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A breakage kernel for use in population balance modelling of twin screw granulation

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Abstract

This paper presents a novel breakage kernel for use in population balance modelling for twin screw granulation using a mechanistic understanding in different screw elements. Breakage-isolated experiments are conducted using conveying and distributive mixing elements for a range of model formulations of widely different yield stresses. The breakage kernel, i.e. the selection and breakage functions, are mathematically formed based on the identification of the dominant breakage mechanisms of chipping and fragmentation in the conveying and distributive mixing elements, respectively, and the unique geometries of the two screw elements. A parametric study for the proposed breakage kernel is performed to identify the influential parameters on the breakage kernel. This is the first breakage model specifically developed for a TSG and incorporates a mechanistic understanding of several key parameters, particularly the role of screw geometry. The breakage model is well suited to population balance modelling framework for model-driven design of twin screw granulation.

Keywords: Breakage kernel, Population balance model, Critical breakage size, Screw geometry, Twin screw granulation

1 Introduction

Wet granulation is a key component in the integration of continuous pharmaceutical manufacturing. As an emerging technology for continuous wet granulation, twin screw granulation is becoming increasingly popular due to its large material throughput, flexible screw configuration, short residence time, and small capital costs. Hence, there has been considerable interest in the study of twin screw granulation both experimentally and numerically.

A twin screw granulator consists of two intermeshed co-rotating screws encased in a barrel with powder and liquid injection ports. The positions of the powder and liquid injection ports can be adjusted easily. The screws are assembled using individual screw elements available in different screw geometries. The material is conveyed along the length of the screw and granulation occurs by mechanical mixing of the powder and the granulating liquid in the granulator.

Several mechanistic studies have been conducted in twin screw granulators to understand governing rate processes. A twin screw granulator operates in the mechanical dispersion regime, relying on mixing elements to disperse a liquid throughout the powder mass [1,2]. Thus, granule breakage has been shown to be a key rate process affecting granule properties since breakage is necessary for good liquid distribution [3].

Granule breakage varies considerably with different screw geometries, resulting in a variety of granule properties. It has been shown that conveying elements primarily transport material and cause minor attrition of granules. Conveying elements do not cause intense mixing of the powder and the binder [1,4–6], resulting in a bimodal distribution of granules marked by a fines mode in the granule size distribution corresponding to ungranulated material [4,7,8]. Kneading elements cause intense mixing of material by shearing and extruding the wet mass, resulting in dense granules with flat, elongated shapes [9–12]. Distributive mixing elements also cause intense mixing of the wet mass via a chopping and fragmentation breakage mechanism [3-6, 13, 14]. As a result, the granules from distributive mixing elements are more porous compared to kneading elements and rounder in shape. Since twin screw granulators have a small free volume compared to high shear or fluidized bed granulators, screw geometry plays an important role in controlling the maximum

1 granule size that can be produced. The maximum granule size can be obtained by estimating
2 the largest sphere that can fit in the free volume of a given screw geometry [4, 5, 15]. The
3 maximum granule size in a conveying element is set by the space available between the two
4 flights of the conveying element and barrel whilst the maximum granule size in a distributive
5 mixing element is the space between the teeth of the elements and the barrel [5].

6 Granule size, shape, and porosity are sensitive to formulation properties (such as API and
7 excipient type, blend particle size distribution, binder viscosity, etc.), process parameters
8 (such as material feed rate, liquid to solid ratio, and screw speed), and screw element
9 geometry [1, 2, 4, 5, 11, 13, 16, 34]. Hence, it is important to understand the effect of
10 formulation properties and process parameters on granule breakage with different screw
11 geometries. The breakage of a wet granule depends on its dynamic yield strength (DYS),
12 which describes the mechanical behaviour of the wet mass. The DHS is dependent on the
13 primary powder particle size, binder viscosity and surface tension, powder binder contact
14 angle, granule porosity and saturation, and strain rate of deformation [35-37]. The material
15 feed rate and screw speed are the key process parameters affecting the granule properties
16 in a twin screw granulator. The interlinked effects of material feed rate and screw speed are
17 captured by the dimensionless Powder Feed Number (PFN) given by [23]:

$$PFN = \frac{\dot{m}_{powder}}{\rho_{bulk}\omega D^3} \quad (1)$$

18 where \dot{m}_{powder} is the powder feed rate in the granulator, ρ_{bulk} is the powder poured bulk
19 density, ω is the screw speed, and D is the screw diameter.

20 The material fill level in the granulator is directly proportional to the PFN. Some studies
21 reported in the literature show that the PFN does not have a statistically significant effect on
22 granule properties [23]. However, some reports have suggested that increasing the material
23 fill level in the granulator increases the mean granule size [8, 14, 31]. As a result, the precise
24 effect that the PFN has on granule breakage remains uncertain.

25 Population balance modelling is recognized to be a powerful model-based design tool for
26 understanding the prediction and optimization of continuous twin screw granulation
27 processes. For example, Paavola et al. [38] defined two rate process kernels, i.e.,
28 consolidation and aggregation, to study the size, porosity, and saturation distributions of

1 granules. However, growth behaviour by layering and breakage is omitted in their study.
2 Barrasso et al. [39] used a multi-dimensional population balance model for continuous twin
3 screw granulation where the rate processes of aggregation, breakage, liquid addition, and
4 consolidation were taken into account. The influence of liquid-to-solid ratio was studied and
5 larger liquid addition rates resulted in higher frequencies of larger particles as well as a
6 reduction in primary particles. Likewise, a population balance model-based analysis of twin
7 screw granulation was carried out for continuous solid dosage manufacturing by Kumar et al.
8 [40]. A 1D population balance model was adopted with aggregation and breakage in the
9 kneading elements. Unknown input parameters were estimated using the experimentally-
10 measured particle size distribution. Recently, the spatial heterogeneity in twin screw
11 granulation was evaluated with a three-compartment population balance model by Liu et al.
12 [41]. The three compartments were composed of wetting (conveying), mixing (kneading),
13 and steady growth (conveying) sections. Within these compartments it was assumed that
14 aggregation occurred in the wetting compartment and breakage occurred in the mixing
15 elements. Aggregation and breakage took place in the steady growth compartment.

16 As inferred from the preceding discussion, one of the main challenges of population balance
17 modelling is development of a reasonable model where the rate process kernels are defined
18 based on the screw configuration. Although several breakage kernels have been used in
19 population balance models [39, 48], there have been two main deficiencies in their
20 formulation. First, the breakage mechanisms are not properly characterised in different
21 screw elements and the majority of existing breakage kernels use the same function
22 regardless of the screw type. Second, a mechanistic-based breakage kernel is yet to be
23 established for twin screw granulation where the process parameters and mechanical
24 properties of the particles are incorporated into the breakage probability function.

25 This paper develops new breakage kernels for use in population balance modelling of twin
26 screw granulation. To characterise the breakage mechanism within the twin screw
27 granulator, breakage-isolated experiments are performed using conveying and distributive
28 mixing element configurations. Breakage experiments for kneading elements are out of the
29 scope of this paper. We recommend similar studies on different configurations of kneading
30 elements (e.g., 30° forward, 30° reverse, 60° forward, 60° reverse, and 90°) to gain insight
31 into the shearing mechanisms associated with kneading elements. From the experimental

1 observations, the dominant breakage mechanisms are identified as chipping and a
 2 combination of chipping and crushing for the conveying and distributive mixing elements,
 3 respectively. The selection and breakage functions are mathematically formed as functions
 4 of the powder feed number (PFN), dynamic yield strength (DYS), and screw element
 5 geometry. These new breakage kernels improve the population balance modelling of twin
 6 screw granulation by providing mechanistic-based breakage kernels that are screw
 7 configuration dependent.

8 **2 Population balance model for twin screw granulation**

9 Population balance modelling has been widely used to track granule attribute evolution in
 10 twin screw granulation. The dimension of the population balance model is dependent on
 11 the number of phases (solid, liquid, and gas) to be considered. Most population balance
 12 models in the literature are one-dimensional, usually considering only the variation of
 13 particle size or volume. One-dimensional population balance models fall short of predicting
 14 all granule properties of interest due to their inability to track granule-to-granule variation
 15 in liquid content and granule porosity. Therefore, 3D population balance models have been
 16 developed to account for the variations in solid, liquid, and gas composition. Most
 17 granulation population balance models include rate process kernels for consolidation,
 18 aggregation, and breakage. The development of breakage kernels is the focus of this paper.

19 **2.1 Governing equations of population balance model**

20 Multi-dimensional population balance models (PBMs) have been developed to track granule
 21 solid, liquid, and gas volumes. A typical 3D population balance model may be written as [42]:

$$\begin{aligned} \frac{\partial}{\partial t} n(s, l, g, t) + \frac{\partial}{\partial s} \left[n(s, l, g, t) \frac{ds}{dt} \right] + \frac{\partial}{\partial l} \left[n(s, l, g, t) \frac{dl}{dt} \right] + \frac{\partial}{\partial g} \left[n(s, l, g, t) \frac{dg}{dt} \right] \\ = B_{nuc}(s, l, g, t) + B_{break}(s, l, g, t) - D_{break}(s, l, g, t) + B_{lay}(s, l, g, t) \end{aligned} \quad (2)$$

22 where (s, l, g) is the vector representing the solid, liquid, and gas volumes of a granule and
 23 $n(s, l, g, t)$ is the population density of a granule with these three components over time.
 24 The three non-temporal partial differential terms refer to the state change due to solid
 25 layering, liquid addition, and gas consolidation, respectively. The quantities $B_{nuc}(s, l, g, t)$

1 and $B_{lay}(s, l, g, t)$ denote the net rates of nucleation and layering, respectively. The terms
 2 $B_{break}(s, l, g, t)$ and $D_{break}(s, l, g, t)$ denote the birth and death rates due to breakage.

3 **2.2 Rate expression for breakage**

4 The population balance model shown in Eq. (2) is a framework to track the granule volume
 5 development considering three phases, i.e., solid, liquid, and gas. Breakage events are a
 6 function of factors such as the granule properties (size, shape, porosity, mechanical
 7 properties, etc.) and the operational variables. It is assumed that broken granules will have
 8 the same composition as the original granule. Therefore, we can write the breakage
 9 equations in one internal dimension, with the granule size evolution as a function of the
 10 aforementioned factors,

$$D_{break}(v) = S(v)n(v, t) \quad (3)$$

11 where $S(v)$ is the specific breakage rate of granules of volume v and $v = s + l + g$.

12 A granule of volume v can be created from the breakage of a larger-sized granule of volume
 13 w . Hence, the birth term of a granule is,

$$B_{break}(v) = \int_v^\infty S(w)b_M(v, w)M(v, t)dw \quad (4)$$

14 where $S(w)$ is the specific breakage rate of the mass fraction of granules of volume w .

15 When breakage is the only rate process, the population balance model for the mass-based
 16 breakage equation can be derived by combining Eqs. (2), (3), and (4) [43],

$$\frac{dM(v, t)}{dt} = \int_v^\infty S(w)b_M(v, w)M(v, t)dw - S(v)M(v, t) \quad (5)$$

17 where $M(v, t)$ is the mass of granules with volume v at time t . The breakage function
 18 $b_M(v, w)$ denotes the breakage size distribution probability between the volume range v
 19 and w , with $b_M(v, w) = B_{w,v} - B_{w-1,v}$ where B is the cumulative distribution of particle in
 20 different size fractions.

21 The breakage kernel is composed of two important functions: the selection function (S) and
 22 breakage function (B_m). The selection function represents the breakage rate of granules

1 whilst the breakage function represents the size distribution after breakage. The
2 development of the selection and breakage functions for conveying and distributive mixing
3 elements are described in the following sections.

4 **3 Experimental protocol**

5 Prior studies on twin screw granulation (TSG) focus on understanding the effects of screw
6 configuration, formulation properties, and process properties on granule attributes [2].
7 However, granule properties are controlled by several rate processes. In order to
8 understand the governing factors for granule breakage in a TSG, novel experiments that
9 isolate breakage from other granulation rate processes were carried out using conveying (CE)
10 and distributive mixing element (DME) configurations [44]. The experimental protocol and
11 granule breakage probability and daughter size distribution measurements have been
12 previously reported [5]; however, the setup of the breakage-isolating experiments is briefly
13 described here for the reader's convenience.

14 **3.1 Materials**

15 To understand the influence of screw element geometry on breakage probability for
16 different granule sizes, breakage experiments were first conducted using Play Doh (Hasbro
17 Inc., USA) spheres of different diameters. For the CEs, Play Doh spheres with diameters of
18 1.0 ± 0.1 mm, 2.0 ± 0.1 mm, 3.0 ± 0.1 mm, and 4.0 ± 0.1 mm were prepared. For the DMEs,
19 spheres of diameter 1.0 ± 0.1 mm, 2.0 ± 0.1 mm, and 3.0 ± 0.1 mm were prepared. Twenty
20 Play Doh spheres were prepared for each diameter.

21 The effects of material properties and process parameters on granule breakage
22 characteristics were studied using pellets prepared from model powders and liquid binders.
23 Glass ballotini (Potters Industries LLC, OH, USA) with five size ranges, i.e., 0-10 μ m, 63-90 μ m,
24 125-128 μ m, 180-250 μ m, and 355-500 μ m, were selected as the model powder material
25 due to its well-controlled properties. A Malvern Mastersizer 2000 (Malvern, UK) was used to
26 measure the size distribution of the glass ballotini using water as the wet dispersing medium.
27 The particle size distribution of the glass ballotini with the aforementioned five size ranges
28 can be found elsewhere [44]. Two model binders of different viscosities were used, namely,
29 silicone oil (Sigma-Aldrich Corp, MO, USA) and a glycerol solution (Sigma-Aldrich Corp., MO,
30 USA), the viscosities of which were 64 Pa.s and 0.7 Pa.s, respectively. Twenty cylindrical

1 pellets (diameter = height) were prepared for each model material system, having diameters
2 of 2 mm and 3 mm, using a Natoli punch and die set and an Instron ElectroPlus E1000 to
3 punch the pellets. Two replicate breakage experiments were performed for the 3 mm
4 pellets in conveying and distributive mixing elements, and 2 mm pellets in distributive
5 mixing elements as summarized in Table 1. The details of the pellet preparation method are
6 described in previously published work [5]. It is important to note that breakage is a
7 probabilistic process and a statistically significant number of pellets should be used to
8 account for the randomness in the breakage of the pellets. In this work, we have not
9 explored the effect of sample size of feed pellets on the scatter in the data. A sample size of
10 twenty feed pellets was used. It is worth noting that previously published breakage-only
11 experiments in high shear granulation literature have also used twenty feed pellets for each
12 experiment [50, 51]. For future studies, we recommend performing studies with a larger
13 sample size to refine the data.

14 The dynamic yield strength (DYS) of Play Doh and the model materials was measured using
15 an Instron ElectroPlus E1000. As discussed in Section 1, the mechanical behaviour of wet
16 granules resembles an elasto-plastic material. The material undergoes elastic deformation
17 until the stress reaches the dynamic yield strength value, following which, the material
18 plastically deforms and the granule is considered broken [45]. The details and results of the
19 dynamic yield strength measurement are given in a previous publication [5].

20 **3.2 Breakage-isolating experiments**

21 The breakage-isolating experiments [5] were carried out in a Thermo Fisher Scientific
22 EuroLab 16 mm Twin Screw Granulator with 25:1 length-to-diameter. The TSG barrel length
23 is 380 mm and is composed of six 60 mm zones and one 20 mm zone at the end. A
24 combination of conveying and distributive mixing elements are used in the experiments. The
25 experimental set up is shown in [Figure 1](#). For the CE breakage experiments, all six 60 mm
26 zones and the 20 mm zone are comprised of conveying elements. Both the powder and the
27 pellet are fed from zone 4 for the CE breakage specific experiments. For the DME breakage
28 experiments, the six 60 mm zones are comprised of conveying elements and the 20 mm
29 zone consists of the three DME pairs and a part of the adjacent conveying element. For the
30 DME experiments, the powder is fed from zone 4 whilst the pellet is fed from an aperture in
31 the middle of the 20 mm section in front of zone 1 to ensure that the pellets only

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1 experience the DME zone. In all of these experiments microcrystalline cellulose (MCC) was
2 used as the surrounding free flowing carrier powder medium to simulate the powder fill in
3 the twin screw granulator. The powder feed number (given in equation 1) incorporates the
4 feed rate of MCC in the granulator and the screw speed to evaluate the effects of process
5 parameters on the breakage behaviour in conveying and distributive mixing elements.

6 Figure 1. Schematic of the experimental setup using conveying and distributive mixing
7 elements (reproduced from Pradhan et al. [5])

8 The experiments were performed at three screw speeds (200 RPM, 400 RPM, and 800 RPM)
9 and two MCC feed rates (2 kg/h and 4 kg/h), which results in three different powder feed
10 numbers (PFN = 0.011, 0.022, and 0.045) [23].

11 For 3 mm pellets in conveying elements, previously performed work [5] showed that the
12 breakage probability at a PFN of 0.022 (resulting from a screw speed of 400 RPM and
13 powder feed rate of 4 kg/h, as given by equation 1) was a function of the material DYS.
14 Hence, breakage experiments at low and high PFN were performed to understand the
15 effects of process parameters on the breakage probability. Furthermore, an additional
16 breakage experiment was performed at the center point PFN of 0.022, albeit using different
17 individual values of the screw speed and powder feed rate to investigate if the results
18 depend on individual values of the process parameters.

19 We have previously shown that 2 mm pellets in conveying elements did not show breakage
20 at a PFN of 0.022 [5]. Hence, the breakage experiment was performed at a larger value of
21 PFN (and, thus, a larger fill level in the granulator) to understand if doubling the fill
22 enhances breakage.

23 Likewise, breakage experiments for 2 mm pellets in distributive mixing elements were
24 performed at low, center point, and high PFNs, and an additional experiment was
25 performed at a PFN of 0.011 but with different values of the individual screw speed and
26 powder feed rate. For 3 mm pellets in distributive mixing elements, previously performed
27 breakage experiments at the center point PFN showed complete breakage of the pellets
28 regardless of material strength [5]. Hence, an additional breakage experiment was

1 performed at a low PFN to observe if lowering the PFN results in a reduction of breakage for
2 the 3 mm pellets.

3 The experimental design of the breakage experiments using model granular materials is
4 summarized in [Table 1](#).

5 The pellet remnants and the MCC powder were collected at the outlet of the granulator for
6 breakage probability and breakage fragment distribution analysis. The breakage probability
7 was measured by counting the number of survivor pellets out of the twenty feed pellets.
8 Each broken pellet constitutes a 5% breakage probability. The breakage size distribution
9 was measured using a $\sqrt{2}$ series of sieves from 0.5 mm to 2.8 mm.

10 Table 1. Experimental design of the breakage specific experiments in CEs and DMEs

11 3.3 Results

12 In this section, the results from the breakage-isolating experiments that are used to develop
13 the breakage kernels are described. The experiments focused on the influence of material
14 properties and screw element geometry on the breakage probability and daughter size
15 distribution have been previously published [5]. The following section describes the
16 development of a breakage kernel using this previously published data [5] and additional
17 experimental data.

18 3.3.1 Breakage probability in conveying elements

19 The effect of granule size on breakage probability was first investigated in CEs with a PFN
20 equal to 0.022 using Play Doh spheres. The breakage probability results for the Play Doh
21 spheres from three replicates are shown in [Figure 2](#).

22 Figure 2. Breakage probability of a Play Doh sphere as a function of size in CEs (reproduced
23 from Pradhan et al. [5])

24 There is no breakage for a sphere smaller than 3 mm while a 4 mm sphere has a 100%
25 breakage probability. For the elements used in the experiments described in this paper, the
26 maximum granule size in the CEs was 3.49 mm as measured using CAD analysis [5].

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1 Considering the calculated maximum sphere size is 3.49 mm in CEs, it is expected that the
2 breakage probability would be 100% above this critical value.

3 The effect of material properties and process parameters on granule breakage was
4 measured using model material pellets of different DYS values, of size 2 mm and 3 mm, as
5 per the experimental design in [Table 1](#). The breakage probabilities of 3 mm and 2 mm
6 pellets are plotted as a function of DYS for varying PFN for CEs in [Figure 3](#) and [Figure 4](#). In
7 [Figure 3](#), the breakage probability of a 3 mm pellet decreases when the DYS is increased
8 until 9 kPa. The breakage probability drops to almost zero when the pellets are stronger
9 than 9 kPa irrespective of the operating conditions. The breakage probability increases with
10 increasing PFN, particularly for weaker materials, i.e., smaller DYS values. It is worth noting
11 that the breakage probability is similar for the same PFN, even though the screw RPM and
12 mass flow rate are different. It is important to note that one broken pellet accounts for 5%
13 breakage probability and, considering the probabilistic nature of granule breakage, small
14 differences observed in the data for the same PFN can arise from the randomness of the
15 breakage itself. There is no breakage of 2 mm granules regardless of the DYS and PFN
16 (Figure 4). The weakest material shows a 5% breakage probability for a PFN of 0.022.
17 However, we consider this point as an outlier because the same material showed zero
18 breakage for a larger PFN and, thus, a larger fill level. The weakest material is subject to the
19 largest scatter in the data because the material strength is low.

20 The most important parameter in determining granule breakage is the size of the granule.
21 All granules greater than the geometrically determined maximum size (3.49 mm) break.
22 Just below the critical size (3 mm), granule breakage is a function of granule strength (DYS)
23 and powder flow number (PFN). Well below the critical size (2 mm), no breakage occurs
24 regardless of material properties and process parameters.

25 Figure 3. Breakage probability of 3 mm pellets as a function of DYS for varying PFN using
26 CEs

27 Figure 4. Breakage probability of 2 mm pellets as a function of DYS for varying PFN using
28 CEs

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1 3.3.2 Breakage probability in distributive mixing elements

2 [Figure 5](#), shows the breakage probability of the Play Doh spheres as a function of size at a
3 screw speed 400 RPM and powder feed rate of 4 kg/h (PFN=0.022) [5]. The breakage
4 probability in DMEs increases gradually from 0 to 100% breakage as size increases from 1
5 mm to 3 mm. In contrast, the breakage probability in CEs over the size range from 1 mm to
6 3 mm is observed to be nearly zero. The maximum granule size in the DMEs is 3.19 mm
7 using a CAD model analysis [5]. The DME breakage probability is 100% at 3 mm, which is
8 close to the predicted critical size, confirming that the breakage pattern is strongly screw
9 geometry dependent.

10 Figure 5. Breakage probability of Play Doh spheres as a function of particle size in DME
11 (reproduced from Pradhan et al. [5])

12 The model material breakage specific experiments in DMEs were carried out using 2 mm
13 and 3 mm pellets. The breakage probability of the 2 mm model materials as a function of
14 DYS is given in [Figure 6](#), for three PFNs (as described in [Table 1](#)). Similar to the CEs, the
15 breakage probability increases with decreasing DYS and increasing PFN. The influence of
16 PFN is more pronounced for weaker materials.

17 Figure 6. Breakage probability of 2 mm pellets as a function of DYS for varying PFN using
18 DMEs

19 [Figure 7](#), displays the breakage probability of 3 mm pellets as a function of DYS and PFN. The
20 breakage probability is 100% irrespective of the DYS and PFN. This result is due to the 3 mm
21 pellets being at approximately the DME geometric limit and, thus, are subject to
22 fragmentation.

23 Figure 7. Breakage probability of 3 mm pellets as a function of DYS for varying PFN using
24 DMEs

25 For both CEs and DMEs, the breakage probability is a function of PFN, DYS, and granule size.
26 Granules at or above the maximum critical size will break. For granules slightly smaller than

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1 the maximum critical size, the breakage probability increases with decreasing DYS and
2 increasing PFN. In particular, the effect of PFN is more pronounced for the weaker materials.
3 Small granules do not break, independent of material properties and process conditions.
4 The breakage pattern is observed to be strongly screw geometry dependent. Any
5 mechanistic TSG breakage kernel should be consistent with these findings. In particular, we
6 expect the breakage kernel must be screw element specific.

7 3.3.3 Breakage fragment size distribution

8 The breakage fragment size distributions of pellets broken in CE and DME elements have
9 been reported in a previous study [5]. It was concluded from those breakage fragment
10 distributions that chipping and fragmentation were the dominant breakage mechanisms in
11 the conveying elements and distributive mixing elements, respectively. Here, the daughter
12 size distribution in each screw element is presented and will be used to model the breakage
13 function. The data points shown are the average of two replicate measurements with the
14 scatter bars showing the range. For each replicate, the pellets with five ranges of DYS are
15 sampled and collected for breakage fragment size measurement. There are 10 datasets for
16 CEs and 16 datasets for DMEs in two replicates. The data for the individual replicates is
17 provided in the supplementary information. The large scatter bars are due to the
18 randomness of granule breakage and the small masses in each sieve cut. The breakage size
19 distributions of 3 mm pellets in CEs and DMEs are shown in [Figure 8](#), and [Figure 9](#),
20 respectively. The PFN for the CE data is 0.045 at a feed rate of 4 kg/h and screw speed of
21 200 RPM while the PFN for the DME data is 0.022 at a feed rate of 4 kg/h and screw speed
22 400 RPM.

23 Figure 8. Breakage fragment distribution from 3 mm pellets in CEs (PFN = 0.045) (a) Mass-
24 based particle size distribution (b) Mass-based cumulative size distribution (Data from [44])

25 Figure 9. Breakage size distribution of breakage particle in DMEs (PFN = 0.022) (a) Mass-
26 based particle size distribution (b) Mass-based cumulative size distribution (data from [44])

27 Due to the chipping mechanism in CEs, the fragment frequency distribution in [Figure 8a](#) is
28 bi-modal with one peak at 0.605 mm and the other peak at 2.4 mm in the size fraction
29 immediately smaller than the parent pellet. On the other hand, [Figure 9a](#) shows the mono-

1 modal fragment frequency distribution for DMEs with a mode at 1.7 mm. The DMEs
2 produce extensive granule breakage as the granule breaks into small fragments. In
3 comparison, the CEs cause granule chipping, as indicated by the bimodal distribution. A
4 good breakage model must capture these differences in fragment size distribution.

5 **4 Breakage kernel development**

6 Compared to other rate processing kernels, the published TSG breakage kernels for PBM are
7 mainly borrowed from milling or high shear granulation, which results in a discrepancy in
8 the type of stressing events in a TSG and, thus, inaccuracies in the prediction of granule size
9 distributions. The findings from the breakage specific tests using the CEs and DMEs indicate
10 that breakage probability is a function of the geometry of the screw element, PFN, and
11 material DYS. There are currently no existing breakage kernels in TSG that capture these
12 parameters in the selection and breakage functions. Hence, the development of TSG
13 breakage kernels incorporating these parameters is needed in order to improve the
14 predictive capacity of TSG PBMs. This section presents the development of selection and
15 breakage functions based on the findings from the breakage specific experiments for the
16 two screw elements.

17 **4.1 Selection function (SF) development**

18 4.1.1 Breakage pattern in TSG

19 Pradhan et al. [5] proposed breakage mechanisms in the TSG, i.e., chipping in CEs and
20 fragmentation in DMEs. Chipping is subsurface material removal from the particle due to
21 local damage, such as edge or corner detachment. Fragmentation denotes the splitting of
22 the original particle into several pieces. Based on the results in Section 3, we propose two
23 different functions for breakage probability as a function of size for the different element
24 types and breakage mechanisms, shown schematically in [Figure 10](#).

25 [Figure 10](#). Schematic outline of two breakage patterns. (a) chipping in CEs and (b)
26 fragmentation in DMEs

27 In [Figure 10\(a\)](#) (CE, chipping), the breakage probability increases with increasing granule size
28 between the minimum and maximum breakage sizes. The breakage probability

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1 corresponding to chipping is reported to follow a power law in the literature [46] before a
 2 sudden jump to 100% breakage due to the geometric constraints in the screw element. In
 3 [Figure 10\(b\)](#) (DME, fragmentation), the breakage probability increases smoothly for sizes
 4 greater than the minimum breakage size until reaching 100% at the maximum breakage size.
 5 The model is described using a Weibull law expression, which is often used for
 6 fragmentation probability distributions [46]. For both CEs and DMEs, there exist two critical
 7 sizes: the minimum breakage size x_{lc} and the maximum breakage size x_{uc} . The minimum
 8 breakage size x_{lc} is a material dependent parameter, above which particle breakage takes
 9 place. The maximum breakage size x_{uc} is a screw-dependent parameter, which is defined as the
 10 largest available gap size allowing particles to pass through and remain unbroken. It should
 11 also be noted that the breakage size region (x_{lc}, x_{uc}) in DMEs is usually broader than that in
 12 CEs due to more intensive stressing events in DMEs leading to a smaller x_{lc} .

13 4.1.2 SF in conveying elements

14 The breakage rate S is found by multiplying the number of breakage events per unit time
 15 and the breakage probability:

$$S = N * P_x \quad (6)$$

16 where N is the number of breakage events per unit time (proportional to the screw speed)
 17 and P_x is the breakage probability relevant to the process parameters and particle
 18 properties [47].

19 The breakage probability P_x was found to increase with an increase in PFN and granule size
 20 and a decrease in DYS. Taking these parameters into account along with the upper and
 21 lower granule size limits for breakage, an empirically-derived selection function for
 22 conveying elements may be written as:

$$P_x = \begin{cases} 1 & x \geq x_{uc} \\ a * \exp\left(-\frac{DYS}{b} * \frac{1}{PFN}\right) * (x/x_{uc})^c & x_{lc} < x < x_{uc} \\ 0 & x \leq x_{lc} \end{cases} \quad (7)$$

23 where the parameters a , b , and c are fitting constants.

1 The fitting results of Eq. (7) against the breakage data for 3 mm pellets of nine different
2 model materials in the TSG with only CEs subject to two feed rates and three screw speeds
3 are shown in [Figure 11](#).

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4 Figure 11. Predictive breakage probability vs. breakage dataset for 3 mm pellets in CEs

5 Relatively good agreement is observed between the predictions and data for the sets of
6 conditions. The parameters a , b , and c for each set of data were estimated using a
7 nonlinear least squares method in MATLAB based on a global fitting of the four data sets.
8 Global fitting herein means the estimation of parameters a , b , and c based on the four
9 datasets of breakage probability subject to varying rotary speed and feed rate (varying PFN
10 as a result). This method is different from that of parameter estimation using an individual
11 dataset, resulting in four sets of different values of a , b , and c . The decision to use global
12 fitting is made based on the model universality to show its predictive powder applied to all
13 of the operational conditions.

14 Note that the parameters a and c are combined as $\hat{a} = a * (x/x_{uc})^c$ for fitting since the
15 pellet size is constant at 3 mm. The fitting parameters of \hat{a} and b are tabulated in [Table 2](#).
16 The minimum breakage size for the model material x_{lc} is taken as 2 mm and the maximum
17 breakage size x_{uc} is 3.49 mm. The confidence interval of the fitting parameters is 95% by
18 default unless stated elsewhere.

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19 Table 2. The fitting parameters of \hat{a} and c in CEs

20 The predicted and measured breakage probabilities in Figure 11 are plotted again in [Figure](#)
21 [12](#), with the measured breakage probabilities on the horizontal axis and predicted values on
22 the vertical axis. It is observed that the majority of the data follows the 45 degree line,
23 indicating that the proposed fit is a good one.

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24 Figure 12. Fitted vs. measured breakage probability for 3 mm pellets in CEs

1 4.1.3 SF in distributive mixing elements

2 The breakage probability in DMEs is found to be a strong function of the screw geometry,
3 DYS, and the powder feed number (PFN). We propose the following empirically-derived
4 three parameter model for the breakage selection function in DMEs:

$$P_x = \begin{cases} 1 & x \geq x_{uc} \\ 1 - a * \exp\left(-PFN * \frac{b}{DYS} * \left(\frac{x}{x_{uc}}\right)^c\right) & x_{lc} < x < x_{uc} \\ 0 & x \leq x_{lc} \end{cases} \quad (8)$$

5 As with Eq. (7), the parameters a , b , and c are fitting parameters.

6 The fitting results of Eq. (8) against the measured DME breakage data for two feed rates and
7 three screw speeds are shown in [Figure 13](#). The minimum breakage size is 1.0 mm based on
8 [Figure 5](#), and the maximum breakage size is measured as 3.18 mm from the screw element
9 geometry. Good agreement between the predictions and the experimental data is observed.

10 Note that the parameters b and c are combined as $\hat{b} = b * (x/x_{uc})^c$ for the fit since the
11 pellet size is constant at 2 mm. The parameter values for a and \hat{b} are summarized in [Table 3](#),
12 using a global fitting method based on the four DME data sets.

13 Figure 13. Fitted breakage probability predictions vs. measurements for 2 mm pellets in
14 DMEs

15 Table 3. The fitting parameters of a and \hat{b} in DMEs

16 [Figure 14](#), plots the same data in Figure 13, but as the predicted breakage probability as a
17 function of the measured breakage probability. The data following the 45 degree line
18 indicates that the proposed fit is a good one.

19 Figure 14. Fitted vs. measured breakage probability for 2 mm pellets in DMEs

20 Note that the developed model of breakage probability has the ability to account for the
21 breakage of granules formed by other rate processes such as coalescence or nucleation in
22 the real twin screw granulator system. This will be achieved by defining the relevant process
23 kernels including, but not limited to, coalescence and breakage in an overarching population

1 balance framework. Once the granule size reaches or exceeds the minimum breakage size,
2 x_{lc} , granule breakage is subject to the selection function $S = N * P_x$. Development of the
3 full PB framework is beyond the scope of this paper, but the breakage kinetic model is
4 presented in a way that makes its directly applicable within such a framework.

5 4.2 Breakage function (BF) development

6 The breakage function describes the size distribution of fragments and number of fragments
7 in a single breakage event and, thus, is a key component in a population balance model. A
8 detailed description of breakage functions proposed in the literature has been provided in
9 [46].

10 4.2.1 Breakage size distribution in TSG

11 [Figure 15](#) shows schematically the expected breakage functions for CEs (chipping) and DMEs
12 (fragmentation). Chipping leads to a bimodal breakage function distribution where the large
13 mode is only slightly smaller than the original particle size and the small mode represents
14 the small chips or fines ([Figure 15a](#)). In contrast, fragmentation ([Figure 15b](#)) results in a wide
15 range of particle sizes and a unimodal distribution with the mode in the breakage function
16 distribution well below the original particle size.

17 Figure 15. A generic breakage size distribution for chipping in CEs and fragmentation in
18 DMEs

19 4.2.2 Modified Weibull distribution in CEs and DMEs

20 Previous studies have used a simple breakage function for modelling TSGs, with the granule
21 assumed to break into two halves with equal volume regardless of the applied stress [48].
22 The simplicity of such a breakage function limits the model's accuracy. However, the single
23 particle breakage data presented here ([Figure 8](#) and [Figure 9](#)) can be used to develop a
24 more sophisticated breakage function. A modified Weibull distribution is proposed to
25 describe the breakage fragment size distribution from DMEs via fragmentation,

$$B_x = 1 - \exp\left(-a * \left(\frac{x}{x_{uc}}\right)^b\right) \quad (9)$$

1 where B_x is the cumulative size distribution and a is the scale parameter and b is the shape
2 parameter in the Weibull function.

3 To represent the distribution of coarse and fine particles that result from chipping in CEs, a
4 bimodal distribution is proposed,

$$B_x = \nu B_{x1} + (1 - \nu) B_{x2} \quad (10)$$

5 where ν is the proportion of fine and coarse particles produced in Eq. (10) and B_{x1} and B_{x2}
6 are the modified Weibull distributions identical in form to Eq. (9).

7 To test the accuracy of the proposed breakage function in Eq. (9) and Eq. (10), the fitting
8 results of the breakage fragment size distributions of 3 mm granules, based on the breakage
9 size distribution dataset in [Figure 8](#), and [Figure 9](#), are shown in [Figure 16](#) and [Figure 17](#). The
10 results indicate that the modified Weibull distribution gives good agreement in both
11 conveying and distributive mixing elements. The fitting parameters and goodness of fit are
12 summarized in [Table 4](#). The maximum breakage size x_{uc} is defined as 3.5 mm (rounded from
13 3.49 mm) and 3.2 mm (rounded from 3.18 mm). Note that there are extensive datasets of
14 breakage particle distribution in the literature and, thus, it would be worthwhile to make a
15 comprehensive assessment of the developed breakage functions against the literature data.

16 Figure 16. Modified Weibull prediction of breakage size distribution using conveying
17 elements

18

19 Figure 17. Modified Weibull prediction of breakage size distribution using distributive
20 mixing elements

21 Table 4. Fitting parameters of the modified Weibull distribution in the conveying and
22 distributive mixing elements

23 [Table 4](#) demonstrates that the two fitting parameters in the modified Weibull distribution
24 are sufficient to produce a good fit to the experimental dataset. There may exist other
25 breakage size distribution forms that fit the experimental data, but the proposed forms are
26 accurate and simple to implement.

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1 5 Parametric study

2 The input parameters in the proposed breakage kernels (selection function and breakage
3 function) can be categorized into four types: material-dependent parameters (DYS and the
4 minimum breakage size), a process-dependent parameter (PFN), screw-dependent
5 parameters (maximum breakage size), and fitting parameters (a , b , and c). The parametric
6 study in this work employs a univariate approach to quantifying the influence of the first
7 three types of parameters on the selection and breakage functions. A reference case is first
8 defined based on the breakage results from pellets. Next a univariate analysis of selected
9 parameters is carried out and their influences on the selection function are summarized. In
10 terms of the parametric study on the breakage function, the maximum breakage size in Eqs.
11 (9) and (10) is employed for univariate analysis whereas the fitting parameters a , b , and v
12 are kept constant with their values summarized in Table 4.

13 5.1 Reference parameters

14 Our reference case study is based on pellets as the reference material. The reference values
15 for the input parameters are listed in Table 2 and Table 3. It should be noted that the CE and
16 DME power exponents c must be arbitrarily specified in the current parametric study since
17 experimental data sets for varying granule size in the range $x_{lc} < x < x_{uc}$ are not available.
18 For pellet size 3 mm in CEs, we assume that the power exponent c is 2 in the expression
19 $\hat{a} = a(x/x_{uc})^c$ giving a value of $a = 0.4072$ when $\hat{a} = 0.9162$. Likewise, for the lumped
20 parameter $\hat{b} = b * \left(\frac{x}{x_{uc}}\right)^c$, the exponent c is assumed to be 10 giving a value of $b = 0.0303$
21 when the lumped parameter is $\hat{b} = 31.0142$. The fitting parameters a , b , and c are
22 summarized in Table 5, based on the fitting of the data in Figure 3 and Figure 6. The
23 maximum breakage size in CEs and DMEs are determined from the CAD model analysis, for
24 which the data is shown in Figure 2 and Figure 5.

25 Table 5. The reference values of the input parameters for pellets in CEs and DMEs

26 The predicted breakage probabilities using Eq. (7) and Eq. (8) in a CE and DME, respectively,
27 are depicted in Figure 18a and Figure 18b. Note that the symbols in Figures 18 (a) and 19(b)
28 are experimental data for comparison to the proposed breakage model.

1 Figure 18. Breakage model prediction of pellet (a) in the conveying and (b) distributive
2 mixing elements

3 The selection function is capable of predicting the effect of granule size on breakage
4 probability irrespective of the breakage mode in different screw elements. However, the
5 fitting curve with the input values in Table 5 is least accurate at the smallest breakage
6 probability, which is consistent with the finding in Figure 14.

7 **5.2 Influence of critical breakage size range**

8 The critical breakage size range is bounded by the material-dependent minimum breakage
9 size x_{lc} and the screw-dependent maximum breakage size x_{uc} . The variation for the
10 minimum breakage size is chosen as $\pm 20\%$ of the reference value. The impact of varying x_{lc}
11 for conveying elements between 1.6 and 2.4 mm on the breakage probability is shown in
12 [Figure 19a](#). The impact of varying x_{lc} for distributive mixing elements between 0.8 and 1.2
13 mm on the breakage probability is shown in [Figure 19b](#). In the CE, there is relatively little
14 breakage below x_{uc} and the breakage probability is insensitive to x_{lc} . In contrast, the
15 predicted breakage probability is a strong function of x_{lc} for DMEs. This trend also occurs
16 for different values of the exponent c .

17 Figure 19. Influence of minimum breakage size on breakage probability (a) in CE and (b) in
18 DME

19 The maximum critical size is a geometry-defined parameter that is determined by the
20 largest gap size through which the granule can pass. For comparative purposes, the
21 variation for the maximum breakage size is chosen as $\pm 20\%$ of the reference value.
22 Therefore, the ranges of maximum breakage size are chosen as 2.8 mm to 4.2 mm in the CE
23 and 2.56 mm to 3.64 mm in the DME. The input values of fitting parameters a , b , and v are
24 from Table 4. [Figure 20](#) displays the influence of maximum breakage size on the cumulative
25 granule size distributions in the CEs and DMEs.

26 Figure 20. Influence of maximum breakage size on the cumulative breakage size distribution
27 (a) in CEs and (b) in DMEs

1 The plots indicate that the maximum critical size has a moderate effect on the breakage
2 function. Increasing the maximum critical size moderately increases the proportion of larger
3 granules. However, the increase of maximum critical size in CEs has a bigger influence on
4 the larger particles than the fine particles.

5 **5.3 Influence of PFN**

6 The PFN is a function of powder feed rate, powder bulk density, shaft angular velocity, and
7 the barrel diameter. The influence of PFN on the granule size distribution was found to be
8 minor for the granule size distribution D_{10} and D_{50} , but statistically significant for D_{90} [49].
9 The influence of PFN on the breakage probability in the CE and DME is shown in [Figure 21a](#)
10 and [Figure 21b](#). Increasing PFN results in increasing breakage probability in both the CE and
11 DME. The influence of PFN on the breakage probability is more pronounced in the DME,
12 which is consistent with the observation from the breakage specific experiments.

13 [Figure 21. Influence of PFN on the breakage probability \(a\) in CE and \(b\) in DME](#)

14 **5.4 Influence of DYS**

15 The DYS of material is an important indicator affecting granule deformation in a TSG [5, 44].
16 There exists a threshold of DYS above which the granule breakage is merely dependent on
17 the screw geometry (approximately 9 kPa in the current work). The influence of DYS on the
18 breakage probability in CEs and DMEs is shown in [Figure 22a](#) and [Figure 22b](#), respectively. It
19 is found that the DYS plays a negative role on the breakage probability in both the CE and
20 DME. The breakage propensity in the DME is much larger than that in the CE using the same
21 value of the DYS. In particular, the breakage probability of a pellet with a 9 kPa DYS is nearly
22 zero in the CE regardless of the pellet size. However, the breakage probability of a pellet
23 with a DYS equal to 9 kPa increases to 100% when the pellet size increases to 3 mm.

24 [Figure 22. Influence of DYS on breakage probability \(a\) in CE and \(b\) in DME](#)

25 The influences of minimum breakage size, maximum breakage size, DYS, and PFN on the
26 selection function and the breakage function are summarized in [Table 6](#),

27 [Table 6. Influence of input parameters on the developed breakage kernel](#)

1 It should be noted that interactive effects play an important role in the final granule
2 attributes, which cannot be achieved by OAT (one-at-a-time) analysis. However, as a
3 prelude to explore the interactive effects of the parameters in a PBM, OAT analysis serves to
4 identify the effects of individual parameters on the final attribute by singling out the most
5 influential parameters.

6 A Global System Analysis (GSA) is a valuable tool for an interactive analysis, but it is not
7 considered here due to the research scope in this paper. However, a GSA for the PBM
8 parameters is currently under investigation by incorporating the new breakage models in a
9 PBM modelling package for TSG.

10 **6 Discussion**

11 A breakage kernel in the population balance modelling of a TSG was developed based on
12 breakage specific experiments. The advantages of the developed kernel include the
13 influence of different screw elements, the piecewise breakage probability based on the
14 critical breakage size, and the incorporation of key parameters such as DYS and PFN.
15 However, several issues remain to be addressed:

16 1. The breakage specific experiments demonstrate that the breakage probability increases
17 with an increase in PFN and a decrease in DYS. Although the effect of PFN and DYS are
18 incorporated in the developed selection function, the challenge in the breakage model
19 development is whether it is possible to develop a unified selection function accounting for
20 both chipping and fragmentation in different screw elements.

21 2. Although the modified Weibull distribution was developed to describe the breakage size
22 distribution, further efforts are required to provide insights between the two Weibull
23 parameters and mechanical property (DYS) as well as the process parameter PFN. There are
24 many breakage functions in the literature and their applicability in TSG has not yet been
25 fully tested. The majority of the breakage functions display a mono-modal distribution of
26 breakage particle size while less attention is given to bi-modal distributions. A
27 comprehensive assessment of mono-modal and bi-modal size distributions will be valuable
28 for the practical guide of defining the most appropriate breakage selection in PBM.

29 3. The breakage specific experiments in TSG were carried out in CEs and DMEs. Due to the
30 discrete nature of the particle size, the chipping data of a granule between 3.0 mm and 3.49

1 mm is unavailable. Moreover, there is no literature data available for breakage-isolated experiments for CEs. In the current work, arbitrary but reasonable input values were assumed for the exponent c in the CE and DME breakage probability functions. Additional breakage specific experiments of varying particle size are still required to validate this assumption. Breakage-isolated experiments in kneading elements (KEs) should also be carried out to investigate the applicability of the developed breakage kernel as KEs are a key screw element widely used in TSGs.

4. The parametric study of the input parameters in the developed breakage kernel indicates that the influence of DYS and PFN on the selection function is more pronounced in a DME compared to a CE. However, the influence of these input parameters on the granule product attributes in the context of PBM are not yet fully identified and a systematic analysis of the input parameters in the rate process kernels is still scarce. The category of the PBM input parameters should also be clarified to reduce the modelling uncertainty. Hence, a global sensitivity analysis of full factorial parameters in the rate process kernels should be performed to identify the significance of each parameter on the granule product attributes.

7 Conclusions

This paper has presented the breakage kernel development in the population balance modelling of twin screw granulation. It was found that the breakage probability increases with an increase in PFN and a decrease of DYS. The breakage probability is dependent on the screw geometry for material DYS values smaller than a threshold value (9 kPa), but independent of DYS and geometry above DYS = 9kPa. There exists a material dependent parameter, the minimum breakage size (x_{lc}), below which no breakage occurs and a screw geometry dependent parameter, the maximum breakage size (x_{uc}), above which all granules are broken. The breakage of particles takes place between the minimum breakage size and the maximum breakage size and the breakage size regime ($x_{uc} - x_{lc}$) is typically broader in DMEs than that in CEs.

A piecewise breakage selection function was used to describe the breakage probability in CEs and DMEs taking into account the material dependent parameters (DYS, granule size, and minimum breakage size), the process parameter PFN, and the screw dependent parameter (maximum breakage size). The selection function gave very good agreement with

1 the experimental observations in both the CEs and DMEs. A modified Weibull distribution
2 was used to describe the breakage size distribution for DMEs and gave a good fit to
3 experimental data. For CEs, a bimodal breakage size distribution was required to describe
4 the experimental data, reflecting that chipping is the predominant breakage mechanism for
5 CEs.

6 This work presents the first breakage model specifically developed for a TSG and
7 incorporates a mechanistic understanding of the process, particularly the role of screw
8 geometry. The model is suitable for incorporating into a population balance framework to
9 describe twin screw granulation.

10 **8 Nomenclature**

a	Fitting parameter, -
b_M	Breakage function, -
$B(v, t)$	Birth rate, $\text{m}^{-3}\text{s}^{-1}$
B_{break}	Birth rate of breakage, $\text{m}^{-3}\text{s}^{-1}$
B_{lay}	Birth rate of layering, $\text{m}^{-3}\text{s}^{-1}$
B_{nuc}	Birth rate of nucleation, $\text{m}^{-3}\text{s}^{-1}$
c	Fitting parameters, -
D	Screw diameter, mm
$D(v, t)$	Death rate, $\text{m}^{-3}\text{s}^{-1}$
D_{break}	Death rate of breakage, $\text{m}^{-3}\text{s}^{-1}$
$D_{m_p, nuc}$	Death rate of powder particles, $\text{kg m}^{-3}\text{s}^{-1}$
$M(v, t)$	Mass of granule with volume v at time t , kg
\dot{m}_{powder}	Feed rate of powder, kg/h

n	Population density of length function, m^{-3}
N	Number of breakage events, -
P_x	Breakage probability of particle size x , -
S	Breakage rate, s^{-1}
x	Particle size, mm
x_{lc}	Minimum breakage size, mm
x_{uc}	Maximum breakage size, mm
ν	Proportion of fines and granules, -
ω	Angular velocity of the shaft, $rads^{-1}$
ρ_{bulk}	Particle bulk density, $kg\ m^{-3}$
DYS	Dynamic yield strength, kPa
LSR	Liquid solid ratio,-
PFN	Powder feed number,-

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3 (CPI) for research under the project of Models for Manufacturing of Particulate Products.
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5 (DEM Solutions Ltd.), Johnson Matthey, Pfizer, Procter & Gamble, PSE (Process Systems
6 Enterprise), and the University of Edinburgh for their feedback and many helpful discussions.

7 **Appendix**

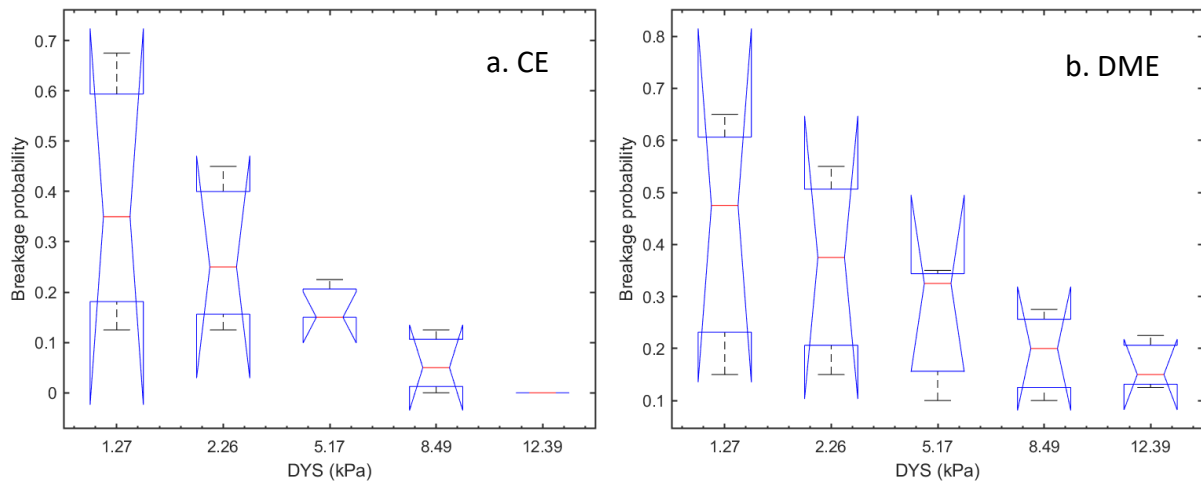
8 To support the conclusion that the influence of PFN is more pronounced for weaker
9 materials and in DMEs as compared to CEs, an ANOVA analysis was carried out to
10 corroborate the conclusion stated in this paper. The breakage probability subject to varying

- 1 DYS and PFN values are shown in Table A1 for CEs and Table A2 for DMEs, respectively. The
- 2 ANOVA analysis was performed based on the data in Tables A1 and A2.
- 3 Table A1 Breakage probability of pellet (3 mm) subject to varying DYS and PFN in DME

DYS (kPa) \ PFN	Breakage probability		
	0.011	0.022	0.045
12.38899	0	0	0
8.49463	0.125	0	0.05
5.16542	0.15	0.15	0.225
2.25964	0.125	0.25	0.45
1.27398	0.125	0.35	0.675

- 4 Table A2 Breakage probability of pellet (2 mm) subject to varying DYS and PFN in DME

DYS (kPa) \ PFN	Breakage probability		
	0.011	0.022	0.045
12.38899	0.125	0.225	0.15
8.49463	0.1	0.275	0.2
5.16542	0.1	0.325	0.35
2.25964	0.15	0.375	0.55
1.27398	0.15	0.475	0.65



1
2 Figure A1 Comparison of Kruskal-Wallis ANOVA analysis of PFN subject to varying DYS
3 in (a) CE and (b) DME

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