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3D Population Balance Model for Continuous Twin Screw Granulator

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Continuous processes could be applied to improve cost-efficiency of pharmaceutical manufacturing that has traditionally relied on batch processing due to regulatory requirements and small lot sizes. However, in order to utilize this new approach and to meet the end-product requirements, understanding of the dominating granulation sub-processes is needed. One tool for gaining such knowledge is population balance (PB) modeling.
This paper describes initial steps in developing a three dimensional PB model for a continuous twin screw granulator. The focus is on the modeling of the rate processes considered dominant in the screw elements of the granulator, namely consolidation and aggregation. In formulating the three-dimensional PB the particle properties (size, porosity and saturation) are presented in terms of volumes of solid, liquid and gas. The results demonstrate correct behavior of the model and thus, the proposed solution could be used as a basis for further development.

1. Introduction

Traditionally, the pharmaceutical manufacturing has relied on batch processes mainly due to regulatory requirements and small lot size. The use of continuous processes, however, would provide several benefits such as improved cost and process efficiency, optimal use of equipment, and flexibility in production capacity.
An important pharmaceutical process that could benefit from continuous mode of operation is granulation, which is applied to convert solid fine particles to granular materials with the aid of a liquid binder. To achieve this, understandings of the dominant granulation sub-processes as well as tools for process monitoring and control are required. One tool for gaining such knowledge is PB modeling. It has a wide range of applications in particle technology, for example in coating (Li et al., 2012), mixing (Bárkányi et al., 2011), grinding of fine powders (Fadda et al., 2009) and crystallization (Gherras and Fevotte, 2012). PB modeling can be utilized in granulation process design for determining the controlling mechanisms, analyzing the effect of operating conditions, predicting the granule properties, and for process optimization and control (Litster and Ennis, 2010). In the context of continuous granulation the applications of PB are rare, however. A recent study (Ramachandran and Chaudhury, 2012) utilised PB modeling in model-based design of control of a continuous drum granulation process.
This paper describes the initial development of a three dimensional PB model for a continuous twin screw granulator. The approach enables the mathematical representation of the physical phenomena taking place during granulation thus making possible to describe the evolution of particle property distributions during the process. These phenomena are described by the granulation rate processes that include nucleation, layering, aggregation, consolidation, and attrition and breakage. The focus of the modeling in this work is the rate processes considered dominant in the screw elements of the twin screw granulator, namely aggregation and consolidation.

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The rest of the paper is organized as follows. In the next Section, the granulator is briefly introduced. Then, the three dimensional PB model for the granulator is presented in Section 3 followed by the modeling results and discussion Section 4. Finally, conclusions are given in Section 5.

2. Twin screw granulation and rate processes

The twin screw granulator with its operating principle is presented in Figure 1. It is assumed that the liquid distribution and nuclei formation take place in the kneading blocks. Nucleation is the formation of new granules from liquid or fine powder feed, increasing both mass and number of granules (Litster and Ennis, 2010).

The screw elements convey the material. Additionally, growth by coalescence and consolidation of particles occurs in the elements. Coalescence, also referred to as aggregation, creates a new granule but does not change the total volume or mass of the granules (Litster and Ennis, 2010). In modeling of this rate process, it is convenient to use volume-based granule size distribution instead of size, since volume is additive in binary collisions (Verkoeijen et al., 2002). A central term in modeling of the coalescence is the coalescence kernel (coalescence rate constant) which describes the overall rate of coalescence as well as the size dependent coalescence. Different kernels are available and the selection of the kernel has a major effect on the shape and evolution of the distribution (Litster and Ennis, 2010).

Consolidation decreases the granule porosity with time, with a small change (usually negligible) in the granule size. However, the indirect effect on granule deformability and liquid saturation is very important: granule saturation increases as the granule consolidates and the probability of the coalescence is very sensitive to liquid saturation distribution (Litster and Ennis, 2010).

The screws are configurable, i.e. the number of different elements as well as their position can be altered. Moreover, the rotational speed of the screws, cooling of the jacket, and the feed rates of the powder and liquid can be adjusted. A more detailed description about the equipment can be found from (El Hagrasy et al., 2012).

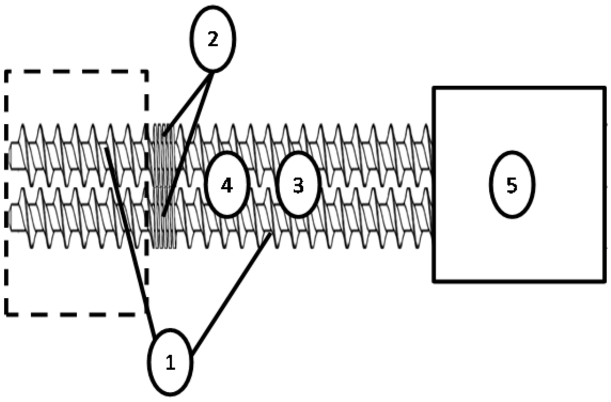

Figure 1: The operating principle of the twin screw granulator (not in scale). The granulator has two screws that consist of screw elements (1) and kneading blocks (2). Powder is fed from the top of the granulator (3) before liquid feeding (4). The drive (5) maintains the desired rotational speed of the screws. The rectangle drawn with a dashed line shows the focus of the model presented in this paper.

The main focus is on modeling the aggregation and consolidation rate processes taking place in the screw elements. Thus layering, which increases granule size and mass by coating new material onto existing granules and its direct opposite, attrition are excluded from the model. Moreover, breakage of granules is not considered dominant in the screw elements, and it is thus omitted.

3. Population balance modelling

In the granulation process, it is necessary to follow the particle population distribution with respect to the particle size, binder content and the porosity of the granules, because the particle population is distributed with respect to each of these three particle properties (Poon et al., 2008). For this, a three-dimensional PB model is used. In formulating the balance, the considered particle properties are presented in terms of volume of solid, volume of liquid and volume of gas (Verkoeijen et al., 2002).

The resulting three-dimensional PB equation with the chosen internal coordinates is given by (Imanuel and Doyle, 2005):

$$\frac{\partial F}{\partial t}(s,l,g,t)+\frac{\partial}{\partial g}\left(F(s,l,g,t)\frac{dg}{dt}\right)+\frac{\partial}{\partial s}\left(F(s,l,g,t)\frac{ds}{dt}\right)+\frac{\partial}{\partial l}\left(F(s,l,g,t)\frac{dl}{dt}\right)=R_{nuc}+R_{agg}+R_{break}. \quad (1)$$

Partial derivatives with respect to solid volume *s* and liquid volume *l* present growth by layering and rewetting / drying of granules, respectively. The partial derivative with respect to *g* presents consolidation, in which there is a continuous decrease in pore volume, while the solid and liquid volumes remain unchanged.

As mentioned in the previous Section, the dominating growth mechanism is considered to be aggregation, and thus, growth by layering, drying; and breaking and attrition are omitted. Additionally, nucleation is out of the scope of the model and also breaking and attrition are not considered dominant mechanisms. However, consolidation is expected to take place in the screw elements. The equation therefore becomes:

$$\frac{\partial}{\partial t}F(s,l,g,t)+\frac{\partial}{\partial g}\left(F(s,l,g,t)\frac{dg}{dt}\right)=R_{agg}\,. \quad (2)$$

Considering aggregation and consolidation in a specific control volume *V* and taking into account also the flows of particles into and out of the process results in:

$$V\frac{\partial}{\partial t}F(s,l,g,t)+V\frac{\partial}{\partial g}\left(F(s,l,g,t)\frac{dg}{dt}\right)-VR_{agg}=Q(F(s,l,g)_{in}-F(s,l,g)_{out}). \quad (3)$$

Furthermore, substituting $\tau = V/Q$ yields:

$$\frac{\partial}{\partial t}F(s,l,g,t)+\frac{\partial}{\partial g}\left(F(s,l,g,t)\frac{dg}{dt}\right)-R_{agg}=\frac{(F(s,l,g)_{in}-F(s,l,g)_{out})}{\tau}. \quad (4)$$

The change in the gas volume (*dg/dt*) is treated as negative growth by layering, and it is defined as in (Verkoeijen et al., 2002):

$$\frac{dg}{dt}=-c\frac{s+l+g}{s(1-e_{min})}\left[l-\frac{e_{min}s}{1-e_{min}}+g\right]. \quad (5)$$

Here, constant c and e_{min} are defined as compaction rate and minimum porosity of granules, respectively. Aggregation consists of formation and depletion terms:

$$R_{agg}=R_{agg}^{formation}-R_{agg}^{depletion} \quad (6)$$

and it also utilizes the approach derived in (Poon et al. 2008), based on the work in (Ramkrishna, 2000). The aggregation kernel β used in the model presented in this paper is based on equipartition of kinetic energy (EKE) –model (Hounslow et al., 2001), as in (Ramachandran and Barton, 2010).

$$\beta(s',s-s',l',l-l',g',g-g')=$$

$$\beta_0(D(s',l',g')+D(s-s',l-l',g-g'))^2*\sqrt{\frac{1}{D^3(s',l',g')}+\frac{1}{D^3(s-s',l-l',g-g')}}, \quad (7)$$

where D is particle diameter and β_0 the aggregation rate constant. Particle diameter is obtained from *D(s,l,g) = [6(s+l+g)/π]1/3*.

The granulator is assumed to be a plug-flow system. The plug-flow is approximated applying continuous stirred tanks (CSTR) in series. The input of the first CSTR is the particle distribution leaving from the kneading blocks, modeled using a Gaussian multivariate probability density function *f*:

$$F(s,l,g,t)_{in}=af(x,\mu,E), \quad (8)$$

where x is a matrix including the total ranges of solid, liquid, and gas volume distributions, μ is the mean vectors, E is the covariance matrix. Coefficient a adjusts the total number of particles of the input flow.

After the first CSTR, the input of the each subsequent CSTR is the output of the previous one. For each tank, representative overflow is assumed:

$$F(s,l,g,t)_{i,out}=F(s,l,g,t)_i\,, \quad (9)$$

where i denotes order of tank in series.

As in Li et al. (2012), the model was solved using finite volume method. The particle property domain was divided into 3D cells and, then backward Euler method was applied. In the implementation of the model, it was assumed that at the lower property boundaries, only depletion of particles takes place as they grow. At the upper property boundaries, on the other hand, only formation was considered in order to prevent the particles leaving from the defined grid.

4. Results and discussion

The parameters of the PB model (Table 1) were defined manually based on the solution stability, execution time and experimental results presented in (El Hagrasy et al., 2012). Figure 2a and b present the granule distributions of the input particle flow leaving from kneading blocks to the screw elements as a function of solid, liquid and gas volumes. The input of the first CSTR was defined so that the particle distribution with respect to gas volume was located in the middle of the grid, since it may increase due to aggregation and decrease due to consolidation (Figure 2a). The solid and liquid distributions were at the lower boundaries of the grid to enable aggregation (Figure 2b). The grid steps for solid and liquid volumes were defined so that the liquid-to-solid (L/S) –ratio resulted in 0.3 which is the mean of the experimental results for measured granule porosity presented in (El-Hagrasy et al., 2012). For gas volume, the grid steps were so that the initial porosity was higher than the mean of the measured ones obtained with L/S-ratio 0.3 in (El-Hagrasy et al., 2012). The grid steps were not scaled according to any particular raw material, and thus the volumes are arbitrary from that point of view.

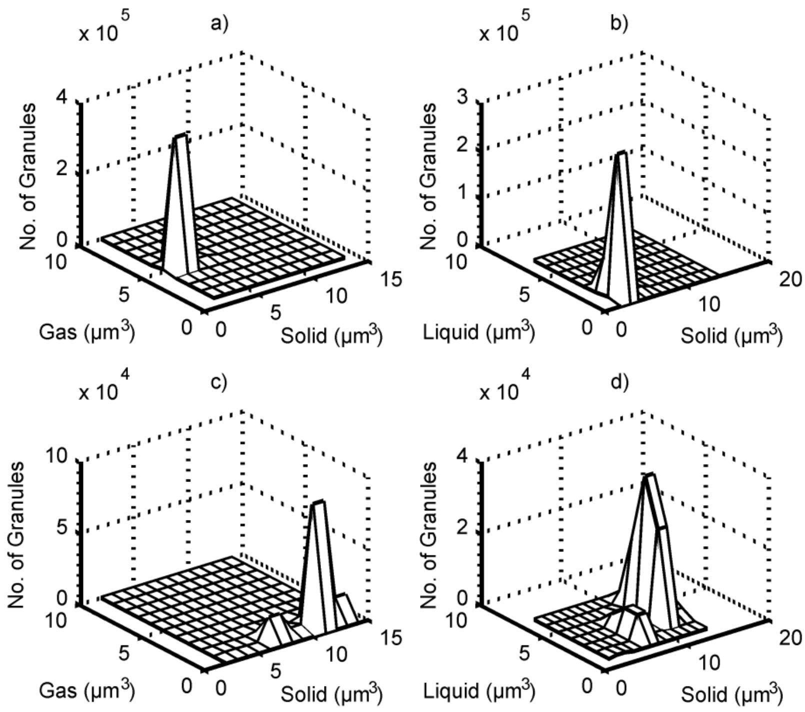

Figure 2: The granule property distribution of input (a, b) and output flows (c, d).

Next, the simulation was executed for 15 s. The evolution of particle property distribution was then investigated (Figure 2c and d). It can be observed that the gas volume has decreased due to the consolidation, as expected (Figure 2c). Moreover, the solid and liquid volumes have increased due to the growth of granules (Figure 2c and d).

The particle size, porosity and saturation distributions were then calculated based on the volume distributions and investigated (Figure 3). It can be observed that both the particle size and the variation of the distribution increase (Figure 3a and d). The resulting particle size distribution slightly resembles the experimental one presented in El Hagrasy et al. (2012) having, however, a notably smaller size range. A wider range would require increased grid size. For this the computational efficiency of the solution should be improved.

The evolution of porosity (Figure 3b and e), and saturation (Figure 3c and f) distributions, seem to be correct as well. The porosity of the particles is expected to decrease due to consolidation, which can be clearly observed from the results. Correspondingly, the saturation increases as the volume of the pores filled by the liquid gets smaller.

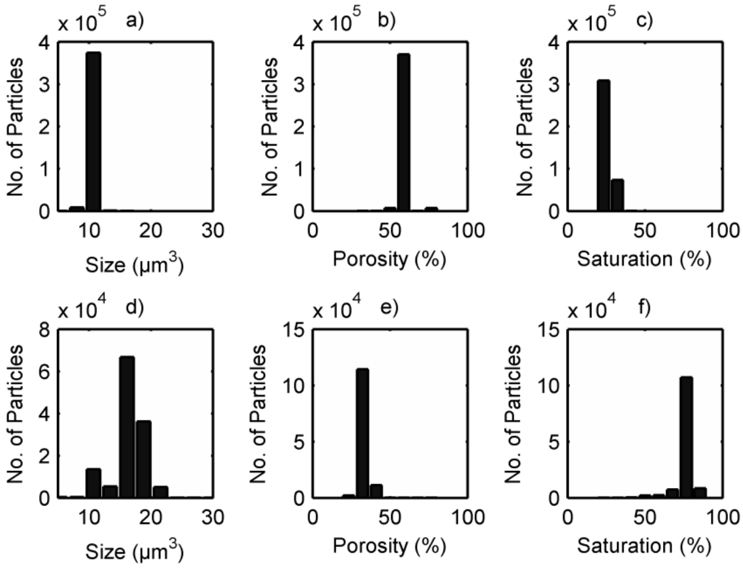

Figure 3: The property distributions of the input (a, b, c) and output flow (d, e, f) of the particles. The distributions were calculated based on the simulated volume distributions applying equations (s+l+g), porosity [(l+g)/(s+l+g)], and [l/(l+g)] for size, porosity and saturation, respectively.

From modeling point of view, the most important steps could include increasing knowledge about the nucleation in the kneading blocks. Moreover, studying the different aggregation kernels with respect to the experimental results could be useful. Additionally, increasing the computationally efficiency of the solution of the model as well as more careful tuning of the model parameters is required.
As a long term goal clarifying the effects of the twin screw granulator control variables (screw speed, powder feed, liquid feed) on the developed models could be interesting. This would allow utilization of the developed model in studying the control of the process using simulation tools.

Table 1: The parameters of the simulation

Grid size (s, l, g)	Grid steps (μm^3) (s, l, g)	Simulation time step (s)	Total residence time (s)	c, b_0, e_{min}	No. of reactors
7, 7, 10	2, 1, 1	0.025	7.5	0.2, $2 \cdot 10^{-6}$, 0.1	20

5. Conclusions

In this paper, an initial study for a three-dimensional PB model for a continuous twin-screw granulator was presented. The model focused on the screw elements of the granulator, for which consolidation and aggregation were considered dominant rate processes. The results lend support to the model correctness and thus the proposed solution could be used as a basis for further development. The parameters of the model, however, need to be tuned to better describe the twin screw granulator and rate processes. Additionally, grid sizing and computational efficiency of the solution needs to be improved. Moreover, a more detailed study of the different aggregation kernels could be carried out and verified experimentally.
The future enhancements could address improving modeling of the nucleation taking place in the kneading blocks and the effects of the granulator control variables (liquid and powder feed, and screw speed). With these additions, the PB-based simulation could be a very valuable tool for studying different control scenarios for twin screw granulation process.

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References

Bárkányi Á., Németh S., Lakatos B.G., 2011, Effects of mixing on the formation of polymer particles in suspension polymerization, Chemical Engineering Transactions 24, 613-618. DOI: 10.3303/CET1124103

El-Hagrasy A.S., Hennenkamp J.R., Burke M.D., Cartwright J.J., Litster J.D., 2012, Twin screw wet granulation: Influence of formulation parameters on granule properties and growth behaviour, Powder Technology, DOI:10.1016/j.powtec.2012.04.035

Fadda S., Cincotti A., Cao G., 2009, Modelling breakage and reagglomeration during fine dry grinding in ball milling devices, Chemical Engineering Transactions 17, 687-692. DOI: 10.3303/CET0917115

Gherras N., Fevotte G., 2012, On the use of process analytical technologies and population balance equations for the estimation of crystallization kinetics. A case study, AIChE Journal 58, 2650-2664. DOI: 10.1002/aic.12776

Hounslow M.J., Pearson J.M.K., Instone T., 2001, Tracer studies of high-shear granulation: II. Population balance modelling, AIChE Journal 47, 1984-1999, DOI: 10.1002/aic.690470910

Imanuel C.D., Doyle F.J. III, 2005, Solution technique for a multi-dimensional population balance model describing granulation processes, Powder Technology 156, 213-225. DOI: 10.1016/j.powtec.2005.04.013

Li J., Freirech B., Wassgren C., Litster J.D., 2012, A general compartment-based population balance model for particle coating and layered granulation, AIChE Journal 58, 1397-1408 DOI: 10.1002/aic.12678.

Litster J.D., Ennis B., Liu L. (Ed.), 2010, The Science and Engineering of Granulation Processes, Particle Technology Series, Ed. Scarlett, B., Kluwer Academic Publishers, the Netherlands

Poon J.M.-H., Immanuel C.D., Doyle F.J. III, Litster J.D., 2008, A three-dimensional population balance model of granulation with a mechanistic representation of the nucleation and aggregation phenomena, Chemical Engineering Science 63, 1315-1329. DOI: 10.1016/j.ces.2007.07.048.

Ramachandran R., Barton P.I., 2010, Effective parameter estimation within a multi-dimensional population balance framework, Chemical Engineering Science 65, 4884-4893. DOI: 10.1016/j.ces.2010.05.039

Ramachandran R., Chaudhury A., 2012, Model-based design and control of a continuous drum granulation process, Chemical Engineering Research and Design, 90, 1063-1073. DOI: 10.1016/j.cherd.2011.10.022.

Ramkrishna D., Population Balances, 2000, Academic Press, San Diego, USA.

Verkoeijen D., Pouw G.A., Meesters G.M.H., Scarlett B., 2002, Population balances for particulate processes- a volume approach, Chemical Engineering Science 57, 2287-2303. DOI: 10.1016/S0009-2509(02)00118-5.