

Determination of the Relative Importance of Process Factors on Particle Size Distribution in Suspension Polymerization Using a Bayesian Experimental Design Technique

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Received 16 January 2006; accepted 2 June 2006

DOI 10.1002/app.24889

Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: The use of a Bayesian experimental design technique to determine the relative importance of factors that control particle size distribution (PSD) in suspension copolymerization of styrene and divinylbenzene is reported. Six factors and two responses are considered in this study. The experimental trials are of the two-level factorial type designed with a Bayesian method. The experiments were carried out in a 5-L pilot plant reactor. The matrix of variances of the parameter means (the prior knowledge) was estimated with the use of a preliminary compartment-mixing (CM) model for PSD in suspension polymerization and our subjective judge-

ment (process understanding). The responses, mean particle size and coefficient of variation, were calculated from distributions obtained with a Coulter particle counter. The results of this study provided the criteria needed to guide the future improvement of our CM-PSD model in a balanced and effective way. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 102: 5577–5586, 2006

Key words: experimental designs; suspension polymerization; particle size distribution; copolymerization; cross-linking

INTRODUCTION

Suspension polymerization is a rather old process that presently is aimed at producing specialty resins. Although many studies on particle size distribution (PSD) in suspension polymerization have been published in the last few decades, the understanding of the influence and importance that the known key factors have on the shape and spread of the PSD is still unclear and incomplete. In the critical review on suspension polymerization presented by our group,¹ we proposed a systematic approach to the study of PSD in suspension polymerization, which was aimed at providing an adequate framework for the development of an effective mathematical model for the

calculation of the PSD. Some of the stages of that approach included the development of an effective model for crosslinking free-radical copolymerization kinetics,² the selection of the polymerization conditions using a mechanistic model-based experimental design technique,³ and the development of a preliminary mathematical model for the PSD using a compartment-mixing (CM) model approach to account for the nonhomogeneous mixing in the tank reactor.⁴ Our original idea of using a CM modeling approach for calculation of the PSD in suspension polymerization, calculating the intensity of mixing for each compartment from rigorous computational fluid dynamics simulations of the actual tank reactor, has also been used by others since then.^{5–8} The homogeneous mixing approach (single CM model) is still used in the context of proposal or evaluation of different variations of the breakage-coalescence models, or evaluation of numerical techniques to solve the population balance equations.^{9–11} An interesting issue not considered in previous modeling studies is the effect of deviations of droplet density and shape on the PSD in suspension polymerization.¹²

In the present article, a Bayesian experimental design technique is used to determine the relative

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Contract grant sponsor: Science and Technology National Council (CONACYT), Mexico.

Contract grant sponsor: Natural Sciences and Engineering Research Council (NSERC), Canada.

TABLE I
Polymerization Conditions and Vessel Dimensions

Parameter	Value
Temperature (°C)	80
[BPO] (mol/L)	0.02
f_{DVB}^0	0.001
[CTA] (mol/L)	Variable (see Tables II, V, and VI)
[PVP] (g/L water)	Variable (see Tables II, V, and VI)
Tank diameter (T) (cm)	15.8
Tank height (H_t) (cm)	28.0
H_2 (cm; length of baffle, defined in Fig. 1)	21.3
Impeller diameter (D) (cm)	Variable (see Tables II, V, and VI)
Z_2 (cm; distance from top lower impeller, defined in Fig. 1)	20.1
Z_1 (cm; = $Z_2 - \text{Sep}$)	Variable (see "Sep" in Tables II, V, and VI). If Sep = 0, only one impeller is being used
Z/T (see Fig. 1 for definition of Z)	1.2
Agitation speed (N) (rps)	Variable (see Tables II, V, and VI)

importance that the different factors of the process have on the PSD. This Bayesian technique was chosen for two main reasons: first, the possibility of easily incorporating the prior knowledge about the process into the design and, second, its flexibility to change the levels of the factors with relative ease. Although the Bayesian design of experiments used in this study is still a factorial type of design, the technique is not restricted to a linear model. A detailed explanation of the technique and a step-by-step illustration of its application to the systematic study of an emulsion terpolymerization system were presented by Dubé et al.¹³

The experimental data obtained from this design were used to calculate the contributions of the main factors and their two- and three-factor interactions on the mean values of mean particle size (MPS) and the coefficient of variation (CV) of the PSD. The knowledge of the relative importance of the factors and their interactions not only indicate how good (or bad) our prior knowledge is, namely how good our preliminary mathematical model is for PSD, but they also provide valuable information as to which aspects of the model are poorly explained. This will serve as a measure of how much greater a degree of complexity is needed about the different phenomena that affect the PSD to improve the mathematical model. This interplay of models, experimentation, and statistical design techniques represents the most systematic approach one can follow to clarify complex processes.

EXPERIMENTAL

Styrene monomer (Aldrich S 497-2, 99% pure), divinylbenzene (DVB) crosslinker (Aldrich 41456-5, technical grade, 80% mixture of isomers), benzoyl peroxide (BPO) initiator (Aldrich 17998-1, 97%), carbon tetrachloride (CTA) (Caledon Laboratories, Ontario, Code 2700-1, 99.9%), and polyvinylpyrrolidone (PVP) stabi-

lizer (Aldrich 85647-9, $M_w = 360,000$) were used as received. Water was filtered and deionized to 0.2 M Ω cm using a Nanopure ion-exchange system.

The polymerization conditions were designed using a kinetic model-based experimental design technique.³ The selected conditions for monomer concentration, crosslinker mole fraction (f_{DVB}^0), initiator concentration, and temperature are listed in Table I. The concentration of CTA was one of the factors studied with the Bayesian experimental design. The lower limit was 0 mol/L, and the upper limit was 0.125 mol/L (of the organic phase). The initial levels for the remaining factors are listed in Table II. As it will be explained later, the levels of some of the factors were changed at different points of the experimental stages.

The experiments were carried out in a 5-L pilot plant reactor. The configuration and dimensions of the vessel are shown in Figure 1 and Table I, respectively. Either one or two 4-bladed 45° pitched bladed turbine impellers were used, depending on the design conditions. For each batch, the PVP in water solution would be prepared a day before the polymerization was carried out. The pH of the PVP solution was adjusted to 8.0 for every batch, except for the first one, by adding a small amount of ammonium hydroxide solution. The reagents were added to the reactor in the following order: PVP solution,

TABLE II
Factors and Their Initial Levels

Factor	Low level	High level
(1) N (rps)	5	9.717
(2) Dispersed phase holdup (φ)	0.37	0.47
(3) [PVP] (g/L water)	2.0	5.0
(4) D (cm)	5.9	9.1
(5) Sep ($Z_2 - Z_1$) (cm)	0 (1 impeller)	8.5 (2 impellers)
(6) [CTA] (mol/L)	0	0.125

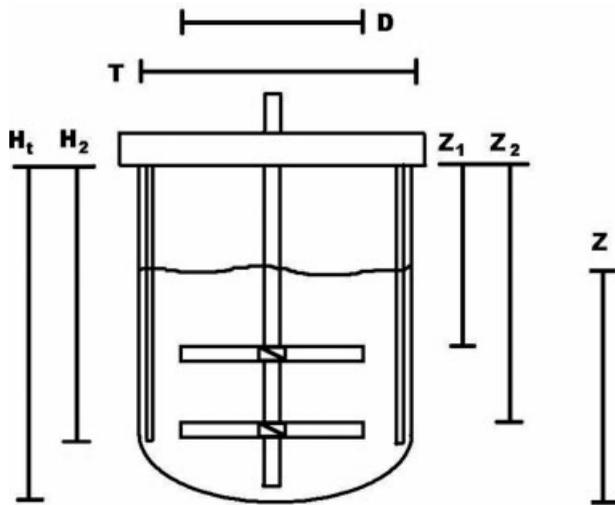


Figure 1 Tank reactor configuration.

styrene monomer, DVB (in 50 mL of styrene), the CTA (if present), and finally the initiator, previously dissolved in 50 mL of styrene. Oxygen was removed from the reactor by repeatedly pressurizing with liquid nitrogen and then drawing a vacuum. This was done thrice. The contents of the reactor were stirred for 15 min at 20°C prior to starting the heating cycle. The reactor was pressurized to 3 bar with nitrogen. The temperature in the reactor was controlled with a West 3300 PID controller.

Once the reactor was discharged, the polymer was washed thrice with methanol (Caledon laboratories Ltd., reagent grade) and rinsed thoroughly with distilled water in a Buchner funnel. It was then transferred to a large flat container and left to dry overnight. A sample of about 3 g was obtained, by taking small portions of polymer from different zones of the flat container.

The PSDs were measured with a Coulter particle counter. A cell with an aperture size of 560 μm was used. Particle sizes lower than 20 μm could not be detected with this cell. The weight fraction of the particles lower than 20 μm was negligible, typically lower than 0.1 wt %. The maximum expected drop diameter was in the order of 400 μm .

BAYESIAN DESIGN OF EXPERIMENTS

Background

Dubé et al.¹³ presented a brief theoretical background on the Bayesian approach to experimentation, which was based on an internal report by Reilly.¹⁴ In this subsection we will include the equations required to use the technique.

The technique requires a model equation for the process response(s) as a function of the factors or

variables under study, and a distribution function, which contains the prior knowledge about the process. In our study, as in Dubé et al.'s study,¹³ we will use a linear regression model and a multivariate normal distribution for the prior knowledge, although a nonlinear model could also be used. The model is then represented by eq. (1), and the prior knowledge by eq. (2).

In eqs. (1)–(6), y is an $n \times 1$ vector of observations, X is an $n \times p$ matrix of the coefficients of the parameters, and θ is the $p \times 1$ vector of parameters (note that the effect is defined as twice the parameter value). A dot superscript (\bullet) denotes the true value of the parameter θ and a "hat" denotes the posterior mean of the parameter θ . ε is the error, I is the identity matrix, σ^2 is the variance of the response(s) (σ being the corresponding standard deviation), α is a $p \times 1$ known vector of the parameter means, U is a positive definite $p \times p$ known matrix of the variances of the parameter means, n is the number of trials, and p is the number of parameters or effects.

$$y = X\theta^\bullet + \varepsilon \quad (1)$$

$$\theta^\bullet : N[\alpha; U] \quad (2)$$

The posterior distribution of θ^\bullet , after application of Bayes' theorem, is given by eq. (3).

$$(\theta^\bullet/y) : N \left\{ \left[U^{-1} + \left(\frac{1}{\sigma^2} \right) X'X \right]^{-1} \left[U^{-1}\alpha + \left(\frac{1}{\sigma^2} \right) X'y \right]; \left[U^{-1} + \left(\frac{1}{\sigma^2} \right) X'X \right] \right\} \quad (3)$$

The "best" set of experiments represents an n -trial fraction of a full factorial experiment. The search for the best set of trials involves maximizing the determinant ("Det") shown in eq. (4).

$$\text{Det} = \left| I + \left(\frac{1}{\sigma^2} \right) XUX' \right| \quad (4)$$

After the completion of a set of experiments (design sequence), the vector of parameter means α and the matrix U of variances of the parameter means are updated using eq. (3) or, more explicitly, eqs. (5) and (6).

$$\hat{\theta} = \left[U^{-1} + \left(\frac{1}{\sigma^2} \right) X'X \right]^{-1} \left[U^{-1}\alpha + \left(\frac{1}{\sigma^2} \right) X'y \right] \quad (5)$$

$$U = \left[U^{-1} + \left(\frac{1}{\sigma^2} \right) X'X \right] \quad (6)$$

Selection of the design factors and levels

Six factors and two responses were considered in this study. The factors were speed of agitation (N), disperse phase hold-up, ϕ (defined as the ratio of volume of the dispersed phase, V_d , to the total volume of the dispersion, V_t), concentration of stabilizer ([PVP]), diameter of the impeller (D), distance of separation between impellers (Sep), and concentration of chain transfer agent ([CTA]). The selected factors are known to heavily influence the PSD in suspension polymerization.¹ The responses were MPS and CV. The selection of these factors and their low and high level values were based on a detailed and critical analysis of the literature (e.g., Vivaldo-Lima et al.¹), combined with some of our previous experience about the process. The initial levels for each factor are listed in Table II.

Incorporation of previous knowledge

The prior knowledge about the process is incorporated into the design through the initial estimates of the vector of parameter means, α , and the matrix of the variances of the means, \mathbf{U} . The initial values of α and \mathbf{U} will depend on the selected response. As mentioned before, we decided to use MPS (measured as mean particle volume) and CV (σ_{vol}/MPS) as the responses.

The prior information about the mean and the various effects was obtained from a mechanistic model-based $2^6 - 1$ conventional fractional factorial design. The 32 trials of the fractional factorial design were simulated with a computer program based on our CM-PSD model.⁴ The CM-PSD model⁴ takes into account the effect of nonhomogeneous mixing in a balanced way, avoiding solving a very rigorous time- and position-dependent description of the flow in the tank reactor, but not oversimplifying the effect of mixing by using an homogeneous mixing ap-

proach. The specific use of a two-compartment mixing approach, which consists of assuming that a single reactor can be modeled as a circuit of two CSTRs interconnected among themselves, is represented graphically in Figure 2. V_i in Figure 2 is the volume of the impeller zone, whereas V_b is the volume of the bulk zone (the remainder of the tank). Figure 3 shows a typical PSD obtained with the CM-PSD model, for a styrene suspension homopolymerization. As observed, there was a significant improvement on the prediction of the PSD by using a two-compartment model, as compared with the homogeneous mixing approach, but the case of the copolymerization with DVB was not sufficiently well captured with that version of the CM-PSD.⁴

Calculated values for MPS and CV were recorded for each one of the 32 trials. The vectors of means of the parameters, α_{MPS} and α_{CV} , were obtained by performing linear regression on the data of MPS and CV calculated with the CM-PSD model. The regression calculations were made using an electronic spreadsheet. The regression analyses provided estimates of the coefficients (means of the parameters), standard error of the mean, and standard error of the coefficients. The calculation of the standard error of the coefficients was possible due to the intentional omission of some of the three-factor interactions during the regression procedure.

Some of the standard error estimates were altered based on our knowledge of the characteristics and assumptions of the CM-PSD model. Since the CM-PSD model had been developed putting emphasis on nonhomogeneous mixing, we felt that the effects of speed of agitation, impeller diameter, and impeller separation (accounted for by the volume of the compartments and the rate of energy dissipation at the impeller zone) on PSD were better explained by the model than the other effects. Therefore, we assumed the magnitudes of the means of these parameters to be equal to 6σ on a normal distribution

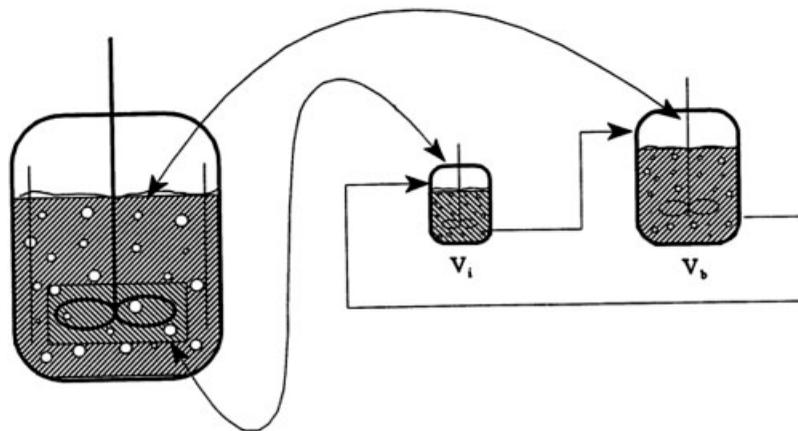


Figure 2 Conceptual representation of the two-compartment model.

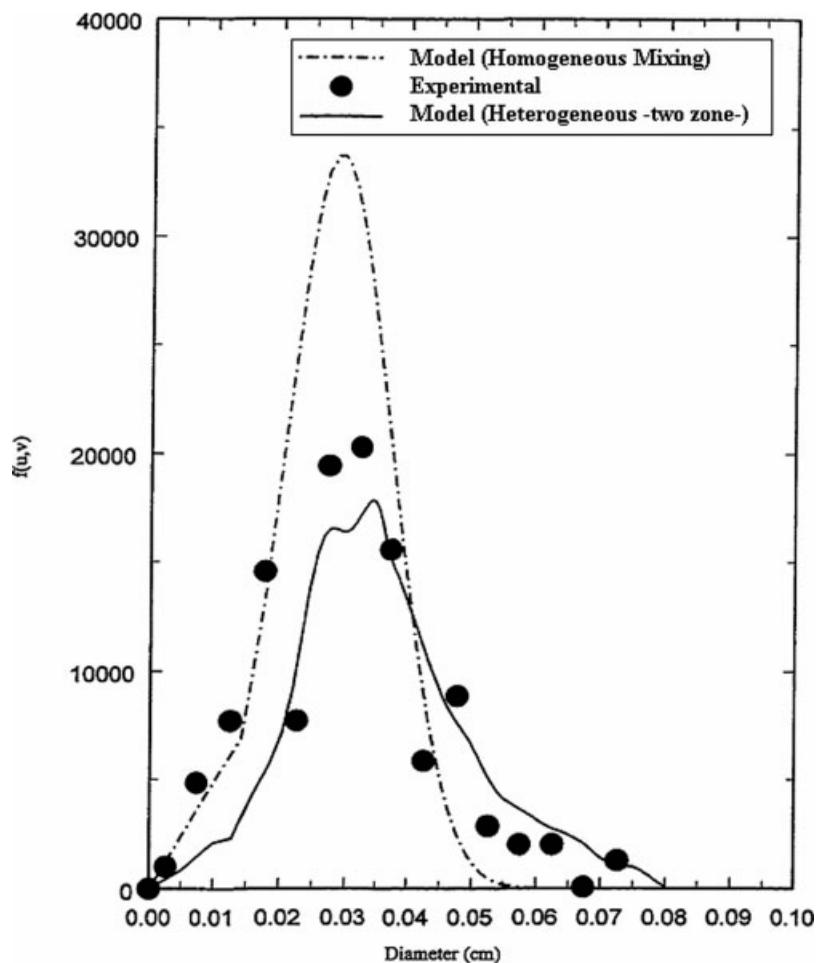


Figure 3 Typical representation of the PSD in suspension polymerization calculated with the single and the two compartment models.

curve. For [PVP] and some of the two factor interactions we assumed the magnitude of the parameters to be equal to 3σ . For the remaining factors and two- and three-factor interactions, we assumed their standard deviations to be the higher than that of the magnitude of the parameter representing 3σ or the standard deviation estimated during the linear regression calculations. Squaring σ gave the diagonal elements of \mathbf{U} ; the off-diagonal elements were initially all set to zero. Table III shows the initial estimates of α and \mathbf{U} for the mean and the main factors for each of the two measured responses.

The error variance of the responses [the variance of ε in eq. (1)] was calculated from a previous set of experiments.⁴ The PSD of seven samples from two different batches at the same polymerization conditions were measured (five samples from one batch and two from the other), and the corresponding MPS and CV values calculated from the experimental data. From these data, the variance for MPS (measuring size in terms of droplet volume) was estimated to be $\sigma_{\text{MPS,Vol}}^2 = 5.26 \times 10^{-4} \text{ cm}^6$, whereas variance for CV was $\sigma_{\text{CV}}^2 = 2.902 \times 10^{-3}$.

RESULTS AND DISCUSSION

It was decided to run a total of eight experiments in two sequences of four experiments each. The reason for running only eight experiments was that we wanted to improve our knowledge about a fairly old process, and we did not expect to uncover striking new phenomena about the process. We just wanted to quantify the relative importance that the already

TABLE III
Elements of Initial α and \mathbf{U} : Mean and Main Effects

Effect	$\alpha_{i,\text{MPS}}$ (10^5 cm^3)	$U_{i,\text{MPS}}$ (10^{10} cm^6)	$\alpha_{i,\text{CV}}$	$U_{i,\text{CV}}$ (10^6)
Mean	3.5	2.958	0.3273	11906.52
N	-2.63	0.192	0.0146	23.73
ϕ	0.124	0.092	0.0057	100.0
[PVP]	-2.27	0.572	0.0161	79.21
D	-1.79 (-0.447)	0.089	0.0096 (0.0024)	79.21
Sep	-1.1	0.034	0.0071	79.21
[CTA]	0.001	0.092	0.0001	100.0

Numbers in brackets for D are explained in the Results and Discussion section.

TABLE IV
First Sequence of 4-trial Experiments (Original Coding)

Run	N	φ	[PVP]	D	Sep	[CTA]
1	-1	1	-1	1	1	1
2	-1	-1	-1	1	-1	-1
3	1	1	-1	1	-1	-1
4	-1	1	1	-1	-1	-1

known key factors have on the characteristics of the PSD. The decision to run two sequences of four trials each, instead of running a single 8-trial sequence, was made because we were not certain that the chosen factor levels were the most adequate (optimal). It should be emphasized that the Bayesian technique allows one to design any number of trials per sequence, and any number of sequences. We chose four trials per sequence in two sequences for convenience. In the following paragraphs, the sequence of chronological events to design and run the two design sequences is documented. This will serve to illustrate some important aspects related to the implementation, flexibility, and interpretation of results with the Bayesian experimental design technique.

As explained in Dubé et al.,¹³ the methodology for selecting an optimal set of experimental trials involves generating several suboptimal designs (>500) and choosing the one with the highest value of "Det" from eq. (4). We varied the number of designs from 500 to 10,000 in each run, and ran the "Bayesian Design" program 20 times for MPS and 15 times for CV. We noticed that the suboptimal designs for CV did not change much the "Det" value (<10% variation), whereas the suboptimal designs for MPS did show significant differences in "Det" (up to an order of magnitude, or even more). We therefore chose the best suboptimal design for MPS (the one which produced the largest "Det" value using eq. (4)) as the one to be executed, which was indeed nearly optimal for CV. The first sequence of four trials that resulted from the previous procedure is shown in Table IV.

The first run of the first design sequence resulted in a suspension set-up (massive agglomeration of the dispersed droplets). After careful analysis of the chronological events for this run, we found some possible explanations for this incident. An undetected nitrogen leak had occurred through one of the feed lines to the reactor. So, it was possible that oxygen was present during the reaction. Another abnormality was that although the pH was measured (pH = 4.5), it was not raised to 8.0, as recommended by Villalobos.¹⁵ It has been demonstrated that lowering the pH of the stabilizer solution increases the coalescence rate.¹⁶ It was also noticed that several of the factors were at levels promoting large beads and possible suspension instability. Namely, the speed of agitation was at its low level, the dispersion phase

hold-up at its high level, and the concentration of stabilizer at its low level. All these conditions favor the formation of large beads, and the possibility of massive agglomeration.

Some changes were made based on the previous analysis. The recipe was modified by adding ammonium hydroxide to control the pH at a value of 8.0. The lower and upper levels for N , φ , and [PVP] were modified. The speed of agitation was increased to assure operation in the turbulent region for the two impeller diameters used in the design, the dispersion phase hold-up was decreased to reduce the risk of agglomeration, and the stabilizer concentration was increased to promote better suspension stability. The new levels of these factors are listed in Table V. Since the differences between the upper and lower levels were not altered, it was not necessary to update the values of the means of the parameters and their variances at this point and, therefore, it was not necessary to generate a new design for this sequence.

The four trials of the first design sequence were carried out in the pilot plant reactor described previously. Runs 1, 2, and 3 did not show any problem. In all three cases, well-formed, white beads of small (latex size) and medium size (<300 μm) particles were obtained. Run 4, however, behaved differently. Although the samples taken from the reactor at different times of reaction for run 4 showed that the particles were small (latex size and beads no larger than 100 μm), when the reactor was opened, it was noticed that a partial set-up had occurred. What happened was very interesting. Run 4 had been produced using the upper level of stabilizer concentration, but low speed of agitation, and a single impeller with a small diameter. The impeller was positioned in the lower third section of the reactor (see Z_2 in Fig. 1). As observed in Figure 4 (a photograph of the shaft and the impeller after the reactor was opened), a cone-shaped "block" of polymer was attached to the shaft of the impeller. Medium size (mostly smaller than 1 mm in diameter) and small size (polymer latex in the order of microns) beads were formed at the bottom of the reactor. What this photograph shows is that there were at least three populations of polymer particles. The populations with the medium and small particle sizes had been formed in

TABLE V
Factors and Their Updated Levels After First Run

Factor	Low level	High level
(1) N (rps)	10	14.717
(2) φ	0.27	0.37
(3) [PVP] (g/L water)	3.5	6.5
(4) D (cm)	5.9	9.1
(5) Sep ($Z_2 - Z_1$) (cm)	0 (1 impeller)	8.5 (2 impellers)
(6) [CTA] (mol/L)	0	0.125



Figure 4 "Single bead" obtained at the poor mixing zone in Run 4. At least two other populations of medium and small sizes were obtained in the lower half of the tank reactor.

the lower third of the reactor, in the surroundings of the impeller, and the single, large cone-like "bead" had been obtained in the upper section of the reactor. The small section of the cone started right at the impeller position in the shaft, and it increased in diameter up to almost the reactor diameter at the top of the suspension volume, as we moved further away from the impeller. This photograph is an indication that the CM approach for modeling of the PSD in suspension polymerization⁴ can be considered as a realistic approach. The CM modeling approach divides the tank into two or more regions of different intensities of mixing. The fact that latex size particles are also obtained when the concentration of stabilizer is high could be considered as an indication that the mechanism of satellite daughter drop distribution breakage mechanism of Chatzi and Kiparissides^{17,18} is also a plausible mechanism for bimodal PSD formation under these conditions.

On the basis of the partial suspension set-up result obtained in run 4, likely caused by the poor mixing under those conditions, we decided to change the lower level of the impeller diameter. Therefore, two new impellers of 8.2 cm in diameter were built. The final levels used in this study are listed in Table VI. This change in diameter modified the difference between the upper and lower levels for this factor. It was therefore necessary to recalculate the means for this parameter (elements α_4 and all the α_{4i} or α_{i4} of the α_{MPS} and α_{CV} vectors) and all its interactions to design the second 4-trial sequence and calculate the updated α_{MPS} and α_{CV} vectors. The new values for this parameter are shown in brackets in Table III. The means for the two- and three-factor interactions that contain fac-

TABLE VI
Factors and Their Updated Levels After First Design Sequence

Factor	Low level	High level
(1) N (rps)	10	14.717
(2) ϕ	0.27	0.37
(3) [PVP] (g/L water)	3.5	6.5
(4) D (cm)	8.3	9.1
(5) Sep ($Z_2 - Z_1$) (cm)	0 (1 impeller)	8.5 (2 impellers)
(6) [CTA] (mol/L)	0	0.125

tor 4 (impeller diameter) are not shown (the variation was negligible) in the tables of this paper, but were also recalculated.

To determine the second 4-trial design sequence we needed the "posterior" variance matrix, \mathbf{U} , of the first design sequence. The "posterior" \mathbf{U} of the first design would become the "prior" \mathbf{U} for the second design. Since the values of the means for parameter 4 and its interactions had been changed, it was necessary to recalculate the posterior \mathbf{U} of the first design. To do so, eq. (6) was used. The prior \mathbf{U} in this calculation was the original matrix of variances used when the first sequence was designed, and matrix \mathbf{X} was the matrix of coefficients of the parameters in terms of the revised coding system (the values of -1 and $+1$ in the \mathbf{X} matrix are defined by the lower and upper levels of the parameters, shown in Table VI). Table VII shows the first 6 columns of the \mathbf{X} matrix in terms of the revised coding system. The remaining columns are formed by taking the corresponding products indicated by the interactions. For instance, the column of elements for the $N \times \phi$ interaction is obtained by multiplying the elements of the column associated to N times the corresponding elements of the column associated to ϕ .

With the corrected "prior" \mathbf{U} (calculated in terms of the revised coding), the second 4-trial sequence was designed. The Bayesian design computer program was executed 17 times for MPS and 7 times for CV. Once again it was observed that the suboptimal designs for CV were equally good, and the best design for MPS was also nearly optimal for CV. The conditions for the second design sequence are shown in Table VIII.

Before running the second 4-trial sequence, we decided to calculate the updated vectors of means of the parameters, α_{MPS} and α_{CV} , based on the results

TABLE VII
Modified First 4-trial Design (Revised Coding)

Run	N	ϕ	[PVP]	D	Sep	[CTA]
1	-1	1	-1	1	1	1
2	-1	-1	-1	1	-1	-1
3	1	1	-1	1	-1	-1
4	-1	1	1	-3.5	-1	-1

TABLE VIII
Second (Final) Sequence of 4-trial Experiments
(Revised Coding)

Run	N	ϕ	[PVP]	D	Sep	[CTA]
5	-1	-1	-1	-1	1	1
6	1	-1	1	-1	-1	-1
7	1	-1	-1	-1	-1	-1
8	1	1	-1	1	1	1

from the first 4-trial sequence, using eq. (5). The initial and updated values of the main and two-factor interaction elements of the vectors α_{MPS} and α_{CV} are listed in the second and third columns of Tables IX and X, respectively. These vectors are called θ_{MPS} and θ_{CV} once updated. It is observed that the mean MPS and mean CV values are underestimated by the CM-PSD model. However, the estimated relative contributions to the mean of each effect do not change significantly for MPS, and the change is moderate for CV.

In a preliminary (screening) stage of our systematic study on suspension polymerization, we had measured the PSD of three batches at the conditions described in Table XI (two repeats at conditions of run "a" and one at conditions of run "b"). Runs "a" (two batches at the same conditions) were used to estimate the MPS and CV variances, and run b was the result of an earlier training session. To decide if it was worth running the second 4-trial sequence, namely, if running the second sequence would provide substantial additional information, we decided to update once more the vector of means of the

effects using the experimental data from runs a and b, and carry out a full analysis. The experimental data of MPS and CV for runs a, b, and 1–4 are listed in Table XII.

Tables IX and X show the results for MPS and CV, respectively. The second column shows the initial values of the means of the parameters (mean, main factors and two-factor interactions), and the third column shows the updated values of the means of the parameters after the first design sequence was completed. Column 4 shows the newly updated values with the results from runs "a" and "b" as well. To quantify the relative importance of the parameters and their interactions, as well as the adequacy of the model used to generate the "prior knowledge," we carried out a series of statistical tests (columns 5–7 in Tables IX and X).

Test 1 is defined as the ratio of the prior means to the prior standard deviations of the means [$\alpha_i/(U_i)^{1/2}$] and tests the null hypothesis that $\alpha_i = 0$ purely in the opinion of the "expert" (the person who assigned the values for the prior effects and variances). It is a measure of the uncertainty of the "expert." A value greater than 2 or less than -2 is considered significant (this is equivalent to a 95.44% confidence interval). Test 2 is a measure of the actual significance of an effect. It is equal to the last updated estimate of the effect, divided by the square root of the diagonal element of the last posterior variance/covariance matrix. Once again, a value greater than 2 or less than -2 implies significance. Finally, test 3 is equal to $(\theta_i - \alpha_i)$ divided by the square root of the diagonal element of the last posterior var-

TABLE IX
Results for Main Effects and Two-Factor Interactions for MPS

Effect	α_i (10^5 cm ³)	θ_{i1} (10^5 cm ³)	θ_{i2} (10^5 cm ³)	Test 1	Test 2	Test 3
Mean	3.5	4.5076	4.548	2.035	11.47	2.643
N	-2.63	-2.8169	-2.797	-6.0	-9.87	-0.589
ϕ	0.124	0.2127	0.2159	0.408	0.814	0.346
[PVP]	-2.27	-1.5556	-1.52	-3.0	-3.93	1.939
D	-0.4475	-0.7042	-0.7019	-1.5	-2.77	-1.004
Sep	-1.11	-1.1099	-1.1048	-6.0	-6.51	0.0306
[CTA]	0.001	0.001	0.0003	0.01	0.003	-0.007
$N \times \phi$	-0.101	-0.2481	-0.2404	-0.332	-1.0	-0.5799
$N \times$ [PVP]	1.69	1.4947	1.5086	3.0	4.63	-0.5567
$N \times D$	1.2	1.3025	1.3067	5.625	7.07	0.5773
$N \times$ Sep	0.76	0.7701	0.773	6.0	6.45	0.1085
$N \times$ [CTA]	0.001	0.0073	0.0069	0.01	0.07	0.0598
$\phi \times$ [PVP]	-0.206	-0.1479	-0.1441	-0.677	-0.559	0.2401
$\phi \times D$	0.0757	-0.1336	-0.1294	0.249	-0.541	-0.5645
$\phi \times$ Sep	0.0172	-0.0397	-0.0281	0.056	-0.1082	-0.1744
$\phi \times$ [CTA]	0.001	-0.0051	-0.0061	0.01	-0.062	0.0722
[PVP] $\times D$	0.8822	0.6877	0.695	2.81	2.69	-0.7246
[PVP] \times Sep	0.495	0.4516	0.45	3.0	2.944	-0.2944
[PVP] \times [CTA]	0.001	-0.0149	-0.0155	0.01	-0.1592	-0.1695
$D \times$ Sep	-0.148	-0.1457	-0.1457	-5.62	-5.547	0.0876
$D \times$ [CTA]	0.0937	0.094	0.094	9.37	9.405	0.03
Sep \times [CTA]	0.001	0.001	0.001	0.1	0.1	0.0

TABLE X
Results for Main Effects and Two-Factor Interactions for CV

Effect	α_i (10^3 cm^3)	θ_{i1} (10^3 cm^3)	θ_{i2} (10^3 cm^3)	Test 1	Test 2	Test 3
Mean	327.35	749.3739	911.3834	3.0	37.66	24.133
N	14.61	13.3483	14.7475	3.0	3.077	0.0287
ϕ	5.74	17.9043	27.262	0.574	2.8505	2.2503
[PVP]	16.07	23.4917	34.4836	1.806	3.99	2.1306
D	2.4	-15.5539	-7.7534	0.2697	-0.9573	-1.2536
Sep	7.17	7.9974	26.2012	0.8056	3.102	2.2531
[CTA]	1.0	2.0395	7.0683	0.1	0.7498	0.6437
$N \times \phi$	11.87	0.8152	-0.849	1.334	-0.101	-1.513
$N \times$ [PVP]	13.63	12.0669	11.1517	3.0	2.4786	-0.551
$N \times D$	12.7	16.9464	16.4194	2.816	3.7438	0.8481
$N \times$ Sep	-0.85	-0.6176	0.1727	-0.17	0.0352	0.2084
$N \times$ [CTA]	0.1	0.1749	-1.3042	0.0316	-0.4146	-0.4464
$\phi \times$ [PVP]	4.54	5.1316	9.7891	0.51	1.1396	0.6111
$\phi \times D$	6.11	-5.022	9.1131	0.6865	1.1324	0.3732
$\phi \times$ Sep	15.61	8.0298	23.014	1.561	2.4457	0.7868
$\phi \times$ [CTA]	0.1	-0.6578	-0.9546	0.0316	-0.304	-0.3358
[PVP] $\times D$	7.36	6.2052	7.7371	2.812	2.968	0.1415
[PVP] \times Sep	7.67	6.7576	6.798	3.0	2.666	-0.342
[PVP] \times [CTA]	0.1	-1.2951	-1.2334	0.0316	-0.3919	-0.4237
$D \times$ Sep	9.19	12.1025	13.65	2.812	4.233	1.3831
$D \times$ [CTA]	0.09	2.8188	2.4729	0.0285	0.7927	0.7638
Sep \times [CTA]	0.1	0.4545	-1.2047	0.0316	-0.3828	-0.4146

iance/covariance matrix. Test 3 is a measure of the quality of the expert's opinion. A significant value ($>|2|$) for test 3 implies that the portion(s) of the mechanistic model (the CM-PSD model in our case) related to the response and the effect in question may need refinement. As explained in Dubé et al.,¹³ caution should be exercised in the interpretation of this test, since correlation and nonlinearity in the model equations could also cause the results of test 3 to become significant.

The results from test 1 for MPS (Table IX) indicate that in the "expert's opinion" (the predictions from the CM-PSD model), the factors and interactions that control the MPS are $D \times$ [CTA], N , Sep, $N \times$ Sep, $N \times D$, $D \times$ Sep, [PVP], $N \times$ [PVP], [PVP] \times Sep, and [PVP] $\times D$, in that order of importance. Although not shown, the three-factor interactions showed no significance at all in either of tests 1 and 2. The results from test 2 confirm that the expert's opinion was correct in most instances (the order of importance changes somewhat, though). It is important to note that the factors (either pure or interactions) that have a major quantitative effect on the MPS are mostly related to the mixing environment in the tank (D , N , and Sep). The results from test 3 show that

the CM-PSD model is adequate for MPS. The only effect which showed a value close (but still lower) to the decision criterion of test 3 was [PVP].

In the case of CV, the situation was rather different. The results from test 2 show that the factors and interactions that control the spread of the distribution are, in order of importance: $D \times$ Sep, [PVP], $N \times D$, Sep, N , [PVP] $\times D$, ϕ , [PVP] \times Sep, $N \times$ [PVP], and $\phi \times$ Sep. In this case there is a more balanced weight on the importance of effects. The effects of stabilizer, mixing, and dispersion concentration are equally significant on the spread of the PSD. The fact that most of the mean values of the effects and their interactions are positive is an indication that broad PSDs are inherent to suspension polymerization processes. The results of test 3 suggest that the CM-PSD model needs improvement. The effects of ϕ , [PVP], and Sep on CV are not sufficiently well captured by our CM-PSD model in its present form. Any attempt to improve this model should pay special attention to these factors.

TABLE XI
Conditions for Preliminary (Screening) Experimental Data (Revised Coding)

Run	N	ϕ	[PVP]	D	Sep	[CTA]
a	-1.12	1	0	1	1	1
b	1	1	0	1	1	-1

TABLE XII
Experimental Data for First Sequence and Preliminary (Screening) Runs

Run	MPS (10^5 cm^3)	CV
1	0.085	0.4761
2	0.0607	0.2442
3	0.00825	0.3632
4	5.0	0.8
a	0.0257	0.5355
b	0.1044	0.4873

Given the fact that the second 4-trial sequence was designed based on MPS as the response (the information content about CV from different additional 4-trial combinations was not expected to improve significantly, as explained before), and considering that the analysis on MPS showed that the CM-PSD model (the source of "prior knowledge") was already effective enough to explain the importance of factors on MPS, we decided not to run the second 4-trial sequence. With the information gathered from the first sequence and the additional experimental data that we had available, we managed to successfully achieve our objectives. We were able to determine the relative importance of the factors that control the PSD, and also identify which aspects of the CM-PSD model need improvement.

If more experiments were to be designed, it would be better to use a mechanistic model-based experimental design technique with an improved version of our CM-PSD model. We have used this experimental design technique before, when our copolymerization kinetic model was validated.³ An alternate way to generate a more effective design is to use an improved version of the CM-PSD model to replace eq. (1) of this paper, and still use a Bayesian approach (but based on a nonlinear model).

CONCLUDING REMARKS

A Bayesian experimental design technique whose prior knowledge was generated with a preliminary CM-PSD model was successfully used to determine the relative importance of the factors that control the PSD in suspension copolymerization of styrene and DVB. The combination of the mechanistic nature of the CM-PSD model, the versatility of the Bayesian technique, and our engineering judgement, allowed us to obtain valuable information about the effect of six factors on two responses of the PSD with only six experiments.

It was corroborated that the effect of mixing on the PSD is more important than most researchers do modeling in this area realize. The photograph shown in this paper seems to indicate that different mixing zones are present in the vessel, and that each zone promotes the formation of different particle size populations. Therefore, it seems to be inadequate to assume that the intensity of mixing is homogeneously distributed in the tank reactor, as most models in the literature for PSD in suspension polymerization assume.

The MPS of the PSD seems to be heavily influenced by the mixing parameters (N , D , and Sep). The spread of the distribution (CV), on the other hand, is equally affected by interfacial ([PVP]), mix-

ing (N , D , and Sep) and dispersion (ϕ) parameters. The effects of ϕ , [PVP] and Sep on CV are not sufficiently well explained by the CM-PSD model in its present state. Further efforts to improve the PSD model will have to put emphasis on these factors. This means that the degree of sophistication about polymerization kinetics and mixing in our present CM-PSD model is adequate and that more sound theoretical models that explain the effects of the stabilizer and the dispersion concentration (dispersed phase hold-up) on the spread of the distribution are needed.

The assistance of Professor Harald Stöver and Ms. Wen-Hui Li (Chemistry Dept., McMaster University) with the PSD measurements is greatly appreciated. Also, many thanks go to Loui Polic for providing the FORTRAN code of the computer program for the Bayesian design. E. Vivaldo-Lima acknowledges the financial support from DGAPA-UNAM (PASPA Program) and the Department of Chemical Engineering of the University of Waterloo for his research stay at the Institute of Polymer Research of the University of Waterloo.

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