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A three-dimensional population balance model of granulation with a mechanistic representation of the nucleation and aggregation phenomena

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Abstract

A comprehensive model is discussed for wet granulation based on a three-dimensional population balance, as an attempt to capture particle-level phenomena and their influence on the population-level behaviour. The three dimensions of population distribution are the particle size, binder content, and porosity of the granules. In formulating the population balance, these three particle traits are represented in terms of three equivalent traits, namely, the solid volume, liquid volume and gas volume of the granules. The model accounts for wetting, nucleation, aggregation and consolidation phenomena. Mechanistic kernels are derived for aggregation and nucleation, employing theories on these particle-level microscale phenomena that have already been validated in previous studies. The three-dimensional population balance is solved numerically using a finite volume-based decomposition algorithm also called the hierarchical two-tier solution strategy [Pinto, M.A., Immanuel, C.D., Doyle III, F.J., 2007. A feasible solution technique for higher-dimensional population balance models. Computers and Chemical Engineering, 31, 1242–1256].

Keywords: Granulation; Population balance; Aggregation; Nucleation; Mechanistic kernels; Batch

1. Introduction

Granulation is a size enlargement process in which fine powdery solids are agglomerated together with a liquid binder to form larger aggregates. It finds applications in a wide range of industries from food processing, detergents, fertilisers, and pharmaceuticals to name the least. Some of the advantages of granulated materials include improved flow properties, increased bulk density, controlled dissolution and delivery rates, uniformity in the distribution of multiple solid components, and even taste and aesthetics. In particular, for batch processes such as in the pharmaceuticals, it is of paramount importance that homogeneity is achieved in granules in terms of the active drug ingredient and the excipients. This and the stringent requirements imposed on the specified size ranges for the granules have made the process difficult to control due to the complex interactions among underlying granulation phenomena. Thus, granulation processes are operated in a highly inefficient manner with large recycle ratios within the process (3–4:1, recycle/product) (Mort et al., 2001). As will be described next, an integrated systems model will be a crucial aid to alleviate this situation (Litster, 2003; Bardin et al., 2004; Knight, 2004; Mort, 2005).

A modern view of granulation is a process that is governed by three predominant sub-processes: wetting and nucleation; consolidation and growth; and attrition and breakage; in addition to any simultaneous drying (Iveson et al., 2001) [see Fig. 1(a)]. The formation of granules is first initiated by the nucleation of the fine powder particles (primary particles). This involves the distribution of the liquid binder over the powder, followed by the penetration of the droplet into the powder where the binder droplet will capture the particles within its immediate vicinity into a nucleus. The nucleus will continue to grow by aggregation and will also undergo consolidation in which the particles are compacted thus squeezing the binder from the pores of the granule onto the surface. Both the amount of liquid present on the surface and within the granule will play a significant role in determining the success of an aggregation event should two particles collide with one another (Liu et al., 2000;

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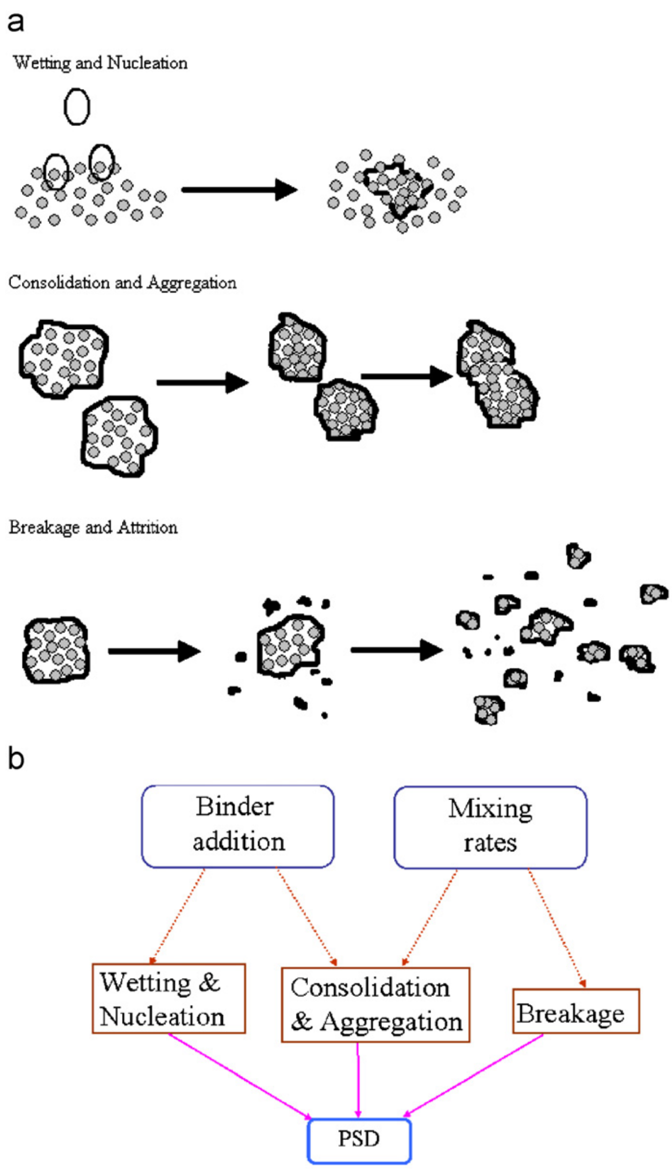

Fig. 1. The granulation mechanisms and the process systems view. (a) Schematic representation adapted from Iveson et al. (2001) showing the underlying granulation phenomena that will determine the particle size distribution. (b) A systems view of the granulation process indicating the multi-scale evolution and inherent interactions.

Immanuel and Doyle, 2005b). The particles may also be involved in fragmentation as a result of collisions either with other particles or by making direct contact with the internal surfaces of the equipment. Thus, the three indicated principle sub-processes will determine the granule size distribution as depicted schematically in Fig. 1(b). An integrated model that accounts for these major sub-processes as well as the effects of the process inputs (binder addition, agitation rate, number of spray nozzles used for the binder spray, etc.) will enable an analysis of the system dynamics and the formulation of a suitable control strategy, thereby alleviating inefficient operation.

Numerous studies are available in the literature, with various aspects of the granulation phenomena being studied in detail. However, the aggregation phenomena have been the main study in the past and as such the level of understanding is much greater when compared with the nucleation and breakage phenomena. The granulation process is usually modelled in the form of a population balance accounting for the nucleation, consolidation, aggregation, and breakage (Adetayo et al., 1995; Verkoeijen et al., 2002; Iveson, 2002; Biggs et al., 2003; Sanders et al., 2003; Immanuel and Doyle, 2005b; Marchisio and Fox, 2005; Tan et al., 2006). A major challenge in developing these population balances is the identification of appropriate kernels for the sub-processes (e.g. nucleation and aggregation). Hounslow et al. (2001) considered three aggregation kernels: a size-independent kernel (SIK), Smoluchowski's shear kernel (SSK) and the equipartition of kinetic energy kernel (EEK). The kernels were fitted with experimental data, and the EEK was the most successful when used in the model for predicting the shape of the tracer distribution. Other alternative forms for the aggregation kernel that have been proposed in the past may also be found in Cameron et al. (2005). On the other side of the spectrum, there are mechanistic kernels derived from first principles as previously described in Immanuel and Doyle (2005b).

With regard to the wetting and nucleation phenomena, Hapgood et al. (2002) and Hapgood (2000) proposed a nucleation regime map based on the drop penetration times of liquid droplets (controlled by the formulation properties) and a dimensionless spray flux (controlled by processing parameters). The nucleation regime map identifies the regions that give rise to a drop-controlled regime wherein each droplet forms one nuclei and a mechanical dispersion regime wherein multiple droplets coalesce onto the bed forming clusters that are then broken by mechanical forces into nucleates. A granule growth regime map was proposed by Iveson and Litster (1998) which seeks to describe the different growth behaviours exhibited by the granule on a qualitative basis. The benefit of this regime map is the ability to infer the dynamic behaviour of the granule based on their formulation properties. Breakage studies for wet granulation processes have not been widely studied in the past. Tardos et al. (1997) used the Stokes deformation number as a criterion for granule breakage. This accounts for the mechanism that given sufficient externally applied kinetic energy, the granules would deform and break in high shear fields (Iveson et al., 2001; Tardos et al., 1997). Several other authors have performed experimental and modelling studies on the breakage phenomenon (Tan et al., 2004; Reynolds et al., 2005; Fu et al., 2005). Discrete element simulations have also been extensively used to predict the granule breakage behaviour (Moreno-Atanasio and Ghadiri, 2006; Ning and Ghadiri, 2006).

Accounting for the microscale mechanisms such as nucleation and aggregation within the macroscale population balance model of a granulation process results in a multi-scale process model. Different computational methods have been adopted to tackle such multi-scale problem. These can be broadly classified as follows, employing the spirit of previous classifications