

# ONLINE OPTIMIZATION OF A TOP-SPRAY FLUIDIZED BED GRANULATION PROCESS BASED ON A THREE-STAGE POPULATION BALANCE MODEL

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## *Abstract*

A multi-scale three-stage population balance model (TSPBM) was developed in combination with the multivariate projection models to obtain the unknown kernel constants in population balance model (PBM), considering the batch and multi-stage characteristics of the top-spray fluidized bed granulation process. Partial least square (PLS) regression is adopted as the particle-scale modeling method in this work to describe the relationship between the manipulated operating variables and kernel constants used in PBM. Population balance model works as process-scale model describing the evolution of granule size distribution (GSD) according to kernel constants. By developing the relationship between the GSD and the manipulated operating variables, the developed multi-scale TSPBM is firstly established as a prerequisite for optimization strategy design. An online optimization strategy is proposed to improve the granule quality of top-spray fluidized bed granulation and to reduce the mismatch between the developed model and the actual system. By adjusting the granule growth trajectory on predefined sample intervals, the new optimal operating variables of pulse frequency, binder spray rate and atomization pressure are determined to ensure the granule size not deviating from desired trajectory. A differential evolution (DE) algorithm is used to solve the problem for online optimization problem and adjust the granulation operating variables. Experimental results and simulation tests are carried out to validate the effectiveness of the proposed TSPBM and the online optimization strategy. The developed TSPBM can accurately predict experimental GSD, which is carried out at randomly selected operating conditions. The proposed online optimization strategy can improve more than 50% prediction capability comparing with the offline optimization method.

## *Keywords*

Three-stage population balance model, Top-spray fluidized bed granulation, Online optimization strategy, Particle size distribution.

## **1. Introduction**

Wet granulation is a process of enlarging solid particles to get granular product with specific size and certain properties such as flowability, dissolution rate, granule strength and bulk density (Liu et al. 2013; Liu et al. 2016). It is an important powder processing technique in

many industries including foods, pharmaceuticals and fertilizers. Among the granulation methods, fluidized bed spray granulation is more popular by combining the traditional mixing, granulating and drying processes together into the same equipment, and therefore produces

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good quality products improving production efficiency. During top-spray fluidized bed granulation, binder liquid is sprayed in form of droplet by a spraying nozzle onto particles bed fluidized by fluidizing air and upon wetting, the particles will be bounded together by liquid bridges to form granules (Tan et al. 2006).

Top-spray fluidized bed granulation is a complex process, which is not only influenced by the original material composition and properties, but also by the operating conditions, such as pulse frequency, binder spray rate and atomization pressure, fluidizing air temperature (Liu et al. 2014(a); Liu et al. 2014(b)). The size distribution is one of the most important properties for granules. In order to obtain granules with specific mean size and size distribution, it is necessary for a top-spray fluidized bed granulation process to work under optimal operating conditions for given material composition and properties. However, the GSD during a granulation process is difficult to be measured online, which causes difficulty in optimally controlling the granule size by changing the operating conditions.

Prediction models based on manipulated operating variables have been widely used in optimization and control of various industrial processes, especially when the quality attributes are difficult to measure (Nagy 2007), while few attempts have been made to optimize fluidized bed granulation process based on process model. This is mainly due to the lack of accurate granulation process model that could be used for process optimization. Although extensive work has been done to understand the granulation process (Iveson et al. 2001; Walker et al. 2006), few direct relationships was found between the operating variables and the granule critical quality attributes (CQAs).

Due to complexity of the top-spray fluidized bed granulation, it is quite difficult to get a pure first principle model that accurately reflects the relationship between the operating variables and the GSD. Considering the multi-stage characteristic of the batch top-spray fluidized bed granulation process, the multi-scale modeling method, which combines the first principle model with partial least square (PLS) regression modeling techniques, is introduced for model development of the granulation process in this work. A multi-scale three-stage population balance model (TSPBM) is established to accurately describe GSD evolution on each stage of the granulation process. Population balance model is used as the process-scale model which models of the basic nature of the granulation process, while the PLS regression model works as particle-scale model to describe the influence that the operating variables have on the unknown granulation kinetics of the PBMs. Among the PLS regression models, a nonlinear multivariate quadratic polynomial is adopted (Liu et al. 2014(a)).

In this paper, a multi-scale TSPBM model is developed to describe the GSD evolution of each stage of the top-spray fluidized bed granulation process. Based on the developed model, an online optimization strategy is

proposed to improve the granule size distribution prediction of top-spray fluidized bed granulation, which utilized an improved differential evolution (DE) algorithm to solve the optimization problem. Experimental results and simulation tests illustrate the effectiveness of both the multi-scale TSPBM and the proposed online optimization strategy.

The remaining parts of this paper are organized as follows: Section 2 introduces the experimental work. Section 3 builds the multi-scale TSPBM for a top-spray fluidized bed granulation process. Section 4 proposes an online optimization strategy based on the multi-scale TSPBM. Section 5 concludes the work.

## 2. Experimental data

The main part of experimental data used for the multi-scale TSPBM development could be found from our previous work (Liu et al. 2013).

A lab-scale batch top-spray fluidized bed granulator (MP-MicroTM, GEA Process Engineering Ltd, UK) was used to carry out the granulation experiment. The microcrystalline cellulose (MCC) was used in the experiment with all the primary particles having diameter from 150 to 180  $\mu\text{m}$  obtained by sieving the original materials (Gamble et al. 2011). The binder material is Hydroxypropyl methylcellulose (HPMC), which is dissolved into ionized water to make 6% w/w binder liquid. Formulation for each granulation experiment is 46.5 g of MCC and 3.5 g of dry binder HPMC. Details of the experimental setup can be found in the same paper (Liu et al. 2013). In summary, in total 15 experiments were carried out to investigate three operating variables of pulsed frequency, binder spray rate and atomization pressure. The pulsed frequency was defined as the ratio of the pulsed and spraying time in a spray cycle which was constant as 2 minutes in the experiments. The range of pulsed frequency from 0 to 1 was investigated. The ranges of binder spray rate and atomization pressure were 0.9–1.5 g/min and 10–20 psi, respectively. In order to keep the same level of fluidization during granulation, the inlet fluidizing air velocity was adjusted manually in real time from 0.6 m<sup>3</sup>/h to 2 m<sup>3</sup>/h in each experiment. For each experiment, samples were taken at three different points of 30%, 70%, and 100% of the total amount of binder liquid sprayed for particle size distribution analysis by sieving method. Further two experiments had been carried for the model validation.

## 3. Three-stage PBM of top-spray fluidized bed granulation

### 3.1 Multi-scale modelling

According to the granule mechanisms occurred on different time period, the top-spray fluidized bed granulation process could be divided into multiple stages. In this work, by preliminary experimental investigation of mean granule size evolution, the top-spray fluidized bed granulation process is divided into three stages with time

percentage and granulation mechanisms as follows: Stage I (first 30% of experiment time) – layering growth and aggregation, Stage II (middle 40% of experiment time) – aggregation, and Stage III (last 30% of experiment time) – aggregation and breakage. On each stage, a population balance model is used to describe evolution of granule size distribution based on their respective granulation mechanisms with the kernel constants. The values of these kernel constants are affected by the operating conditions of the granulation process and once the operating conditions are fixed then the kernel constants values used in PBM of each stage are fixed. Therefore, a relationship should be developed between these undetermined kernel constants and the manipulated operating variables. It is quite difficult to build the relationship simply by mechanistic analysis and deduction. Therefore, PLS regression method is considered to model the relationship between the kernel constants and the manipulated operating variables during the top-spray fluidized bed granulation process based on the experimental data. Diagram of modelling approach of multi-scale TSPBM is presented in Fig. 1, which includes three main steps. The first step is to determine the PLS regression model and to determine the aggregation/breakage kernels used in PBM. Subsequently, parameter estimation was carried out using the PBM based on experimental granule size distribution at time of 30%, 70% and 100% binder sprayed to calculate the kernel constants in PBM of each stage for each experiment. The differential evolution (DE) algorithm is adopted in the parameter estimation. Finally, the parameters of PLS regression model of each stage is fitted based on kernel constants calculated from step II. So far, a multi-scale model with combination of the PLS regression model and population balance model is developed for each stage of the granulation process forecasting the GSD of the granulated product with input of operating variables.

### 3.2 Population balance model

The most widely used population balance equations in granulation system was established by (Hounslow et al. 1988), which could be used to describe changing rates of the GSD density functions, shown as:

Stage I

$$\begin{aligned} \frac{\partial n(t,l)}{\partial t} = & -\frac{\partial(G(t,L)n(t,l))}{\partial L} + \frac{1}{2} \int_0^l \frac{\beta\left(t,(l^3-\mu^3)^{\frac{1}{3}},\mu\right)n\left(t,(l^3-\mu^3)^{\frac{1}{3}}\right)n(t,\mu)}{(l^3-\mu^3)^{\frac{2}{3}}} d\mu - \\ & n(t,l) \int_0^\infty \beta(t,l,\mu)n(t,\mu)d\mu \end{aligned} \quad (1)$$

Stage II

$$\begin{aligned} \frac{\partial n(t,l)}{\partial t} = & \frac{1}{2} \int_0^l \frac{\beta\left(t,(l^3-\mu^3)^{\frac{1}{3}},\mu\right)n\left(t,(l^3-\mu^3)^{\frac{1}{3}}\right)n(t,\mu)}{(l^3-\mu^3)^{\frac{2}{3}}} d\mu - \\ & n(t,l) \int_0^\infty \beta(t,l,\mu)n(t,\mu)d\mu \end{aligned} \quad (2)$$

Stage III

$$\begin{aligned} \frac{\partial n(t,l)}{\partial t} = & \frac{1}{2} \int_0^l \frac{\beta\left(t,(l^3-\mu^3)^{\frac{1}{3}},\mu\right)n\left(t,(l^3-\mu^3)^{\frac{1}{3}}\right)n(t,\mu)}{(l^3-\mu^3)^{\frac{2}{3}}} d\mu - \\ & n(t,l) \int_0^\infty \beta(t,l,\mu)n(t,\mu)d\mu + \\ & \int_l^\infty S(t,\mu)b(l|\mu)n(t,\mu)d\mu - S(t,l)n(t,l) \end{aligned} \quad (3)$$

Where  $n(t,l)$  is the number density function in terms of the particle diameter,  $\beta(t,l,\mu)$  is the length-based aggregation kernel describing the frequency that particles with diameter  $l$  and  $\mu$  collide to form a particle of volume order of  $l^3 + \mu^3$ ,  $S(t,l)$  is the length-based breakage selection rate constant describing the rate at which particle are selected to break and  $b(l|\mu)$  is the breakage kernel describing the formation of particles of diameter  $l$  from the breakup of particle of diameter  $\mu$ .

Population balance equations are extremely complex. Except under special circumstances, it is almost impossible to obtain analytical solutions for the equations, so generally they are solved by numerical methods. In this paper, the discrete method proposed by Hounslow (Hounslow et al. 2001) is used to solve the equations. The granule size domain is divided into a number of size bins in a geometric series, and the number density function in each bin can be derived.

Stage I

$$\frac{dN_i}{dt} = \frac{2G_0}{(1+r)L_i} \left( \frac{r}{r^2-1} N_{i-1} + N_i - \frac{r}{r^2-1} N_{i+1} \right) \quad (4)$$

Stage II

$$\begin{aligned} \frac{dN_i}{dt} = & \sum_{j=1}^{i-2} 2^{j-i+1} \beta_{i-1,j} N_{i-1} N_j + \frac{1}{2} \beta_{i-1,i-1} N_{i-1}^2 - \\ & N_i \sum_{j=1}^{i-1} 2^{j-i} \beta_{i,j} N_j - N_i \sum_{j=i}^{n_{max}} \beta_{i,j} N_j \end{aligned} \quad (5)$$

Stage III

$$\begin{aligned} \frac{dN_i}{dt} = & \sum_{j=1}^{i-2} 2^{j-i+1} \beta_{i-1,j} N_{i-1} N_j + \frac{1}{2} \beta_{i-1,i-1} N_{i-1}^2 - \\ & N_i \sum_{j=1}^{i-1} 2^{j-i} \beta_{i,j} N_j - N_i \sum_{j=i}^{n_{max}} \beta_{i,j} N_j - S_i N_i + \\ & \sum_{j=i}^{n_{max}} b_{i,j} S_j N_j \end{aligned} \quad (6)$$

Where  $N_i$  is the discretized number density function meaning the number of granules in the range of  $(L_i, L_{i+1})$ .  $G_0$  is layering growth constant,  $n_{max}$  is the total number of discrete bins,  $\beta_{i,j}$  is the aggregation kernel between granules in the  $i$ th and  $j$ th size bins.  $S_i$  is the particle breakage selection rate.

As described in discrete PBM of Eq.4-6, a size independent granule layering growth rate  $G_0$  is used, which is modelled as function of operating conditions. An aggregation model can generally be split into two parts as (Iveson 2002)

$$\beta(t,l,\mu) = \beta_0(t,\theta,\Psi)(l+\mu)^3 \quad (7)$$

Where,  $\beta_0(t,\theta,\Psi)$  is the granulation rate constant, which incorporates various system parameters  $\theta$ , such as the binder spray and fluidization operating conditions for a top-spray fluidized bed granulator, and nonequipment parameters  $\Psi$ , such as physical properties of the powder mixtures. In this work,  $\beta_0$  is a function of operating conditions, which will be described in following section.

A breakage selection function can also be described as the following two parts (Tan et al. 2004; Ding et al. 2006)

$$S(t,l) = S_0(t,\theta,\Psi)l^3 \quad (8)$$

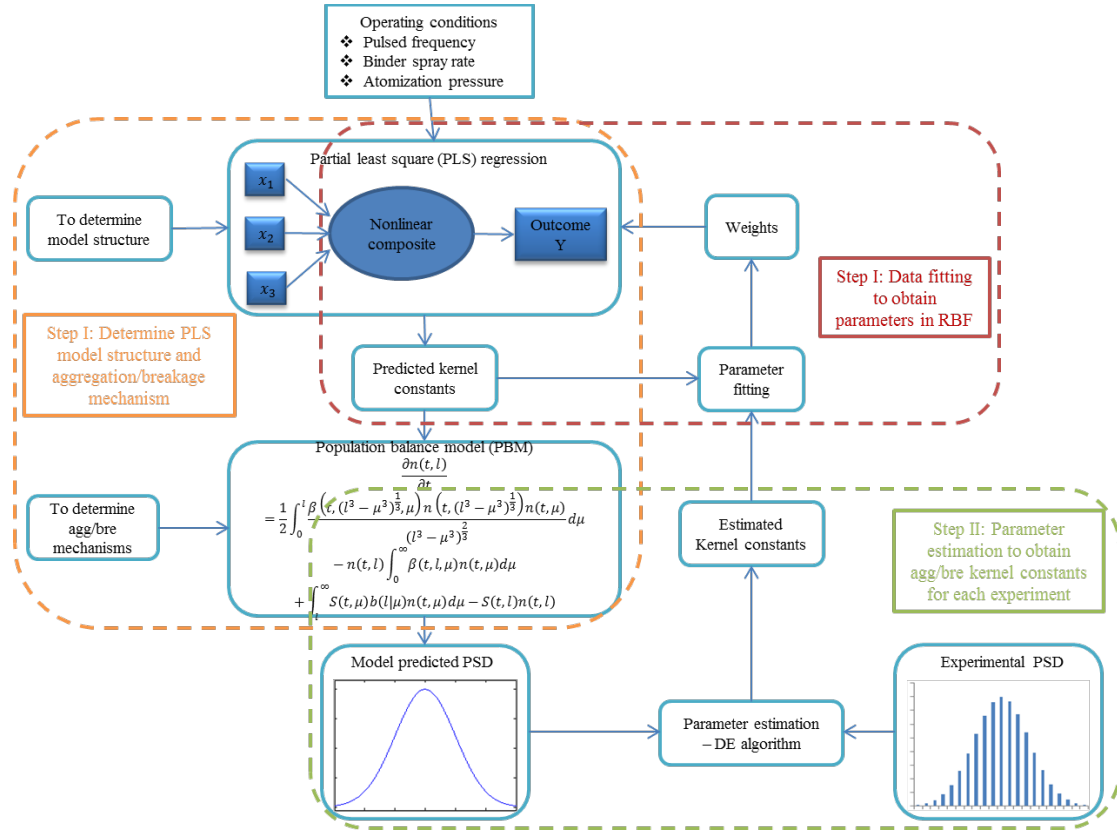


Figure 1. Schematic diagram of modelling approach of TSPBM

Where  $S_0(t, \theta, \Psi)$  is the breakage selection rate constant, which is also modelled in terms of operating conditions. The breakage kernel  $b(l|\mu)$  describes the formation of fragments of diameter  $l$  from the breakage of particles of diameter  $\mu$ , which is described as

$$b(l|\mu) = \frac{6l^2}{\mu^3} \quad (9)$$

Solving population balance equations using the discrete method, the number of particles in each size bin can be determined, and then the GSD can be obtained directly to predict the quality of the final product of the granulation process. However, the population balance equation contains unknown kernel constants including layering growth constant, agglomeration constant and breakage constant. These parameters must be determined in advance in order to solve the balance equations. When the material properties and device parameters have been fixed, these parameters are then determined by the manipulated operating variables during granulation process. Therefore, it is critical to search for the relationships between the kernel constants of population balance equations and the operating variables.

### 3.3 PLS regression model linking operating conditions to kernel constants in PBM

Based on our previous study of a top-spray fluidized bed granulator, it was shown that the quality of end granules was affected significantly by the binder solution spray conditions (Liu et al. 2013). Therefore, for the given materials and formulation, the layering growth rate constant granulation rate constant  $G_0$ , aggregation rate constant  $\beta_0$  and breakage rate constant  $S_0$  should be a

function of the binder solution spray conditions of the pulsed frequency  $x_1$ , binder spray rate  $x_2$  and atomization pressure  $x_3$ , which can be represented as a non-linear quadratic model as

$$G_0(x_1, x_2, x_3) = a_0 + a_1x_1 + a_2x_2 + a_3x_3 + a_{12}x_1x_2 + a_{13}x_1x_3 + a_{23}x_2x_3 + a_{11}x_1^2 + a_{22}x_2^2 + a_{33}x_3^2 \quad (10)$$

$$\beta_0(x_1, x_2, x_3) = b_0 + b_1x_1 + b_2x_2 + b_3x_3 + b_{12}x_1x_2 + b_{13}x_1x_3 + b_{23}x_2x_3 + b_{11}x_1^2 + b_{22}x_2^2 + b_{33}x_3^2 \quad (11)$$

$$S_0(x_1, x_2, x_3) = c_0 + c_1x_1 + c_2x_2 + c_3x_3 + c_{12}x_1x_2 + c_{13}x_1x_3 + c_{23}x_2x_3 + c_{11}x_1^2 + c_{22}x_2^2 + c_{33}x_3^2 \quad (12)$$

Where  $a_0, a_1, \dots, a_{33}, b_0, b_1, \dots, b_{33}, c_0, c_1, \dots, c_{33}$  are constants, which need to be fixed based on estimated kernel constants.

When building the multi-scale model, we first substitute the obtained experimental granule size distribution data into the population balance equations, and estimate the unknown kernel constants. Then the operating conditions and estimated kernel constants will be considered as inputs and outputs to fix the coefficients in the PLS regression model. The DE algorithm is also used in estimating coefficients of PLS regression model. From the obtained 17 batches of experimental data, 15 batches are selected for model development and 2 batches are selected for model validation. Since the entire granulation process is divided into three stages in this work, a model between the kernel constants and the operating variables is needed in each stage. After the multi-scale TSPBM is

developed, the model is utilized to predict the GSD of the 15 experiments used for model development with the comparison shown in Fig 2.

From Fig. 2, it can be seen that the developed multi-scale TSPBM model can predict accurately the GSD for most experiments in each stage, except experiment 1, 7, 9, 13 in stage III, which may be due to the error in sampling and measurement. Comparing the prediction of each stage, it can be seen that the model shows a cumulative prediction error as experiment time increase and has largest prediction error in stage III. This is because that the GSD in previous stage will be used as initial condition in current stage and any prediction error in last stage will be brought into the current stage producing a larger prediction mismatch. Further, the two validation experiments have been shown in Fig 3. For short, only the comparison of GSD for stage III is presented, from which it can be seen the experimental GSD can be accurately predicted by the developed multi-scale TSPBM. In summary, multi-scale TSPBM established in this work works well in describing the GSD evolution during the top-spray fluidized bed granulation process.

#### 4. Online optimization strategy for controlling granule growth

Based on the developed multi-scale TSPBM of the top-spray fluidized bed granulation process in Section 3, the optimal operating conditions of pulsed frequency  $x_1$ , binder spray rate  $x_2$  and atomization pressure  $x_3$  can be determined, with the aim of obtaining the end granules with the desired mean size, by solving the following optimization problem as:

$$\begin{aligned} & \text{Min}_{x_1, x_2, x_3} \{(\bar{D}_m - \hat{D}_m(t_f))^2\} & (13) \\ & \text{s.t. } \frac{\partial n(n,l)}{\partial t} = f(x_1, x_2, x_3, t) \quad (f: \text{Multi-scale TSPBM} \\ & \quad \quad \quad \text{model}) \\ & \quad 0 < x_1 < 1 \\ & \quad 0.9 \text{ g/min} < x_2 < 1.5 \text{ g/min} \\ & \quad 10 \text{ psi} < x_3 < 20 \text{ psi} \end{aligned}$$

Where,  $\bar{D}_m$  is the desired mean diameter of final granules;  $t_f$  is the granulation completion time at which a fixed amount of binder solution has been sprayed;  $\hat{D}_m(t_f)$  is the mean size of the final granules given by

$$\hat{D}_m(t_f) = \sum_{i=1}^{n_{max}} V_{F,i} d_{pi} \quad (14)$$

Where,  $V_{F,i}$  is the volume fraction of end granules at size interval  $i = 1, 2, \dots, n_{max}$ ;  $d_{pi}$  is the geometrical mean of the size interval  $i = 1, 2, \dots, n_{max}$ .

The above optimization is called offline optimization. Once the optimal operating conditions are obtained, they will be implemented into the system and never be changed until the experiments finished. However, it is well known that the drawback of an open-loop optimization problem is that it relies on accuracy of the process model. For a batch top-spray fluidized bed granulation process it is undoubted that there exists the model mismatch between the developed TSPBM and actual granulation process which

contributes to an increasing deviation between real particle size and desired aim as experiment progresses. Hence, an online optimization strategy has been developed, by carrying out two more optimizations on end of stage I and stage II, respectively, based on the current online measured volume-mean granule size at the end of stage I and stage II.

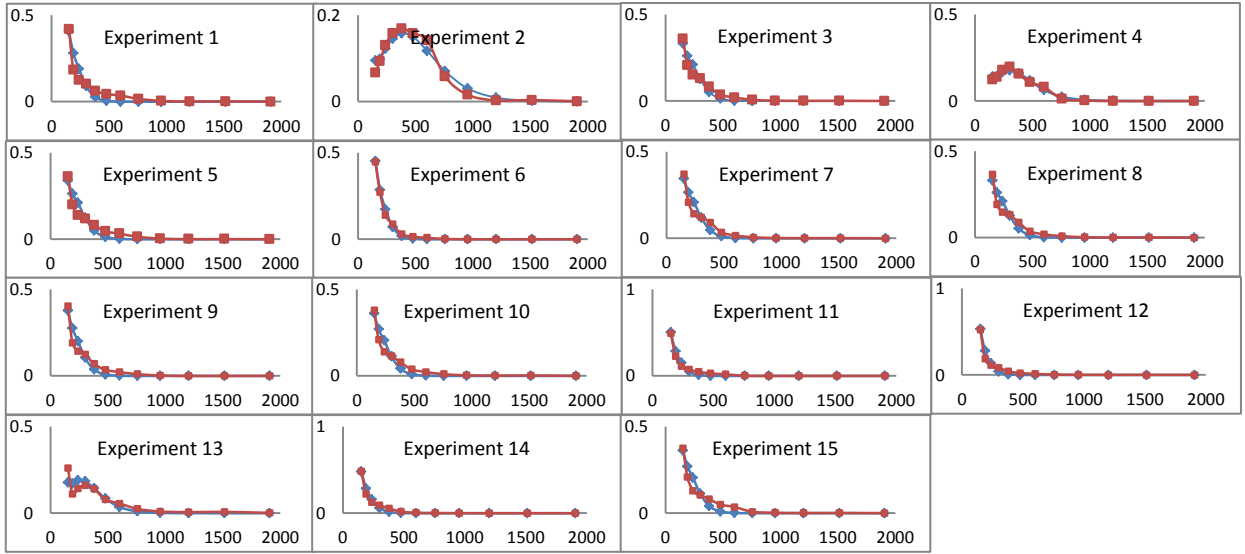
The new optimal operating conditions obtained from the new optimization on end of stage I and stage II will be implemented into the system respectively and help to ensure the real granule growth not deviating from the desired trajectory. A testing case was carried out with desired granule size of 500  $\mu\text{m}$  for comparison of effectiveness between offline optimization and online optimization strategy with results shown in Table 1. From the result, it can be concluded that the proposed online optimization strategy works more accurate than offline optimization in producing desired mean granule diameter.

#### 5. Conclusions

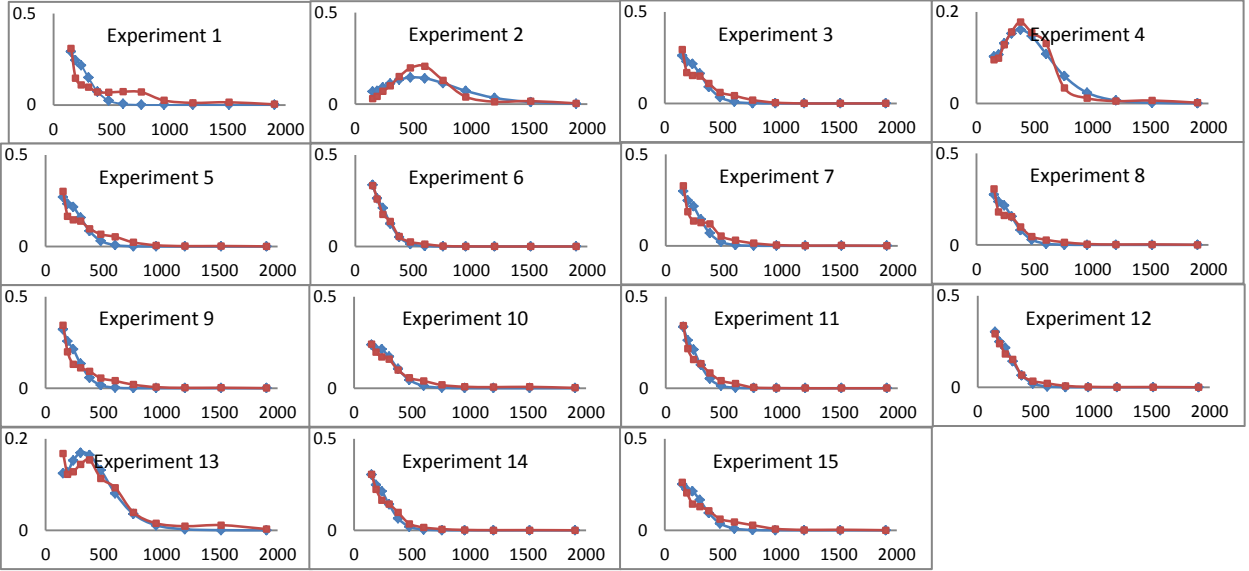
In this work, a multi-scale three-stage population balance model (TSPBM) was developed. By developing the relationship between the GSD and the manipulated operating variables, the developed multi-scale TSPBM is firstly established as a prerequisite for control strategy development. By adjusting the volume-mean granule size increasing trajectory on predefined sample intervals, the new optimal operating variables of pulse frequency, binder spray rate and atomization pressure are determined to avoid the granule growth deviating from desired trajectory. A differential evolution (DE) algorithm is used to solve the problem for online optimization problem and adjustment of the granulation operating variables. Experimental results and simulation tests are carried out to validate the effectiveness of the proposed TSPBM and online optimization strategy. Two experiments at randomly selected conditions were carried out and can be accurately predicted by the developed model. With the aim mean granule size of 500 microns, the online optimization strategy produced final granule size of 512 microns, while the offline optimization provided a value of 542 microns.

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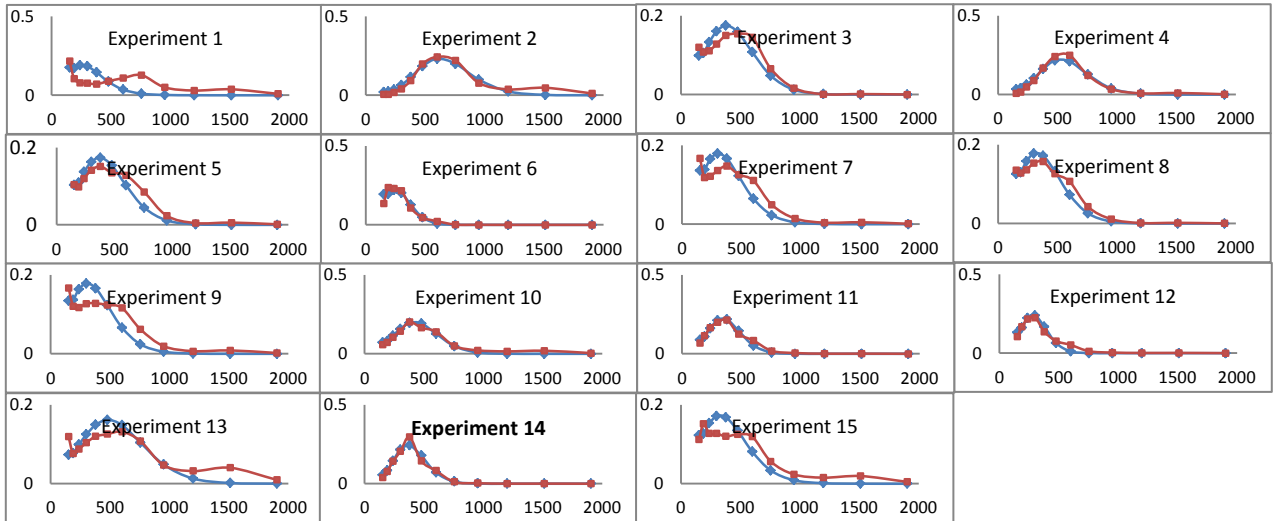
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(a)



(b)



(c)

Figure 2. Comparison between experimental data and multi-scale TSPBM predicted GSD for: (a) stage I, (b) stage II and (c) stage III (red: experiment, blue: predicted, x-axis: particle size in  $\mu\text{m}$ , y-axis: volume fraction)

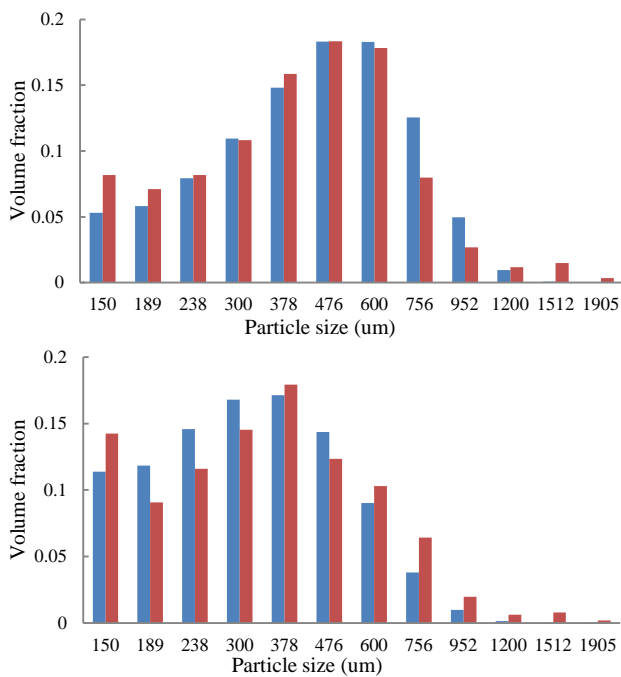


Figure 3. Comparison of GSD between experimental and model predicted for (a) validation 1 and (b) validation 2 in stage III (red: experiment, blue: predicted).

Table 1. Comparison between offline optimization and online optimization strategy

Methods	Final value (um)	Increase from aim value (%)
Aim	500	--
Offline optimization	542	8.4
Online optimization	517	3.4

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