

# Adapting the process conditions and performance in planetary roller melt granulation (PRMG) via the planetary spindle number

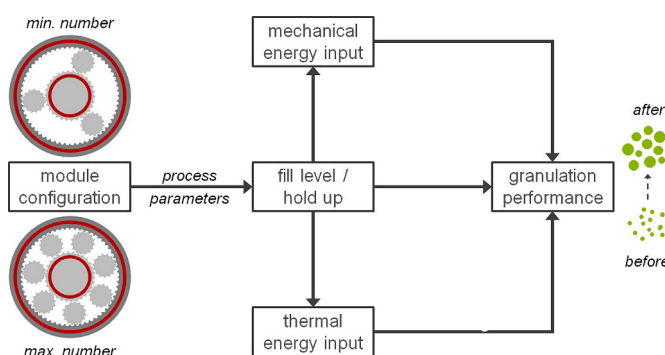
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## HIGHLIGHTS

- Planetary roller melt granulation as new continuous method.
- Fill level higher and hold-up nearly constant for lower free processing volume.
- Normalization of mechanical and thermal energy input.
- Energy input efficiency higher for lower specific feed load.
- Adaption of granulation regime by process settings.

## GRAPHICAL ABSTRACT



## ARTICLE INFO

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## ABSTRACT

Continuous melt granulation with a planetary roller granulator is a new continuous method based on the orbital motion of planetary spindles driven by a rotating central spindle in a surrounding roller cylinder. Here the configuration of the processing section is a central design aspect, which defines the processing conditions and process performance. In this study, the number of applied planetary spindles as part of the module configuration was varied.

As a result, a correlation between direct process parameters, processing conditions and process performance was identified. Hereby, the data normalization relativized successfully the effect of the module configuration. The results are also suitable to identify a module configuration and process settings in the context of a process optimization towards energy input efficiency or energy consumption. Finally, the accounting of the particle modification in terms of size was suitable to link the effect of the investigated parameters to the granulation regime.

## 1. Introduction

In recent years, research endeavors on continuous melt granulation have expanded, which is affiliated to three main aspects. First of all,

granulation is a central unit operation of powder processing [1–3]. Hereby, the main objective of modulating the particle size distribution is usually to tailor the flow properties of a bulk material. Positive side effects of the grain enlargement include for the handling the reduction of

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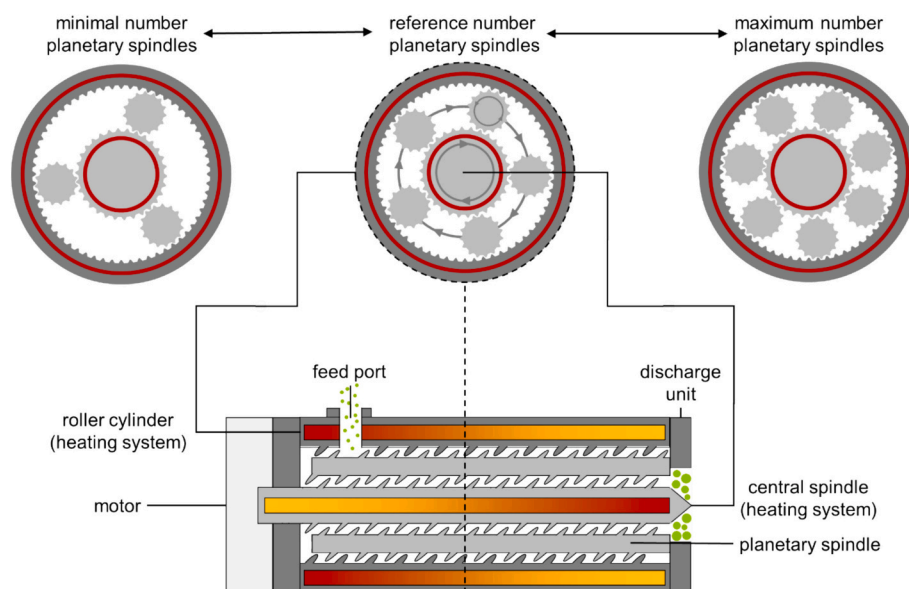
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**Fig. 1.** Radial cross section of planetary roller processing section with different number of incorporated planetary spindles (top) and axial cross section of lab-scale extruder with one module including central spindle, planetary spindle and roller cylinder (bottom). Heating systems for central spindle and roller cylinder are independent. Adapted and adjusted from [40,41].

dust development or the prevention of segregation, as well as the improvement of properties crucial for further processing [4]. Second, melt granulation offers advantages in comparison to the more established methods of wet or dry granulation. These include the sufficient handling of moisture sensitive materials with respect to hydrolytic effects [5], high dose compositions [6], the improvement of tabletability properties [7] or minimizing fines generation [8]. Further aspects to consider as a solvent-free technology are that an energy intensive drying of the product is not required and the consumption of the resource water is omitted. However, due to the complexity of melt granulation, the other two methods might be considered first at the beginning of a process development [9,10]. Third, the continuous manufacturing of goods in contrast to batch operation is expected to reduce product quality fluctuations due to a processing in a dynamic steady state. This paradigm shift in the field of pharmaceutical technology in production [11] was especially fueled by the introduction of the Quality-by-Design concept for a systematic process design [12,13]. Since then, the design of continuous techniques for different unit operations, e.g. blending [14–16], extrusion [17–19] or powder compaction [20–22], following this approach is one central focus of research.

For pharmaceutical processing, the gold standard for the continuous execution of melt granulation is by now the utilization of twin-screw machines [23]. Hereby, these apparatus were applied first for wet granulation, which is based on the work of Gamlen [24], Lindberg [25–27] or Keleb [28–32]. Later, continuous granulation with twin-screw machines was adopted for the alternative method, where a binder is plasticized due to a processing temperature above the glass transition or melting point [33]. In general, investigations on twin-screw melt granulation relate to the identification of the design space evaluating the interplay of material attributes, process parameters and product properties. This includes amongst others the variation of the binder type and excipients [34,35], binder weight fraction [36,37], feed rate or screw speed [38,39] with respect to the impact on the particle size and shape or properties of a tablet as the product of a subsequent manufacturing step.

Besides the use of a twin-screw machine, lately the application of a planetary roller granulator for continuous melt granulation has been introduced. Hereby, the concept of a central spindle driving planetary spindles in a roller cylinder is expected to enhance the process control in terms of heat transfer. This refers to the orbital circulation of the

planetary spindles, which enlarges in combination with the heating concept the ratio of processed volume to the generated and heated surface. In this context, first investigation in planetary roller melt granulation (PRMG) dealt with the impact of direct process parameters on the particle size distribution of the product, while considering the energy input [40] and the fill level [41] as linking elements. Further on, a central aspect of the process design is the module configuration, which refers to the number and type of incorporated planetary spindles. However, this equipment parameter has been kept constant so far. This is contrary to twin screw melt granulation, where the screw design referring to the sequence of screw elements with the same or varying type as the equivalent equipment parameter for this method is already a central subject to investigations presented in literature [42,43].

Consequently, this study focuses on the impact of the planetary spindle number as part of the module configuration on the process and granulation performance in PRMG. This is necessary to establish this new technology in the emerging field of continuous granulation. The corresponding investigations connect to the previous ones by considering the feed rate and rotation speed of the central spindle as variable parameters in the experimental design. Hereby, the fill level and energy input are applied to reflect the processing performance, while the normalized particle size distribution after granulation serves as one indicator for the granulation performance. This is complemented by evaluating the particle size shift during processing to derive the granulated fraction of the material as surrogate for the yield.

## 2. Materials and methods

### 2.1. Melt granulation experiments

Continuous melt granulation was executed on a granulator at lab-scale (PWE 30, Entex Rust & Mitschke GmbH, Bochum, Germany). The processing section consisted of a single module including rotating cylinder, central spindle and standard planetary spindles and had a net length ( $l_{cs}$ ) of 222 mm with a pitch length ( $h_{cs}$ ) of 55.5 mm. While the reference number of incorporated elements in the cross-section was 5, the minimum was 3 due to mechanical stability aspects and the maximum was 7 due to the machine size (Fig. 1, top). Hereby, the free cross-sectional area ( $A_{free}$ ) varied from 553 mm<sup>2</sup> for the minimum configuration over 430 mm<sup>2</sup> for the reference configuration down to

308 mm<sup>2</sup> for the maximum configuration as the diameters of the main mechanical parts were 8.8 mm for the planetary spindles, 17.7 mm for the central spindle and 35.4 mm for the roller cylinder.

A material pre-mix consisting of 10 wt% meltable binder (Hydroxypropylcellulose, Klucel EXF Pharm, Ashland Inc., Covington, USA) and 90 wt% of a model substance (Lactose monohydrate, Lactose 310, Foremost Farms USA, Baraboo, Wisconsin, USA) with a  $d_{50,3}$  at 112  $\mu\text{m}$  and a span of 0.87 were supplied through a feed port with a loss-in-weight feeder (DDW-M-DS(R) 28, Brabender GmbH & Co. KG, Duisburg, Germany) and discharged at the end through an open orifice. During the experiments, both heating systems were set to a temperature of 150 °C. Hereby, pressurized water was used as heating media, which was flowing through the heating jacket of the central spindle respectively roller cylinder. Thereby, the volume flow on average for all configurations and set points was  $7.69 \pm 0.26 \text{ L min}^{-1}$  for the central spindle heating and  $17.46 \pm 0.40 \text{ L min}^{-1}$  for the roller cylinder heating. The design space of the experimental investigations covered four equidistant levels each regarding the material feed rate ( $\dot{m}$ ) and the rotation speed of the central spindle ( $n_{cs}$ ) from 0.3 up to 1.2 kg h<sup>-1</sup> respectively 60 to 240 min<sup>-1</sup> for all three module configurations. Hereby, during processing the determined rotation speed was equivalent to  $100.2 \pm 0.47\%$  of the set value on average for all configurations and set points. Moreover, the parameter set for the highest throughput at the lowest rotation speed and maximum number of planetary spindles could not be operated as the motor torque limit was exceeded only in this case. However, in general the specific feed load (SFL) is a suitable surrogate to summarize the direct process parameter settings (Eq. 1). This parameter is usually applied for this purpose in twin-screw processes [44,45] and was adapted for planetary roller melt granulation in [40]. Hereby, the untapped bulk density of the material pre-mix ( $\rho_{bulk} = 583 \text{ kg m}^{-3}$ ) has to be considered.

$$SFL = \frac{\dot{m}}{n_{cs} \rho_{bulk} h_{cs} A_{free}} \quad (1)$$

## 2.2. Process characterization

The processing conditions were characterized with respect to the fill level and energy input. In the first case, the starting point was the experimental determination of the residence time at a specific operating point with an on-line camera system (ExtruVis, MeltPrep GmbH, Graz, Austria) via marker (E104, respectively Ponceau 4R) experiments in analogy to [41]. Hereby, the median of the residence time distribution ( $t_{50}$ ) represents the average transportation velocity of the material in steady state, which is assumed to be constant over the length of the processing section. In comparison, the hydrodynamic residence time ( $\tau$ ) reflects the material transport duration through the processing volume in case this is fully-filled. Then, the ratio of median and hydrodynamic residence time (Eq. 2) is a surrogate for the machine fill level (MFL).

$$MFL = \frac{t_{50}}{\tau} = \frac{t_{50} \dot{m}}{A_{free} l_{cs} \rho_{bulk}} \quad (2)$$

Second, the energy input during processing was determined in terms of the specific mechanical energy (SME) and the specific thermal energy (STE). Hereby, motor torque ( $M$ ), the density ( $\rho_{hm}$ ) and the heat capacity ( $c_{p,hm}$ ) of the heating media as well as the volume flow for the central spindle ( $\dot{V}_{hm,cs}$ ) and roller cylinder ( $\dot{V}_{hm,rc}$ ) and the corresponding temperature differences ( $\Delta T_{cs}, \Delta T_{rc}$ ) between in- and outlet were taken into account. In both cases (Eq. 3, Eq. 4), the applied energies are considered with respect to the set feed rate.

$$SME = \frac{2 \pi n_{cs} M}{\dot{m}} \quad (3)$$

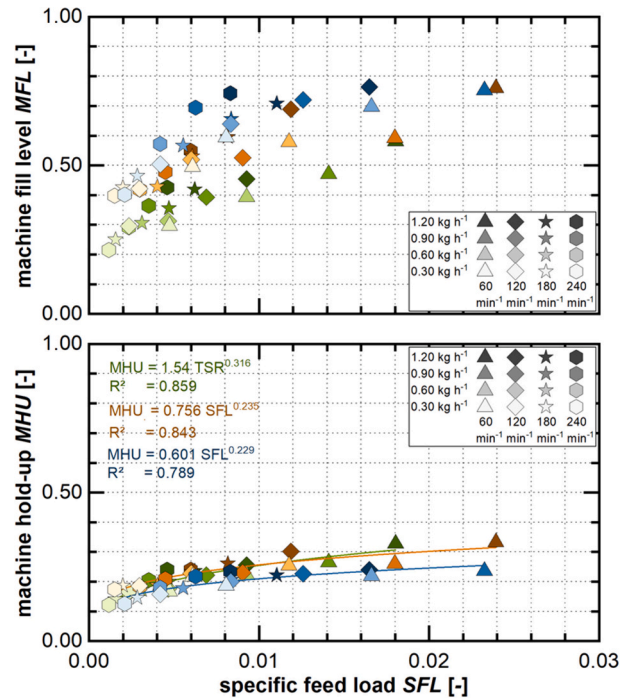


Fig. 2. Machine fill level(top) and hold-up (bottom) during PRMG for different configurations and process settings. Colors encode for three (green), five (orange) and seven (blue) planetary spindles within the module, color saturation for the feed rate and symbol type for the rotation speed within the experimental design space. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

$$STE = \frac{\rho_{hm} c_{p,hm} (\dot{V}_{hm,cs} \Delta T_{cs} + \dot{V}_{hm,rc} \Delta T_{rc})}{\dot{m}} \quad (4)$$

## 2.3. Product characterization

The product samples were sieved first through a mesh with a size of 2.5 mm and then the particle size distribution of the fine sample fraction was measured via dynamic picture analysis (QICPIC, Sympatec GmbH, Clausthal-Zellerfeld, Germany). This system consisted of a dosing unit (VIBRI/L), a gravity disperser (GRADIS/L) and a sensor (QICPIC). Particle size is represented by a sphere with an equal projection area. The derived data was analyzed via a software code based on MATLAB (MathWorks, Natick, USA), which was originally designed for this purpose in crystallization processes [46]. The average number of analyzed particles per sample was roughly 110.000 for all configurations and set points. Due to the preparative sieving step, the normalized volumetric particle size distribution ( $Q_{3,norm}$ ) must be considered to guarantee an objective comparison of the different process settings and module configurations with respect to the granulation performance. Therefore, the data concerning the cumulative distribution ( $Q_3$ ) of the analyzed fine product in dependency of the particle size for a class ( $d_p$ ) is corrected (Eq. 5) by the fine weight fraction of the granular sample ( $w_{fine}$ ).

$$Q_{3,norm}(d_p) = Q_{3,product,fine}(d_p) w_{fine} \quad (5)$$

By the comparison of the volumetric density distribution for the model compound ( $q_{3,model\ compound}$ ) to the granular product in the normalized form ( $q_{3,norm}$ ) as a function of the representative diameter for an individual particle class ( $\bar{d}_p$ ), the shift of the volume density distribution ( $\Delta q_{3,shift}$ ) was determined (Eq. 6). This approach was reported to be suitable for the evaluation of granulation processes in [40] by deriving the net weight fraction of granulated particles during

processing ( $w_{net,granulated}$ ) as performance indicator (Eq. 7). In this parameter, all particle size changes during granulation related to the different rate processes [47] are accumulated, which is reasonable as only the net variation between initial and final stage are a perceptible modification of the material particle size. Hereby, the width of an individual particle class ( $\Delta d_p$ ) has to be considered.

$$\Delta q_{3,shift}(\bar{d}_p) = q_{3,norm}(\bar{d}_p) - q_{3,model\ compound}(\bar{d}_p) \quad (6)$$

$$w_{net,granulated} = - \sum \Delta q_{3,shift}(\bar{d}_p) \Delta d_p \text{ for } \Delta q_{3,shift} < 0 \quad (7)$$

### 3. Results and discussion

#### 3.1. Machine fill level and hold-up

A key factor of the processing conditions during PRMG is the actual mass within the processing section involved in the material transformation via the fundamental rate processes [47]. This aspect was addressed in the first place by determining the machine fill level (MFL), which refers to the material covered volume in steady state in relation to the free processing volume, which directly depends on the screw configuration.

For the different configurations tested in this study, in each case the machine fill level increases as the feed rate increases or the rotation speed is reduced, while the other direct process parameter is kept constant (Fig. 2, top). This is in agreement with results of previous investigations [41] and is related to the balance between the contrary forces of transferred energy by the spindles to the material converted into material transportation and friction of the material depending on the transportation velocity. Hereby, the fill level is a linking element representing the covered area of the radial cross section, which determines the contacted surface of the moving parts and the axial material speed for a constant volume flow in steady state. The opposite impact on both forces results in the logarithmic shape of the identified correlation.

At the same time, an increase of the applied planetary spindles within the module leads to an increase of the fill level for higher specific feed loads as well for constant processing settings related to feed rate and rotation speed. However, this effect might be addressed to the reduction of the free cross-sectional area by the variation of the planetary spindle number in the processing section as the information on the machine fill level is relative per definition (see Eq. 2). In order to fade this out, the ratio of the free cross-sectional area to the inner cross-sectional area of the roller cylinder ( $A_{inner,rc}$ ) is considered (Eq. 8) to normalize the machine fill level. Thereby, the machine hold-up (MHU) is derived. This parameter represents the actual material volume constantly inside the granulator during processing in steady state in relation to the machine scale.

$$MHU = MFL \frac{A_{free}}{A_{inner,rc}} \quad (8)$$

Overall, the hold-up in the granulator is nearly constant for a specific process parameter combination of feed rate and rotation speed despite a module configuration with a minimum or reference number of planetary spindles (Fig. 2, bottom). At the same time, the material inside the granulator for the minimum free radial cross section decreases slightly in comparison.

For the evaluation of these observations, first thing to consider is the reference scale for the force transmission determining the fill level respectively hold-up during processing in PRMG. This is a single planetary spindle or the central spindle and each individual one has an own field of action, e.g. for material shearing at and near by the moving surface. Second, the number of planetary spindles determines the spacing between these. This results in a defined overlap of the individual fields of action for a specific module configuration.

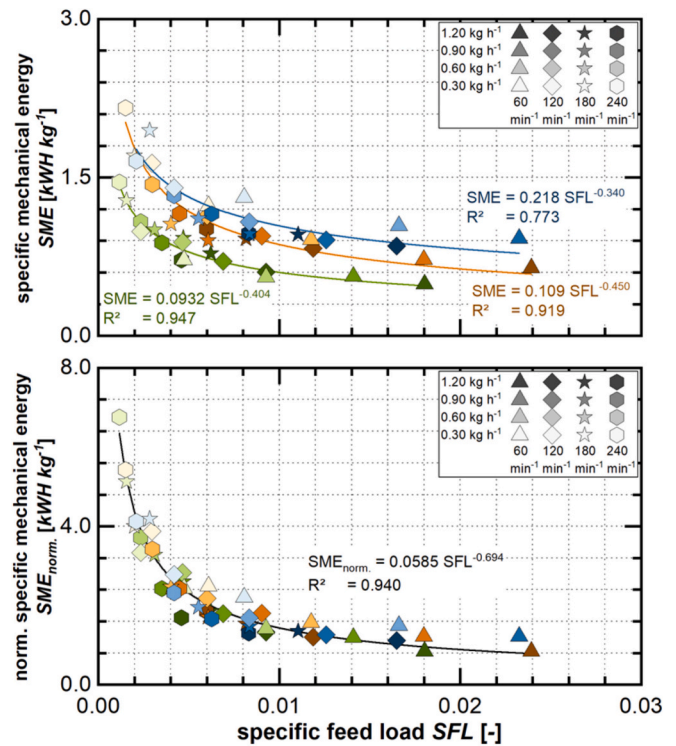


Fig. 3. Specific mechanical energy (top) and normalized specific mechanical energy (bottom) during PRMG for different configurations and process settings. Colors encode for three (green), five (orange) and seven (blue) planetary spindles within the module, color saturation for the feed rate and symbol type for the rotation speed within the experimental design space. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

In this respect, the experimental results imply a shortfall under a critical distance of the planetary spindles for a maximum number within a module in comparison to the other ones tested in this study. Due to enhanced overlap, the effective field of action shrinks, which in turn leads to a more effective force transmission as each individual element covers less space. Ultimately, the hold-up is reduced in order to balance the increase of energy transfer to the material.

Furthermore, the representation of the experimental data for the configurations with a minimum and reference number of planetary spindles with a Power-approach is considered sufficient. At the same time, the fit quality for the configuration with the maximum number of elements is reduced in comparison. Here, the overlap effect of the fields of action potentially leads to a higher sensitivity of the transportation force balance in steady state towards natural process fluctuations, e.g. related to feeding. This results in some fluctuations of the experimental data.

#### 3.2. Energy input

With respect to the processing concept, the machine fill level respectively hold-up affects directly the mechanical and thermal energy transfer into the material.

In the first case, the specific mechanical energy (SME) decreases for an increase of the SFL induced by a higher throughput at a constant rotation speed or a lower rotation speed at a constant feed rate (Fig. 3, top). Both types of parameter adaptations are accompanied by an increase of the machine hold-up (Fig. 2). Hereby, the material is in general assumed to be located around the spindles. At the same time, the shear rate induced by the moving parts remains unchanged or decreases. In consequence, the transferred energy at the surface or in the contact points of these diminishes per processed material. This correlation can

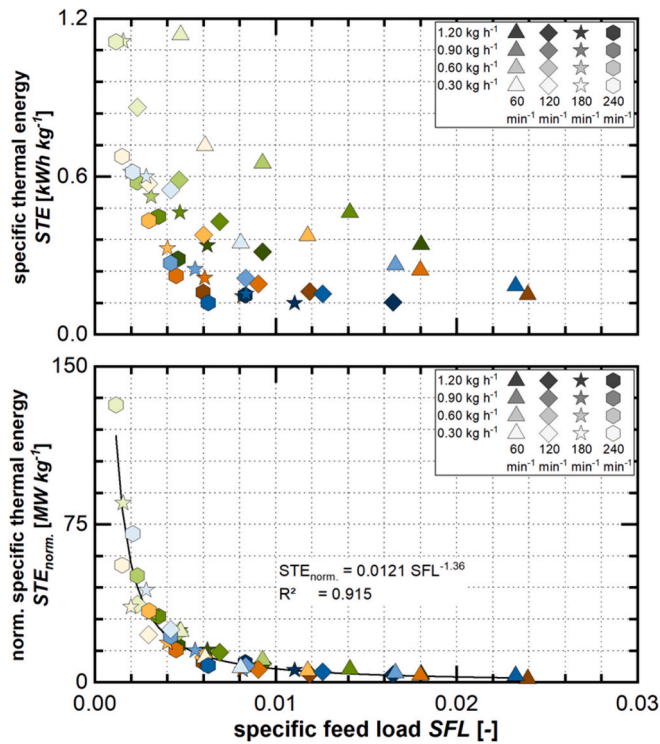


Fig. 4. Specific thermal energy (top) and normalized specific thermal energy (bottom) during PRMG for different configurations and process settings. Colors encode for three (green), five (orange) and seven (blue) planetary spindles within the module, color saturation for the feed rate and symbol type for the rotation speed within the experimental design space. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

be captured with a power approach. For the configuration with a minimum or reference number of planetary spindles, the coefficients of determination with 0.947 respectively 0.919 are considered to be sufficient. The reduced fit quality for the maximum number of planetary spindles is related to the enhanced process sensitivity caused by the overlap of the fields of action for the individual planetary spindles and in consequence to the higher fluctuation of the machine hold-up (Fig. 2, bottom).

Furthermore, the SME increases with a higher number of planetary spindles. This can be attributed to the material distribution inside the granulator. While the material mass represented by the MHU (Fig. 2, bottom) is barely affected for a constant setting of the direct process parameters, the free processing volume directly depends on the specific module configuration. Consequently, the material density around the central or planetary spindles varies. In terms of process characterization, this effect can be addressed to normalize the SME ( $SME_{norm.}$ ) by considering the machine fill level (eq. 9) as this integral parameter reflects the material distribution for a specific configuration.

$$SME_{norm.} = \frac{SME}{MFL} \quad (9)$$

By the proposed transformation, the data sets for the different module configurations coincide to a single curve represented sufficiently by a power approach. This implies a fundamental transfer mechanism for the mechanical energy in PRMG, which is based on the material shearing by the moving parts in combination with the material distribution in the free processing volume of the granulator.

In comparison to the SME, the specific thermal energy (STE) also decreases for an increase of the specific feed load induced by a higher throughput at a constant rotation speed (Fig. 4, top). Here, multiple aspects have to be taken into account. First, the overall material contact

time at the heated surface is reduced due to an in general shorter residence time by this direct parameter variation [41]. At the same time, the material exchange rate at the surface related to a shearing off by the planetary spindles remains constant. Consequently, the number of heating events for an individual volume element is reduced limiting the overall material heating. In addition, the transferred thermal energy is distributed within an enhanced material hold-up (Fig. 3).

In contrast, an increase of the SFL by a lower rotation speed at a constant feed rate barely affects the applied thermal energy. Here, the reduced material exchange rate at the heated surface attenuates the efficiency of the energy transfer and the material hold-up is enlarged, while the overall residence time is prolonged. These alterations of the processing conditions balance each other in terms of the STE.

Furthermore, for a constant direct process parameter set a reduction of the free cross-sectional area by a larger number of planetary spindles in the module results in a lower specific thermal energy input. This indicates a reduced efficiency of the energy transfer at the surface of the central spindle and roller cylinder. This is related on the one hand to the enhanced material exchange due to the higher number of planetary spindles, which limits the individual contact time. On the other hand, the hold-up is only barely affected at the same time in comparison to the other configurations.

Both aspects can be addressed via the rotation speed and machine hold-up in order to normalize the data with respect to the applied module configuration (eq. 10). The opposite impact of these two factors is reflected by considering the ratio of those.

$$STE_{norm.} = STE \frac{n}{MHU} \quad (10)$$

By the proposed transformation, the data sets concerning the STE for the different module configurations coincide to a single curve represented sufficiently by a power approach (Fig. 4, bottom). This implies a fundamental transfer mechanism for the thermal energy in PRMG, which is based on the material exchange rate at the surface related to the rotation speed of the moving parts in combination with the material hold-up in the free processing section of the granulator.

### 3.3. Particle size

The particle enlargement during planetary roller melt granulation is the convolution of the processing conditions defined by the fill level respectively hold-up and energy input in dependency of the process setting related to feed rate and rotation speed. Hereby, the granular product can be represented by the normalized cumulative volume distribution ( $Q_{3, norm.}$ ). The corresponding function values are below 1 in all cases. The difference to this limit value symbolizes per definition the coarse fraction, which was removed during sample preparation. For the depiction of the results, the normalization of the particle diameter ( $d_p$ ) by the median of the model compound ( $d_{50, mc}$ ) provides thereby a perspective on the relative enlargement factor with respect to the input material.

In general, the particle size decreases for higher rotation speeds at constant feed rate as this process parameter variation enhances the shear stress applied to the material promoting the rate process of *breakage and attrition* [47]. At the same time the hold-up decreases, which amplifies the impact of the higher shear rates. The particle size also decreases for lower feed rates at a constant rotation speed. Here, the corresponding reduction of the fill level diminishes the probability of particle-particle interaction, which is fundamental for the rate process of *agglomeration* [47]. Furthermore, the determined particle size distribution highlight a classification according to the module configuration. A reduction of the free processing volume by a higher number of applied planetary spindles results in principle in a finer product. Here, the enhanced number of shear events at a rather constant hold-up (Fig. 2) leading to a higher specific mechanical energy input (Fig. 3) limits the particle size enlargement in comparison.

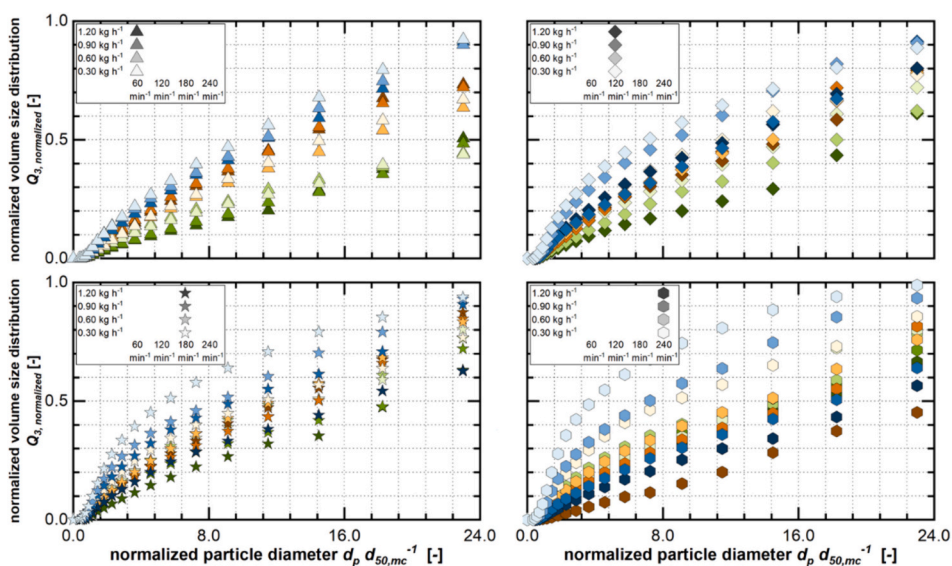


Fig. 5. Normalized volumetric distribution of the granular product after PRMG for different configurations and process settings as a function of the normalized particle diameter. Colors encode for three (green), five (orange) and seven (blue) planetary spindles within the module, color saturation for the feed rate and symbol type for the rotation speed within the experimental design space. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

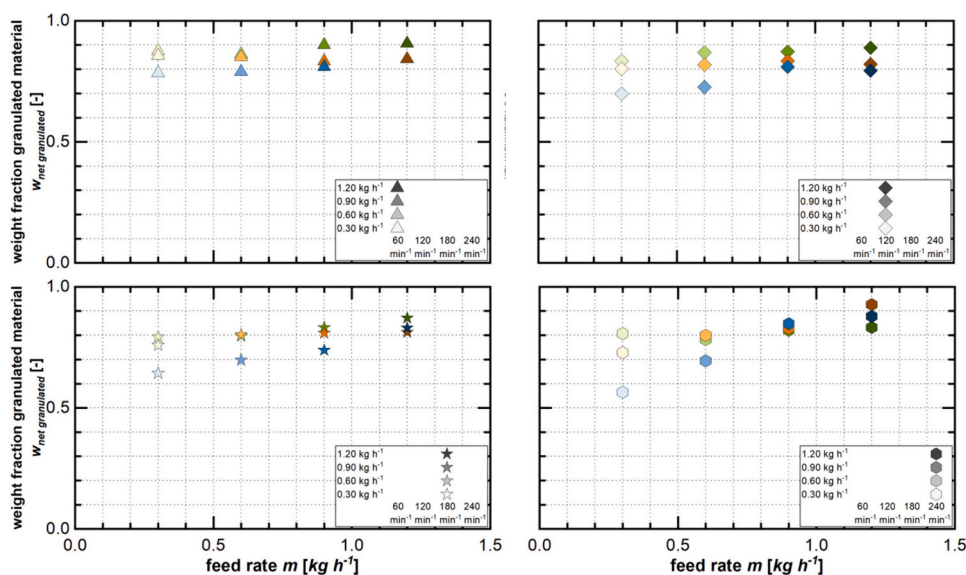


Fig. 6. Net weight fraction of granulated material during PRMG for different configurations and process settings. Colors encode for three (green), five (orange) and seven (blue) planetary spindles within the module, color saturation for the feed rate and symbol type for the rotation speed within the experimental design space. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

However, the combinations of extreme values for the direct process parameters, namely high throughput and rotation speed respectively low throughput and rotation speed, form exceptions for the above mentioned correlations. In the first case, a clear classification regarding the module configuration based on the determined particle size is not feasible as the results are no more aligned in groups. Also, the enhanced rotation speed does not lead to a finer product in comparison to the other settings for a constant throughput (Fig. 5, bottom right). In the second case, especially for the minimum and reference number of applied planetary spindles, a lower feed rate at a constant rotation speed causes a coarse product (Fig. 5, top left). These findings imply a change of the granulation regime by the dominating rate process respectively the combination of these, which is also indicated by the results for the net weight fraction of granulated material in dependency of the process

settings (Fig. 6).

In agreement with the correlations for the normalized cumulative particle size distribution, the net fraction of material modified in the granulation process related to the size shrinks for higher rotation speed at constant feed rate or lower feed rates at a constant rotation speed. These aspects are related to the corresponding effect on the hold-up and energy input. A lower number of planetary spindles results in a higher material conversion as the particle size increases due to a reduced number of shear events and shear stress in consequence. Thereby, the impact of the feed rate is enhanced for the highest rotation speed and maximum module configuration and almost nullifies in turn for the lowest rotation speed. This shift of the correlation between process settings and granulation performance is an indicator for an alteration of the granulation regime during PRMG by the direct process parameters as

different rate processes must be promoted and dominant during processing.

#### 4. Conclusion

Planetary roller melt granulation is a new continuous method for particle size enlargement, which offers a high potential in terms of process control related to the unique process concept. Hereby, a central design piece is the number of planetary spindles applied within a module as part of the module configuration, which is a suitable parameter to adapt the conditions during processing. While the material fill level increases for a reduced free processing volume, the machine hold-up is rather unaffected by this equipment variation. This highlights that the corresponding force balance refers to an individual rotating spindle. Furthermore, the developed data normalization within this study indicate a fundamental mechanism for the mechanical energy transfer based on the material shearing and distribution within the processing section as well as for the thermal energy transfer via the heated surfaces based on the material exchange rate at these and the hold-up. Overall, the energy input efficiency of the granulation related to the processed material is maximized for a low specific feed load, while the energy consumption is minimized for a high specific feed load at high throughputs. Finally, the net weight fraction of granulated particles is a suitable indicator for the granulation performance, which highlighted a change of the granulation regime within the tested experimental design space.

For an ongoing establishment of PRMG in future, further investigations need to be conducted concerning the planetary spindle type as part of the module configuration as well as the formulation impact on the processing conditions. Hereby, the goal must be an identification of models connecting process parameters and product quality attributes to enable at one point a predictive process design.

#### CRedit authorship contribution statement

**Tom Lang:** Methodology, Investigation. **Jens Bartsch:** Writing – original draft, Visualization, Supervision, Project administration, Methodology, Conceptualization.

#### Declaration of competing interest

Jens Bartsch reports equipment, drugs, or supplies was provided by Entex Rust & Mitschke GmbH. Jens Bartsch reports equipment, drugs, or supplies was provided by Ashland Industries Deutschland GmbH. Jens Bartsch reports equipment, drugs, or supplies was provided by Merck Healthcare KGaA. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Data availability

Data will be made available on request.

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#### List of symbols

$A_{free}$  free area of processing cross-section [ $m^2$ ]

$A_{inner,rc}$	inner cross-sectional area of roller cylinder [ $m^2$ ]
$C_{p,hm}$	heat capacity of heating media [ $kJ\ kg^{-1}\ K^{-1}$ ]
$d_{50,mc}$	median of the model compound particle size distribution [mm]
$d_p$	particle diameter [mm]
$\bar{d}_p$	representative particle diameter for a class [mm]
$\Delta d_p$	width of the particle class [mm]
$\Delta q_{3,shift}$	volume density distribution shift [ $mm^{-1}$ ]
$\Delta T_{cs}$	temperature gradient of central spindle heating [K]
$\Delta T_{rc}$	temperature gradient of roller cylinder heating [K]
$h_{cs}$	pitch of central spindle [mm]
$l_{cs}$	length of central spindle [mm]
$M$	applied motor torque during processing [Nm]
$MFL$	machine fill level [–]
$MHU$	machine hold-up [–]
$\dot{m}$	feed rate of material pre-mix [ $kg\ h^{-1}$ ]
$n_{cs}$	rotation speed of central spindle [ $min^{-1}$ ]
$q_{3,model\ compound}$	volume density distribution of model compound [ $mm^{-1}$ ]
$q_{3,norm.}$	normalized volume density distribution of product [ $mm^{-1}$ ]
$\rho_{bulk}$	untapped bulk density [ $kg\ m^{-3}$ ]
$\rho_{hm}$	density of heating media [ $kg\ m^{-3}$ ]
$SFL$	specific feed load [–]
$SME$	specific mechanical energy [ $kWh\ kg^{-1}$ ]
$SME_{norm.}$	normalized specific mechanical energy [ $kWh\ kg^{-1}$ ]
$STE$	specific thermal energy [ $kWh\ kg^{-1}$ ]
$STE_{norm.}$	normalized specific thermal energy [ $MW\ kg^{-1}$ ]
$t_{50}$	median of residence time distribution [s]
$\tau$	hydrodynamic mean residence time [s]
$\dot{V}_{hm,cs}$	volume flow of heating media through central spindle [ $m^3\ h^{-1}$ ]
$\dot{V}_{hm,cs}$	volume flow of heating media through roller cylinder [ $m^3\ h^{-1}$ ]
$w_{fine}$	fine fraction of product sample [–]
$w_{net,granulated}$	weight fraction of net granulated material [–]

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