor and variance due to the error term. This ratio is used to measure the significance of the factors included in the error term. The F value obtained in the analysis of variance is compared with a value from standard F tables for a given statistical level of significance.[7]

Confidence interval, C.I., of the factor effect and estimated value of the result at the optimum condition was computed using the following equation:

$$\text{C.I.} = \pm \sqrt{F_{1,n_2} \times V_e / N_e} \tag{7}$$

Where F_{1,n_2} is the value from F tables (at the required confidence level and the degree of freedom 1 with an error degree of freedom n_2), V_e is mean square of error term and N_e is a quotient of total number of experiments and degree of freedom of factors included in the estimated result plus one.

Results and discussion

After creating a Taguchi orthogonal array, the selected experiments were performed. The results of sieving analysis were median particle size and uniformity grain ratio (Table 2). Median particle size is the 50% size on the cumulative distribution curve and the uniformity grain ratio is the quotient of the particle sizes at 25% and at 75% of cumulative curve. Uniformity grain ratio indicates the width of the CSD. The smaller the uniformity grain ratio is the narrower the CSD curve is.

A statistic analysis summary of the median particle size, called *S*/*N* ratio, is employed to find the optimum level of the selected factors. By taking the numerical values of the median particle size listed in Table 2, the average value for each level of the three factors can be obtained (Table 3).

Table 3. Average *S*/*N* ratios.

	Levels				
Factors	1	2	3	4	5
A	0.76	0.741	0.718	0.76	0.796
B	0.905	0.821	0.711	0.702	0.636
C	0.746	0.785	0.748	0.746	0.75

The relative magnitude of the effect of different factors can be obtained by decomposition of variance, called ANOVA (Table 4). The second column in Table 4 was calculated using equations (2), (3) and (4), the fourth column with equation (5) and the fifth column was calculated with equation (6). It can be seen from Table 4 that linear cooling rate has a large affect on the median particle size (84.71% fraction of importance), the rotational frequency of the stirrer has just a small one (5.15%). Added admixture and interaction between cooling rate and rotational frequency of the stirrer can be pooled. A new table without these two factors was constructed (Table 5). The

sum of squares of pooled factors was added to the error term. The new mean square of the error term was calculated using equation (8):

$$V_e = \frac{\sum_i S_i^p + S_e}{\sum_i f_i^p + f_e} \tag{8}$$

where superscript p indicates the pooled factors.

Table 4. Analysis of variance.

Factor	Sum of squares	Degrees of freedom	Mean square	Fraction of importance/%
A	0.01648	4	0.00412	5.15
B	0.22881	4	0.05720	84.71
A x B	0.01038	4	0.00065	3.89
C	0.00568	4	0.00142	1.10
Error	0.00550	8	0.00069	5.15
Total	0.26685	24	0.01112	100

Table 5. Analysis of variance with pooled factors.

Factor	Sum of squares	Degrees of freedom	Mean square	Variance ratio	Fraction of importance/%
A	0.01648	4	0.00412	3.06	4.16
B	0.22881	4	0.05720	42.45	83.72
A x B			Pooled		
C			Pooled		
Error	0.02156	16	0.00135	1	12.12
Total	0.26685	24	0.01112		100

Since the degree of freedom of the factor term is 4 and of the error term is 16, from the F tables at 0.05 level of significance (95% confidence) we obtain $F_{4,16}$ = 3.0069. Because the computed values of variance ratio in Table 5 are bigger than the value from F tables, there is 95% of confidence that these two factors have an effect on crystal size. Due to the significant effect of cooling rate on particle size, the optimum conditions were found using this factor. The second criterion for the optimum conditions is uniformity grain ratio.

The best design conditions were determined analyzing the results of the designed experiments. Analysis steps are standardized, but the way of how to apply them for the specific purpose is our goal. Depending on the selected performance parameter special criteria for determination of optimal process conditions have to be found. The single

criterion was assumed, which refers to the nature of the performance objectives "smaller is the best".

In Table 6 optimum levels of the factors A and B for producing some particle sizes are presented. Two different criteria were developed. The optimum level of factor B (linear cooling rate) was chosen with comparison of the desired particle size (first column of Table 6) and the mean of the median particle size (fourth row of Table 3). The level of factor B in Table 3, at which the difference between these two values is the smallest, represents the optimum value.

Table 6. Optimum levels of cooling rate and rotational frequency of the stirrer.

Desired particle size/mm	Optimum level of factor B[a]/(K/min)	Optimum level of factor A/(r/min)	Estimated value/mm	Confidence interval/mm
0.65	2.0	160	0.677	± 0.047
0.70	1.5	160	0.707	
0.75	0.8	160	0.716	
0.80	0.4	80	0.807	

[a] According to Table 3.

In the next step the optimum level of factor A (mixing speed) was determined. The uniformity grain ratios for all experiments carried out at the optimum level of cooling rate (Table 2), were considered. The optimum level of the factor A was chosen on the basis of the second criterion, the width of cumulative distribution curve, which should be as narrow as possible. Its narrowness is presented with uniformity grain ratio. The level of factor A (Table 2) at which the value of uniformity grain ratio is the smallest, is the optimum level of mixing speed. For example, for the desired particle size of 0.65 mm, after establishing 2 K/min as the optimum level of factor B, the optimum level of factor A is 160 r/min.

Estimated values of particle size at optimum conditions, calculated using equation (1), together with the confidence interval are also presented in Table 6.

The necessary final step of the research was verifying the optimal process parameters through the confirmation experiment. It may be concluded that the selected criteria for determining optimal process conditions are adequate for describing the dependence of the crystal size on various parameters.

Using Taguchi method the number of experiments has been reduced from 125 to 25. For performing the complete experiment (the crystallization, the filtration and the sieving analysis) about 8 h was required, therefore the total duration of the research work was approximately 200 h. The time consumed for conducting 125 experiments would be 1000 h.

Conclusions

Once the performance parameter is confirmed and the most important factors, which affect it, are selected, they should be optimized using the Taguchi method. It is a set of general design guidelines, which with some modifications are able to cover many industrial applications including crystallization. With the orthogonal array technique as a part of the Taguchi method the number of experiments together with time and cost for their performance could be reduced. Linear cooling rate was found to be the main factor, which had an influence on the crystal size in our study. The results were obtained after 25 experiments only. An application of automated lab equipment allows us to analyze and predict the crystallization behavior at a scale up to larger volumes.

The procedure described in this study cannot be represented as a general one for all crystallization processes, because it depends on the specific product requirements. Therefore, optimal levels of selected crystallization parameters have to be determined for each process separately.

Acknowledgements

The authors gratefully acknowledge Prof. Valter Doleček from the Faculty of Chemistry and Chemical Engineering, Maribor, for his useful comments and the Ministry of Education, Science and Sport of Slovenia for the financial support (fellowship no. 22595).

References

1. H. A. Mohameed, B. Abu-Jdayil, M. Al Khateeb, *Chem. Eng. Proc.* **2002**, *41*, 297–302.
2. N. Kubota, N. Doki, M. Ito, S. Sasaki, M. Yokota, *J. Chem. Eng. Jpn.* **2002**, *35*, 1078–1082.
3. H. Takiyama, K. Shindo, M. Matsuoka, *J. Chem. Eng. Jpn.* **2002**, *35*, 1072–1077.
4. J. Rolfs, S. Kipp, R. Lacman, *J. Crystal Growth* **1997**, *171*, 183–189.

5. J. Nývlt, J. Ulrich, *Admixtures in Crystalization*, Verlag Chemie, Weinheim (Federal Republic of Germany), 1995, pp 161–163.
6. Box G., W. G. Hunter, *Statistics for Experimenters: an introduction to Design, Data Analysis and Model Building*, John Wiley & Sons, N.Y., 1978, pp 75–100.
7. K. R. Roy, *A Primer on Taguchi Method*, Van Nostrand Reinhold, N. Y., 1990, pp 50–105.
8. A. Terence, *Particle Size Measurement, Volume 1,* fifth edition, Chapman&Hall, London, UK, 1997, pp 156–186.
9. M. S. Phadke, *Quality Engineering Using Robust Design*, Prentince-Hall, London, 1989, pp 87.
10. G. Taguchi, S. Konishi, *Orthogonal Arrays and Linear Graphs*, American Supplier Institute, Inc., UK, 1997.

Povzetek

Kristalizacija predstavlja eno najpomembnejših osnovnih operacij v kemijski industriji. Uvajanje vedno novih produktov na tržišče zahteva hitre in učinkovite raziskave. Predpisano kvaliteto produkta lahko dosežemo z optimiranjem procesov eksperimentiranja. V članku je predstavljena metoda eksperimentalnega načrtovanja procesov kristalizacije. V prvi fazi raziskav je bila za načrtovanje minimalnega števila eksperimentov uporabljena standardizirana Taguchijeva metoda. Z določitvijo nivojev izbranih procesnih parametrov in glavnih značilnosti produkta, je metoda primerna za uporabo na procesih kristalizacije. Tehnika ortogonalnih tabel je omogočila hkratno spreminjanje procesnih parametrov in zasledovanje njihovih medsebojnih vplivov. Izračunu statističnega razmerja S/N je sledila analiza variance. V drugi fazi so bili za določitev optimalnih nivojev proučevanih faktorjev razviti posebni kriteriji, odvisni od zahtevane kvalitete produkta.

Eksperimentalno načrtovanje je bilo izvedeno na primeru KNO_3, pri čemer je velikost kristalnega zrna predstavljala merilo za ocenjevanje kvalitete produkta. V našem primeru so bili proučevani faktorji vrtilna frekvenca mešala, hitrost ohlajanja suspenzije in dodatek različnih topil. Kristalizacija je bila izvedena v avtomatskem laboratorijskem reakcijskem kalorimetru RC1 (Mettler Toledo), ki je omogočal vzdrževanje konstantnih parametrov procesa in zagotovil ponovljivost rezultatov. Izvajanje eksperimentov v visoko avtomatizirani opremi omogoča uporabo rezultatov pri povečavah na večje volumne.