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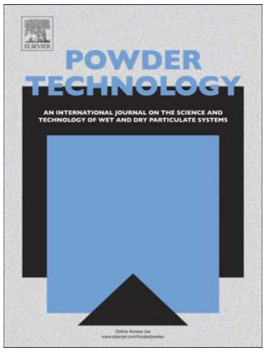

The use of positron emission particle tracking (PEPT) to study milling of roll-compacted microcystalline cellulose ribbons

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THE USE OF POSITRON EMISSION PARTICLE TRACKING (PEPT) TO STUDY MILLING OF ROLL-COMPACTED MICROCYSTALLINE CELLULOSE RIBBONS

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ABSTRACT

Milling is a critical process for controlling the properties of the granules produced by roll compaction. In the current study, the positron emission particle tracking (PEPT) technique was used to examine the milling kinematics of roll compacted ribbons at various milling speeds. Microcrystalline cellulose (MCC, Avicel PH-102) was used as the model feed material and a radioactive particle (tracer) was mixed with the MCC powder and roll-compacted to form sample ribbons. They were then milled using an oscillating mill at various speeds and the kinematics of the ribbons (trajectory, velocity, and occupancy) were quantitatively determined using PEPT. A close examination of the PEPT data reveals that, for milling MCC PH-102 ribbons using the oscillating mill considered in this study, the milling speed plays an important role: at low values, the milling process is dominated by cooperative motion of the ribbons with the blade (i.e. the speeds of the ribbons and the blade are similar, and the ribbons move along with the blade) and the ribbons are milled primarily by abrasion; as the speed increases the ribbons undergo more random motion involving collisions that results in an increase in ribbon breakage and hence an increase in the milling efficiency. It is shown that the PEPT technique is a useful technique for examining milling kinematics of roll compacted ribbons.

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KEYWORDS

Roll compaction, Milling, PEPT, Abrasion, Impact, Granulation.

1. INTRODUCTION

Dry granulation using roll compaction is a preferable granulation technique for powder blends that are sensitive to moisture or heat and it has been increasingly used in a number of industries, including pharmaceutical, agricultural and fine chemicals [1-10]. The process generally involves two stages: i) the compaction of fine powders into ribbons or flakes and ii) milling of roll compacted ribbons/flakes to produce granules. The first process stage (*i.e.* roll compaction) has been investigated extensively in the past two decades [1-10], while the study of milling is still in its infancy.

In practice, oscillating mills are commonly used together with a roll compactor to produce the desired granules [11-15]. An oscillating mill breaks compacted materials (*e.g.* roll compacted ribbons) into granules that pass through a wire mesh screen [11]. The screen forms a milling chamber, in which reciprocating blades with a fixed rotating angle causes the feed ribbons to be milled, as illustrated in Fig.1. The properties of the milled granules are controlled by that of the ribbons, the screen size, the milling speed, and the rotational angle of the blade [12]. Abraham and Cunningham [13] reported that an oscillating mill could be used as a downstream granulator to provide a composition with improved flow characteristics and a reduced amount of fine particles. They showed that these devices produce coarser granules compared to a Comil or Fitz mill with the same mesh size. Sakwanichol *et al.* [14] evaluated the granule properties obtained from an oscillating mill and a roll mill, and investigated the effects of milling conditions on the granule properties. When an oscillating mill was used, four process parameters, *i.e.* milling speed, oscillating angle, aperture of mesh screen and rotor type, were examined, while for the investigation with the roll mill, the throughput, speed ratio in both the first and second stages, roll gap in both stages and roll surface texture were assessed. The granular size distributions obtained with both mills at various process conditions were obtained and examined. They showed that the granule size distribution depends significantly on the process parameters examined when an oscillating mill was used. Using an oscillating mill, the present authors investigated experimentally the effects of solid fraction and fracture energy of roll compacted MCC (Avicel PH102) ribbons and the milling speed on the granule size distributions and the milling performance [15]. The milling performance was characterised using the critical number of milling cycles that was obtained from the evolution of mass throughput. It was shown that the fracture energy of the ribbon increases with its solid fraction. The critical number of milling cycles increases as the ribbon solid fraction and hence the fracture energy increases, implying a decreasing milling performance. It was found that the mean granule size increases linearly with the ribbon solid fraction and the fracture energy but decreases with the milling speed.

Although the milling of roll-compact ribbons has attracted increasing attention over the last 5 years, previous studies were primarily focused on the influence of ribbon properties and milling conditions on the properties of the granules. There is still a lack of mechanistic understanding of the milling process, and little is known about the dominant fracture mechanisms during the milling process. Therefore, in the current study, the milling of roll-compacted ribbons with an oscillating mill is explored using the PEPT technique with the aim of to providing an improved understanding the milling mechanisms.

2. MATERIALS AND METHODS

The feed powder was microcrystalline cellulose (MCC) of the grade Avicel PH-102 (FMC Corporation, USA). It is a white, odourless and tasteless powder with excellent flow property, which is commonly used in the pharmaceutical industry as an excipient. The mean particle size of MCC PH-102 is around 100 µm, and the particles are of needle shape.

2.1. Roll compaction

The feed powder was compacted using a laboratory scale instrumented roll compactor (Fig. 2) with smooth stainless steel rolls (46 mm in width and 100 mm in radius) [4-10]. Unlike most roll compactors used commercially that have floating rolls and the roll compaction can be controlled by the compression pressure (or force), this instrumented roll compactor has fixed rolls and the controllable process parameters are roll gap and roll speeds, from which various roll compression pressures are induced [4-8]. The roll compactor is equipped with a rectangular cross-section gravity powder feeding hopper. For the experiments reported in this study, the hopper was first manually fed with the feed powder and the excess levelled gently so that an initial constant volume of powder was used for each test. Also in the current study, the minimum roll gap and the roll speed were fixed at 1.1 mm and 1 rpm, respectively, so that ribbons with consistent properties were produced for the milling study.

2.2. Milling

An oscillating mill (AR 401, Copley, UK, Fig. 3a) was employed for milling the roll-compacted ribbons since this type of mill is commonly combined with roll compactors in industrial manufacturing. The milling chamber is formed with an exchangeable screen mesh of various screen sizes. In the current study, only the milling experiments with a screen mesh size of 630 µm were reported, we refer the readers to Yu (2013) for details on milling with other screen mesh sizes. In the milling chamber, there is a milling blade with 4 arms made of stainless steel. Each milling blade has a radius of 40 mm (see Fig.3b) and rotates reciprocally with a rotating angle of 90º, which breaks down the ribbons into granules. In order to minimise the effects of variations in the shapes and sizes of feed ribbons, ribbon segments of ~100 g were produced by manually cutting the roll-compacted ribbons to specific dimensions (22 x 22 mm) and fed into the milling chamber before the milling started. The effects of the milling speed were examined in the range 50-330 rpm. The temporal evolution of the mass throughput of the generated granules was recorded using a computerised balance.

2.3. PEPT study of ribbon milling

The milling process was investigated using PEPT since it is a robust method to examine the kinematics of objects in processing equipment [16, 17]. A radioactive tracer particle of similar size to the mean size of the feed powder was placed inside the feed powder during roll compaction in order to produce a radioactive ribbon (i.e. the tracer ribbon). The ribbons were then sectioned to the specific dimension of 22x22 mm and that with the embedded tracer particle was identified as the tracer ribbon using a radioactivity detector to ensure that it was included in the feed ribbons in the milling experiments.

The oscillating mill was placed between two PEPT cameras. Its position was determined by monitoring the location of the radioactive tracers placed at specific locations in the mill. During the milling experiments, the locations of tracer particles as a function of time were determined using PEPT with the data analysis based on the algorithms proposed by Parker *et al.* [17]. The data monitoring frequency was 10 kHz and mean values were calculated at six point intervals. The trajectories of the tracer particles could then be obtained for milling at various milling speeds, from which corresponding temporal evolutions of velocities and the occupancies of the tracer in the ribbon were then determined. Most experiments were terminated once the radioactive tracer was found having passed the mesh (i.e. disappeared from the inline monitoring system).

3. RESULTS

3.1 Milling performance

Yu et al. [15] showed that, for milling of roll-compacted ribbons with an oscillating mill, the variation of mass throughput with the milling time could be described using first order kinetics:

$$\frac{\mathrm{d}m}{\mathrm{d}N} = k\,(m_\infty - m) \qquad (1)$$

where N is the number of milling cycles, and m and m_∞ are the current mass of granules produced and that at the end of the milling process, and k is a rate constant. Integrating Eq. (1) with the limits $m = 0$ at $N = 0$ and $m = m_\infty$ at $N = N_c$ gives:

$$\frac{m}{m_\infty} = 1 - \exp\left(-\frac{N}{N_c}\right) \qquad (2)$$

where N_c is the critical number of milling cycles at which $m = 1 - e^{-1}$. Figure 4 shows the variation of m/m_∞ with the number of milling cycles at various milling speeds. The solid curves represent the multivariate best fit of Eq. (2) to the experimental data. It is clear that, for all milling speeds considered, the data can be well represented by first order kinetics. In addition, the N_c values decrease as the milling speed increases, implying that the milling process becomes more efficient as the milling speed increases, as expected. Consequently, the reciprocal of N_c

(i.e. $1/N_c$) is a direct measure of the milling efficiency, *i.e.* higher values of $1/N_c$ correspond to greater milling efficiencies.

3.2. PEPT study of milling

From the instantaneous velocities of the tracer, the mean velocity at a given location in the milling chamber can be obtained as follows: the milling chamber is divided into specified grids (0.4x0.4 mm) and the mean velocity of the tracer passing each cell is determined by dividing the summation of the tracer velocity on each visit by the total number of visits to this cell. These data can then be collated to produce a velocity field plot in any view plane (i.e., *XY YZ*, see Fig.3). The velocity fields obtained using PEPT at various milling speeds in the *YZ* plane are shown in Fig. 5. In this figure, the data are processed in the laboratory reference frame. The length of the arrows is proportional to the mean speed of the tracer particle embedded in the ribbon; the positions of the cells are offset so that the origin represents the rotational centre of the milling blade. In this and the following figures, the dashed circle of radius of 40 mm (i.e. the radius of the blade) shows the sweep region of the rotating blade. It can be seen from Fig. 5 that at a low milling speed the tracer ribbon only moves with a quarter of the sweep region (Fig.5a), while the tracer ribbons occupy more space in the milling chamber as the milling speed increases. In addition, the velocity circulating patterns can be clearly seen when an intermediate milling speed is applied (see Figs 5b and 5c). At high milling speeds (Figs 5c & 5d), ribbons are frequently projected into the upper region the motion of ribbons become more random.

The corresponding occupancy distributions are shown in Fig. 6, in which the occupancy is defined as the total number of visits of the tracer ribbon in a given cell divided by the total number of visits to all cells during the entire experiments. These data are then mapped to the *YZ* plane in order to obtain the planar occupancy distributions. It is clear that the occupancies of the ribbons were concentrated in the lower part of the milling chamber, especially at the lower milling speeds, but the high occupancy regions were stretched and expanded along the sieve screen and even into the upper region (Figs 6c & 6d) of the milling chamber when the milling speed was sufficiently high. It is also interesting to note that ribbons were primarily located only in a quarter of the sweep region of the blade at low milling speeds (see, Figs. 6a and 6b), which corresponds well to the rotating angle of 90^o in this particular mill. This implies that the ribbons move cooperatively with the blade at low milling speeds. At high milling speed, ribbons appear to occupy a large region in the milling chamber and even in the upper region. This indicates that ribbons could be projected away by the sweeping blades when the milling speed is sufficiently high (say >200 rpm).

4. DISCUSSION

The PEPT data presented in Figs 5 and 6 of the milling processes at various speeds suggest that (a) the ribbons are swept by the blades as a plug while compressed against the sieve mesh and (b) with increasing speed the ribbons are projected by the rotating blade and would probably collide with other ribbons and tool surfaces. The first process would result in abrasion of the ribbons and the second should result in fragmentation of the ribbons. For abrasion dominated milling processes, the critical number of milling cycles N_c should be independent of the milling speed, because the mass of produced granules is governed by the total abrasion surface area and in each milling cycle the abrasion area is identical. This means that the milling efficiency $1/N_c$ is essentially a constant. For fragmentation dominated milling processes, the milling efficiency is determined by the kinetic energy of impacts between blades and ribbons, $i.e. 1/N_c \propto \omega^2$ (ω is the milling speed). To a first approximation, the milling efficiency for a milling process can be treated as a combined contribution of abrasion and fragmentation, thus:

$$\frac{1}{N_c} = \eta + c\omega^2 \tag{3}$$

where η is a constant representing the efficiency of the abrasion dominated milling process and depends upon ribbon properties (*e.g.* solid fraction and fracture energy) and sieve mesh size, and *c* is a proportional constant that is related to the mechanical properties of the ribbons (a lower value of c is expected for ribbons with higher strength) and milling condition (*e.g.*, fill ratio and sieve mesh size) [15,18]. The first term on the right hand side of Eq. (3) represents the abrasion contribution, while the second term represents the fragmentation contribution. It is expected that a lower value of η will be obtained for weaker ribbons. The variation of $1/N_c$ with the milling speed for the milling of the current MCC ribbons at various milling speeds is given in Figure 7 together with the best fit of the experimental data to Eq.(3). It can be seen that Eq. (3) represents a close fit to the experimental data. The best fit gives $\eta=5.26\text{x}10^{-4}$ and $c=1.31\text{x}10^{-8}$ rpm^{-2} for ribbons made of MCC Avicel PH-102. Combining Eqs (2) and (3) yields:

$$\frac{m}{m_\infty} = 1 - \exp\left[-N\left(\eta + c\omega^2\right)\right] \tag{4}$$

Equation (4) can be used to describe the mass throughput of the milling process with an oscillating mill. The increase in efficiency accompanying the increase in fragmentation could arise from both the direct formation of fragments (granules) that are smaller than the mesh size or by allowing greater contact between the ribbons and mesh.

5. CONCLUSIONS

Utilizing the ability to track the motion of tracer particles in processing equipment, the PEPT technique was employed to explore the milling processes of MCC PH-102 ribbons using an oscillating mill at various milling speeds. Experimental data clearly show that there is cooperative motion between the ribbons and blades especially at low milling speeds, indicating that ribbons are swept by the rotating blade. It is expected that ribbons in this regime will primarily experience abrasion against the sieve mesh. In addition, it is shown that ribbons will experience increasing impact fragmentation as the milling speed increases, since the ribbons exhibited greater random motion and the mass throughput increases rapidly. As a first approximation, the milling process can be treated as a combination of abrasion and impact fragmentation, with the former dominating at low milling speeds and the latter making an increasing contribution as the milling speed is increased. This is consistent with the milling efficiency data being described by the sum of an abrasion parameter that is independent of speed and a fragmentation term that is a function of the square of the speed, which will relate to the imposed mean kinetic energy.

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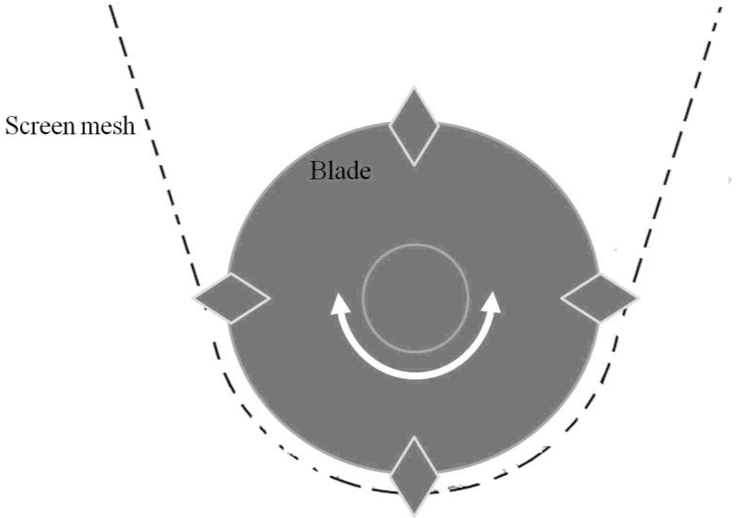


Figure 1 Schematic diagram of an oscillating mill.

Figure 2 The laboratory scale instrumented roll compactor.

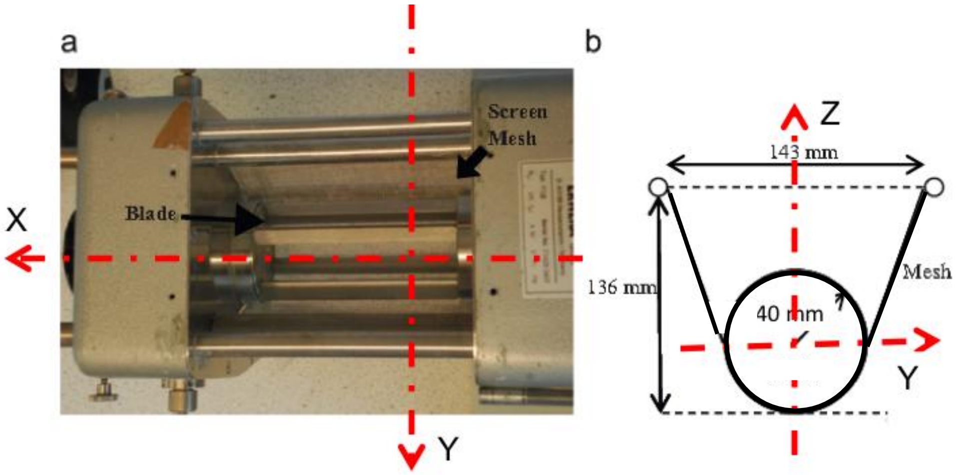


Figure 3. a) Photograph of the oscillating mill showing the blades and screen; b) schematic diagram of the cross-sectional geometry.

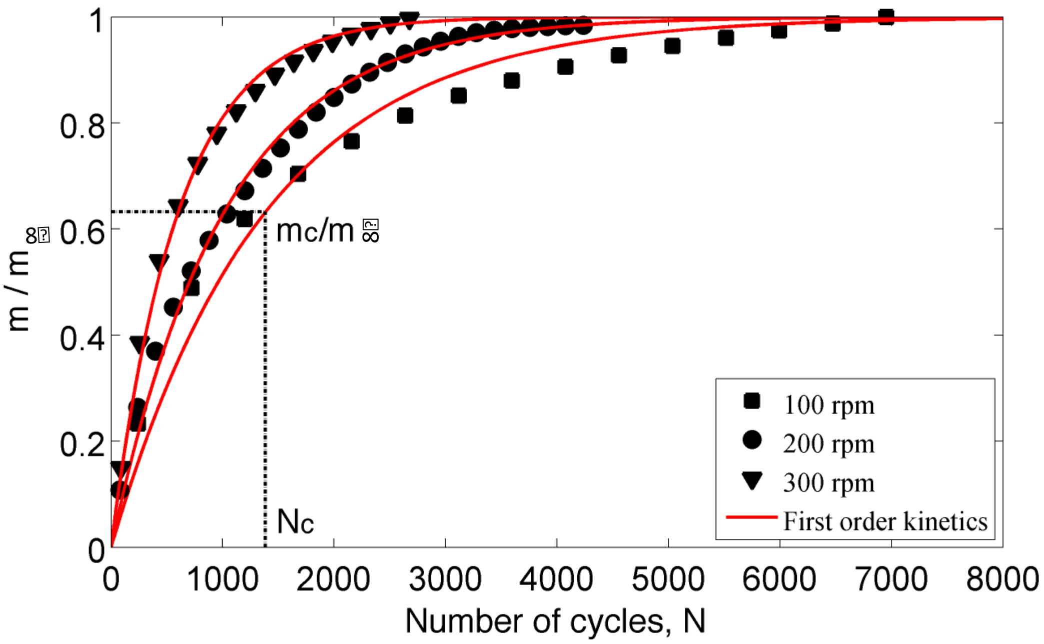
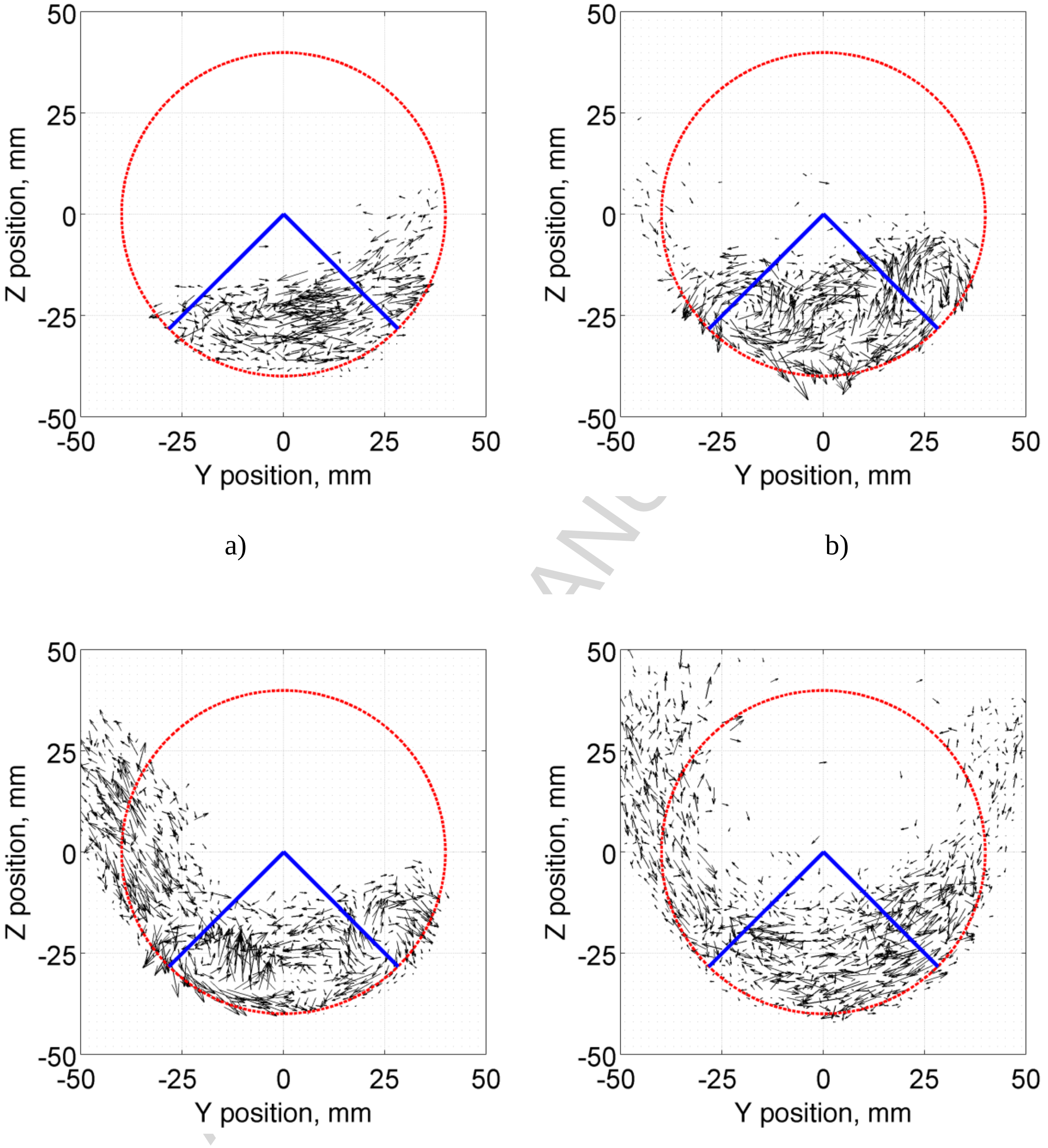


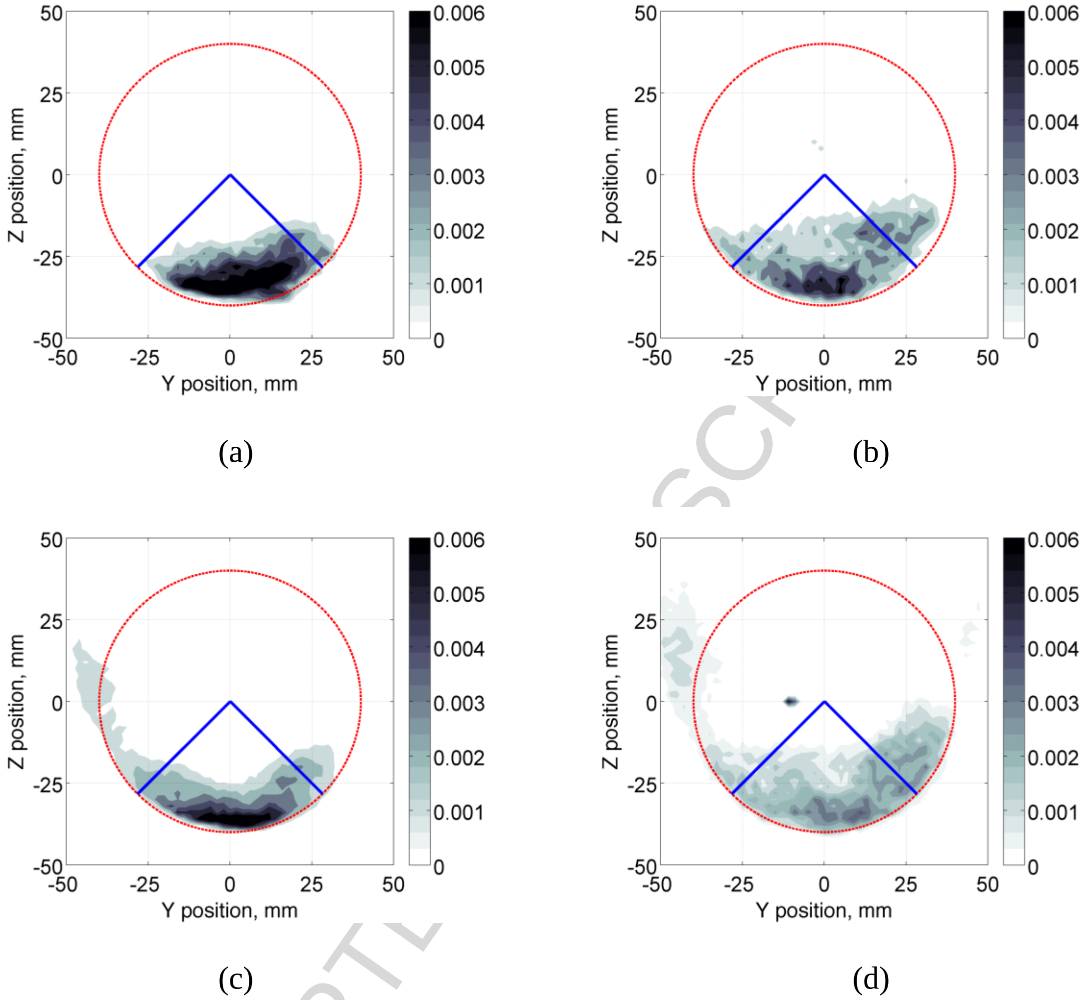
Figure 4. Normalised mass throughput as a function of the milling cycle for milling of MCC (Avicel PH 102) ribbons.



a) b)

c) d)

Figure 5 Velocity mapping on the *YZ* plane for milling of MCC ribbons at a milling speed of a) 50, b) 150, c) 200 and d) 300 rpm. The dashed circles show the outline of the tips of the rotating blades; the solid lines show the sweeping range of the bottom blade (i.e. 45^{o} to both sides, see Fig. 1).



(a) (b) (c) (d)

Figure 6 Occupancy mapping on the *YZ* plane for milling of MCC ribbons at a milling speed of a) 50, b) 150, c) 200 and d) 300 rpm. The dashed circles show the outline of the tips of the rotating blades; the solid lines show the sweeping range of the bottom blade (i.e. 45° to both sides, see Fig. 1). The gray shades represent the occupancy of the tracer ribbons.

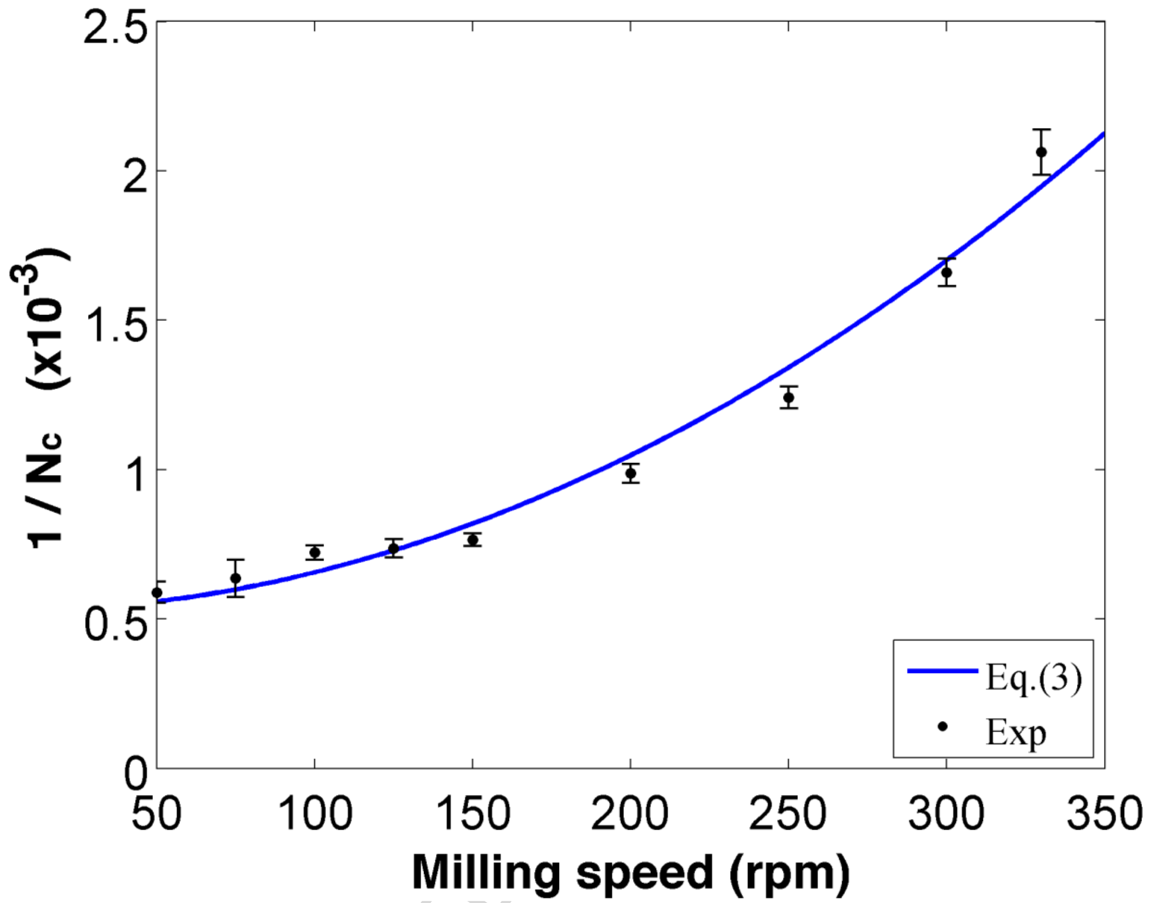
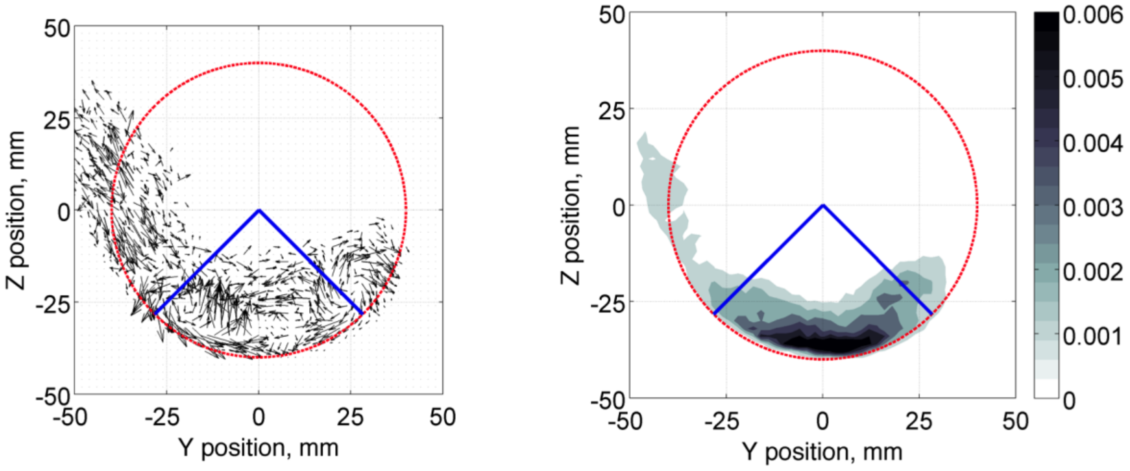


Figure 7. Reciprocal of N_c as a function of milling speed.

Graphical abstract



Velocity (left) and occupancy (right) during milling of MCC ribbons

Highlights

- The milling kinematics of roll compacted ribbons were examined using PEPT.
- At low speeds, cooperative motion of the ribbons with the blade is dominant.
- The ribbons are milled primarily by abrasion at low speeds.
- As the milling speed increases, ribbon breakage and the milling efficiency increase.