Investigation of Phase Transformations of Omeprazole Magnesium during Milling

Hanane Abouhakim[1], Ali Hassanpour[1], Frans Muller[1], Sven Schroeder[1], Mike Quayle[2]

[1] School of Chemical and Process Engineering, University of Leeds, Leeds LS2 9JT, UK
[2] AstraZeneca, Pharmaceutical Technology & Development, Pepparedsleden 1, SE-431 83 Mölndal, Sweden

Key Words
Milling, phase transformation, solid state characterization, omeprazole magnesium, material properties, slip planes

Abstract
Phase transformations of pharmaceutical Active Pharmaceutical Ingredients (APIs) and excipients might cause significant changes to the key particle properties and product performances such as dissolution rate and bioavailability. This poses a challenging problem in the pharmaceutical industry. Phase transformations are often related with high-energy mechanical processes such as milling, which leads to the destruction of the crystalline order and the formation of amorphous components in the sample, or in the extreme case a fully amorphous sample. The extent of the disorder produced varies depending on the material properties and the milling conditions. Nonetheless, phase transitions during milling processes are not well understood, and cannot be predicted due to the complexity of the milling process and the lack of knowledge about underlying mechanisms that lead to such changes. The aim of this work is to investigate material properties and the milling conditions associated with phase transformations. For this purpose, crystallographic and mechanical properties of omeprazole magnesium were determined. Experimentally, omeprazole magnesium was milled at the same conditions using planetary ball mill and single ball mill at different times. The outcome of the calculation shows that Omeprazole Magnesium consists of at least three clear slip planes (111), (011), and (010), and has a bulk modulus of 1.6051 GPa. To evaluate the effect of milling, PXRD, DSC and FTIR were used to characterize the non-milled and milled samples. PXRD showed a significant reduction in crystalline peaks up to 30 min followed by a single halo peak emerging at 2 hours of milling which represented complete transformation from a crystalline to amorphous powder. Similarly, DSC data showed a decrease in the melting and decomposition temperature up to 30 minutes and a complete disappearance of the melting curve at three hours. Moreover, FTIR demonstrated a significant decrease in the percentage transmission as the milling progress.

Methodology to estimate the break force of pharmaceutical tablets with curved faces under diametrical compression

M. Al-Sabbagh[a, b], P. Polak[b**], R.J. Roberts[c], G.K. Reynolds[c], I.C. Sinka[b*]

[a] Department of Mechanical Engineering, College of Engineering, Al-Mustansiriyah University, Baghdad, Iraq
[b] Department of Engineering, University of Leicester, University Road, Leicester, LE1 7RH, UK
[c] Pharmaceutical Technology & Development, AstraZeneca, Macclesfield, SK10 2NA, UK

*ics4@le.ac.uk tel. 44 116 252 2555 (corresponding author)
**pp254@leicester.ac.uk (presenting author)

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Abstract

This poster presents a methodology to estimate the break force of curved faced tablets under diametrical compression. Common excipients used in pharmaceutical tablet formulations, including microcrystalline cellulose, calcium phosphate and mannitol as well as their mixtures were characterised. Compacts of different densities were manufactured and their compressive and tensile strength was measured. The break force of curved face tablets having a comprehensive range of face curvatures and thickness was measured using the diametrical compression method ("hardness" test). Equation $\sigma_d = \frac{F}{\pi D^2}\left(a\frac{t}{D} + b\frac{W}{D}\right)^{-1}$ introduced by Shang et al in 2013 was used to relate the break force (*F*) to tablet geometry (*D, t, W*) and material tensile strength (σ_d). Here, we propose a method to estimate the parameters *a* and *b* using data for curved faced tablets made from three pure excipients. The method was validated for four mixtures. The errors were analysed and compared with the USP29 method $\sigma_d = \frac{10F}{\pi D^2}(2.84(t/D) - 0.126(t/W) + 3.15(W/D) + 0.01)^{-1}$. The proposed method has better accuracy, however, requires additional characterisation of the compressive strength of the material.

Virtual Formulation Laboratory for prediction and optimisation of manufacturability of advanced solids based formulations

I.C. Sinka[1]*, M. Ghadiri[2], J.YY. Heng[3], M.S.A. Bradley[4], R. Davidchack[1], X. Jia[2], M., R. Berry[4]
B. Edmans[1], M. Pasha[2], V. Karde[3], N. di Pasquale[1] and H.S. Kahrizsangi[4]

*ics4@le.ac.uk

[1]University of Leicester, [2]University of Leeds; [3]Imperial College London, [4]University of Greenwich

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Abstract

Virtual Formulation Laboratory (VFL) is a software tool which is being developed to enable the prediction and optimisation of manufacturability and stability of advanced solids-based formulations and considers four processes: powder flow, mixing, compaction and storage. The manufacturability problems are quantified by suitable manufacturability indicators which account for a range of material types, particle structures and blend systems to enable the formulator to test the effects of formulation changes in virtual space and check for potential manufacturing difficulties that could be experienced in production plants.

VFL is being developed through a multi-institutional collaborative project to expand the science base for understanding of surfaces, particulate structures and bulk behaviour to address physical, chemical and mechanical stability during processing and storage. The manufacturability indicators require inputs from bulk properties, particle properties and molecular information. In this poster we present the developments in five distinct areas of research: molecular dynamics, computational mechanics, particle characterisation, surface energy characterisation and characterisation of bulk powder behaviour.

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A micromechanical framework to link particle properties with compact strength

B. D. Edmans, M. N. Al-Sabbagh, I. C. Sinka

Department of Engineering, University of Leicester, Leicester LE1 7RH, United Kingdom

bde2@leicester.ac.uk, mnmas1@leicester.ac.uk, ics4@le.ac.uk

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Abstract

A significant challenge in the pharmaceutical industry concerns reducing the time and cost associated with development cycles for novel solid-based formulations, which includes achieving adequate mechanical properties such as flowability, lack of segregation, stability, compressibility and strength of compacts produced in compaction. Consequently, it is desirable to develop capability to predict macroscopic properties from particle-level information, such as particle size, size distribution, surface energy, mechanical properties, and so forth.

A framework for predicting compaction properties is proposed, based on combining a contact mechanics theory describing binary particle interactions with a micromechanical theory handling large numbers of interactions. In the current work, an analytical elastoplastic-adhesive law **[1]** is used with the anisotropic Fleck-Kuhn-MckMeeking (FKN) model **[2],** which describes envelopes of admissible stress states for compacts. These models are connected by a key intermediate-level parameter, the nondimensional adhesion strength parameter.

The potential of this approach is then investigated by reverse inference followed by forward prediction. An experimental campaign was conducted in which compacts were produced by die compaction from aluminium spheres and various pharmaceutical excipients at a range of relative densities, which were then subjected to uniaxial and diametral loading. By using a numerical fitting procedure with the FKN yield surfaces, estimates of the variation of the adhesion strength parameter with relative density were obtained from the stress states at failure obtained in the experiments. It is concluded that the framework provides a workable and verifiable approach for the prediction of compact strength, which can be further refined by the use of more sophisticated models for both contact mechanics and micromechanics.

References

[1] Mesarovic, S. D. and Johnson, K. L., *Adhesive contact of elastic-plastic spheres*, Journal of the Mechanics and Physics of Solids, 48(10):2009-2033, 2000.

[2] Fleck, N. A., *On the cold compaction of powders*, Journal of the Mechanics and Physics of Solids, 43(9):1409-1431, 1995.

[3] Al-Sabbagh, M. N*., Influence of contact strength between particles on the constitutive law for powder compaction*, PhD thesis, University of Leicester, 2018.

Contact behaviour of compressible particles

B. D. Edmans, I. C. Sinka

Department of Engineering, University of Leicester, Leicester LE1 7RH, United Kingdom

bde2@leicester.ac.uk, ics4@le.ac.uk

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Abstract

Since the original elastic analyses by Hertz **[1],** a wide variety of contact laws have been developed to describe binary particle mechanical interactions, which may include effects such as plasticity **[2]**, viscosity, adhesion and friction, obtained using analytical, numerical and empirical approaches. The dominant approach in modelling elastoplastic behaviour in analytical and numerical studies has been to use standard metal plasticity models using J2 flow plasticity models with isotropic hardening, or deformation plasticity models, both of which are incompressible under plastic deformation. However, many particles of engineering interest do in fact show permanent compressibility at the particle level, notable soil particles and agglomerated particles produced by granulation procedures in the pharmaceutical industry **[3].**

In this work, a systematic set of finite element studies implementing a customisable plasticity model were carried out to investigate contact between spheres implementing different compressible plasticity models and the effect of varying nondimensionalised material parameters. Both the development of plastic zones within the particles and normal force-displacement relationships are presented. A new hybrid Von Mises-compressible plasticity model with density-dependent elastic stiffness is proposed as a homogenised representation of granule material, for which a normal force-displacement relation is obtained and related to the internal development of plastic zones. The influence of model and parameter choice is discussed with reference to internal micromechanics.

References

[1] Hertz, H. *Über die Berührung fester elastischer Körper*. Journal für die reine und angewandte Mathematik, pages 156-171, 1882.

[2] Mesarovic, S. D. and Johnson, K. L. *Adhesive contact of elastic-plastic spheres*. Journal of the Mechanics and Physics of Solids, 48(10):2009–2033, 2000.

[3] Bika, D. G., Gentzler, M., and Michaels, J. N. *Mechanical properties of agglomerates*. Powder Technology, 117:98–112, 2001.

Understanding and improving powders spreadability for a recoater process in Additive Manufacturing

Filip Francqui[a], Geoffroy Lumay[b] and Quentin Ribeyre[a]

[a]Granutools, Rue Jean-Lambert Defrêne, 107, 4340 Awans, Belgium

[b]University of Liège, Allée du 6 aout, 4000 Liège, Belgium

Introduction

Granular materials and fine powders are widely used in several Additive Manufacturing (AM) applications. For example, in SLS (Selective Laser Sintering), SLM (Selective Laser Melting) and EBM (Electron Beam Melting) techniques, successive thin layers of powders are created with a ruler or with a rotating cylinder. Each layer is partially sintered or melted with and energy beam (laser or electron beam). The layer thickness defines a vertical resolution. Therefore, a thin-layer leads to a better resolution.

In order to obtain this effect, the powder is as fine as possible. Unfortunately, when the grain size decreases, the cohesiveness increases and the flowability decreases. Moreover, the powder becomes more and more sensitive to moisture. Thus, a compromise between grains size and flowability must be found. The quality of the part build with Additive Manufacturing is directly related to the powder flowing properties. The flowability must be good enough to obtain homogeneous successive powder layers.

Problematic

Different recent publications have evidencing that the classical flowmeters are unable to give pertinent information about powder flow behaviour in powder-bed-based AM. In shear cell tested and classical rheometers, the existence of a compressive load is incompatible with the free surface flow used in AM devices. However, the measurement method based on the rotating drum is a good candidate because the powder flow is analysed precisely at the powder/air interface without any compressive load. Moreover, the rotating drum geometry allows studying the natural aeration of the powder during the flow.

In this paper we will show that the probability to obtain waves during the layer formation is proportional to the Cohesive Index measured by the GranuDrum instrument. Therefore, four differents titanium powders will be presented. Finally, we will show how this measurement technique can predict the optimal ruler (recoater) speed to obtain a homogeneous powder layer.

International Fine Particles Research Institute (IFPRI) – POSTER SESSION
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Understanding calcium cooping activity of limestone for thermochemical energy storage of concentrated solar power

Pablo Garcia-Trinanes, Faculty of Engineering and Science, Flow, Heat and Reaction Engineering Group, University of Greenwich at Medway, UK
P.GarciaTrinanes@gre.ac.uk

ABSTRACT

The Calcium Looping process, the reversible reaction between $CaCO_3$ and CaO[1], is recently attracting a great deal of interest as a promising thermochemical energy storage system to be integrated in Concentrated Solar Power plants (CaL-CSP). The main drawbacks of the system are the incomplete conversion of CaO and its sintering-induced deactivation. In this work, the influence of particle size in these deactivation mechanisms has been assessed by performing experimental multicycle tests in conditions relevant for CaL-CSP applications. Limestone particles of well-defined and narrow particle size distributions have been used in the deactivation and attrition tests [2]. Results indicate that small particles below a threshold value of significantly benefit CaO multicycle conversion when calcining at low temperature. SEM analysis has been used to identify the morphological changes endured by the material along ensuing cycles, showing that the deactivation is mainly caused by pore-plugging when calcination, whereas it can be attributed instead to a loss of surface area due to extensive sintering when calcination is carried out at high temperature. Understanding dynamic flow and the influence of cohesion and tensile strength of calcium carbonate samples[3] also plays an important role in this study due to the paramount role in the Calcium Looping application.

[1] Valverde, J.M., et al. (2013), Role of looping-calcination conditions on self-reactivation of thermally pretreated CO_2 sorbents based on CaO. *Energy & Fuels*, Vol. 27,(6): pp 3373-3384, 2013
[2] Valverde, J.M. and M.A.S. Quintanilla, Attrition of Ca-based CO2-adsorbents by a high velocity gas jet. *AIChE Journal*, Vol. 59,(4): pp 1096-1107, 2013
[3] Shi, H., et al., Effect of Particle Size and Cohesion on Powder Yielding and Flow. *KONA Powder and Particle Journal*, Vol. advpub: pp, 2018

Ceramic Raw Materials and their effect on Investment Casting Refractories

Emma Jones[a], Professor Stuart Blackburn[a], Dr Jeffery Knight[b] , Dr Stewart Welch[b]

[a]School of Chemical Engineering, University of Birmingham, Edgbaston, B15 2TT
[b]Rolls-Royce Plc, Precision Casting Facility, Wilmore Road, Derby, DE24 9BD

As part of Rolls-Royce's (R-R) Civil Aerospace Division, the Turbine Supply Chain Unit designs, manufactures and supplies turbine modules to their clients. The turbine blades produced by R-R are manufactured by the investment casting process as its high precision offers near or net near shape components.

Investment casting, also known as the lost wax process, derives its name from a wax pattern being invested with a refractory material [1]. This involves dipping the wax pattern into a refractory slurry consisting of a colloidal binder, fine refractory filler and other additives; then coating it with coarse grains of a ceramic called stucco. This process is repeated several times to build up the thickness of the shell mould. After its final coating, it is allowed to dry for up to 24 hours to remove any free water and to ensure complete gelation of the binder, in order to develop the green strength of the shell mould. The wax is then removed, leaving a shell which has a cavity of an exact duplicate of the desired part into which the molten metal is poured. The metal solidifies and finally the surrounding shell is broken off. The figure below illustrates the process in more detail.

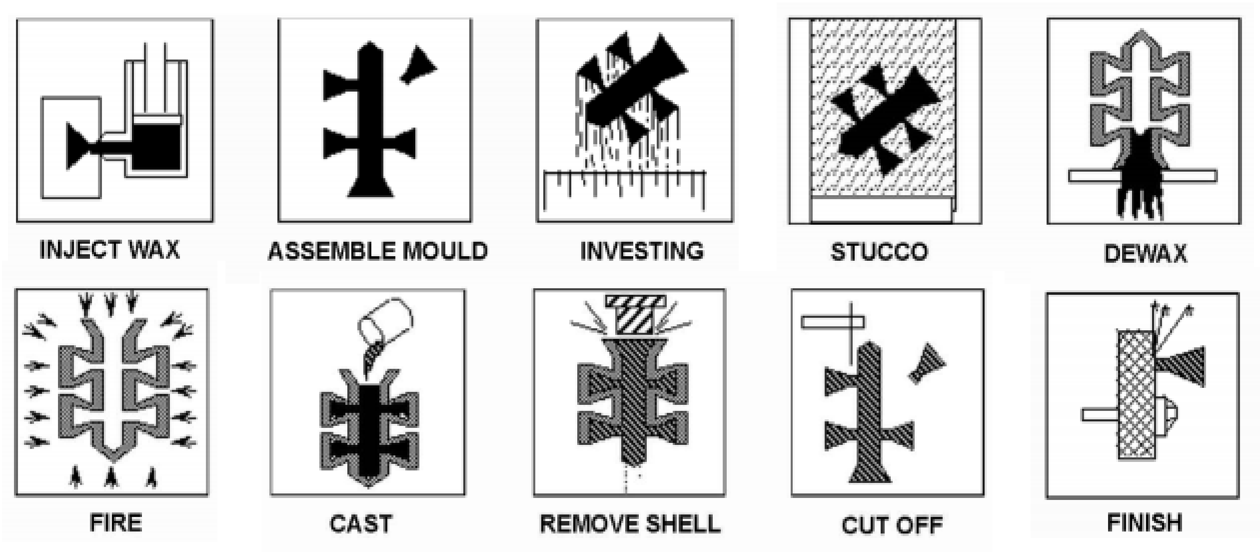

Figure 1: Systematic of basic investment casting process [1].

A key part of the investment casting process is the production of a ceramic shell (the investing and stucco stages in Figure 1) as it provides a strong, inert mould for the metal to be cast. Not only does it provide a 'supportive' role of the refractory material, but it must meet dimensional, visual and metallurgical specifications in order to produce castings which meet the high specifications required in the aerospace industry.

The project will primarily focus on the ceramic powders in the shell system, which includes the filler (zircon). There are various grades of zircon available which can be purchased from different locations, each with particular chemistries and physical properties. Extracted as a by-product of heavy mineral sands mining, zircon production is therefore influenced not only by its direct demand but also by the demand for rutile and ilmenite [2]. Therefore, the investment casting market is subject to the price inelasticity of zircon and supply cost fluctuations. Zircon is used in the refractory slurry because of its low thermal expansion, high thermal conductivity, high melting point and good chemical stability; all of which are desirable properties for a ceramic shell mould. For these reasons, zircon has remained as the refractory of choice despite price fluctuations and the effect chemical variability can have on scrap.

As the demand for more efficient engines increases for R-R, it is important to ensure continuity of supply of the raw materials. In addition, as parts are becoming more complex, there are now tighter dimensional control requirements and any change in the raw material properties can lead to significant changes in dimensional and process yields.

The project will look at commercially available zircon powders in order to characterise the effect of mining location and processing on fundamental physical and chemical properties. It will then relate these to the development of key shell properties and consequential effects on casting dimensions. Detailed understanding of the material's microstructural development through shell manufacture and subsequent casting will allow R-R to drive improvements into the dimensional capability of their cast product.

The main raw material properties to be explored are particle size distribution, composition and chemistry. The effect of particle size distribution will be studied by producing a bespoke PSD and observing what effect this has on dimensional stability of the shell mould. To identify which impurities are present in the samples and to consider what effect they have on the shell system, elemental analysis will be used to compare alternatively sourced zircons. It is expected that different impurities present will affect the thermal stability of zircon as the shell is fired up to high temperatures later in the investment casting process [3]. In regards to the chemistry of the zircon, the influence of calcination and radiation damage on the crystal structure will be explored. As radiation leads to the destruction of the lattice and metamictization of the mineral, it is expected that different levels of radiation damage between the zircon samples will cause them to have different crystal structures, densities and hardness [4].

All of the potential effects due to raw material variation discussed above will be thoroughly investigated and key material properties will be ranked based on their effect on turbine blade attributes. From this, a strategic method can then be proposed which deals with unplanned changes in order to minimise disruption to the business and to ensure product consistency.

References:

[1] S. Jones, S. Bentley and P. Marquis, "Effect of refractory phase separation on investment mould integrity," British Ceramic Transactions, vol. 101, no. 3, pp. 100-105, 2002.
[2] Zircon Industry Association, "Technical handbook on zirconium and zirconium compounds", 2015.
[3] A. Kaiser, M. Lobert and R. Telle, "Thermal stability of zircon," European Ceramic Society, vol. 28, pp. 2199-2211, 2008.
[4] J. A. Woodhead, G. R. Rossman and L. T. Silver, "The metamictization of zircon: Radiation dose-dependent structural characteristics," American Mineralogist, vol. 76, pp. 74-82, 1991.

Development of a New Apparatus for the Investigation of Particles Momentum Transfer in Fluidised Beds

Tobias Matthaeus Piepke[1-2], Stefan Pollak[2], Lyes Ait Ali Yahia[1], Raffaella Ocone[1]

[1]Heriot-Watt University Edinburgh Campus (Edinburgh, Scotland, EH14 4AS)
[2]Ruhr-Universität Bochum (Universitätsstr. 150, 44801 Bochum, Germany)

Fluidised bed technology is largely employed in the process industries. Despite their various applications, such as fluidised bed -reactors, -combustion or -dryers [1], there is still no accurate method to calculate the momentum transfer in fluidised beds [2]. Against this background, the central question that motivates this research project is whether it is possible to characterise the particles momentum transfer in fluidised beds using the same measurement principle as the one used in a Coaxial-Cylinder-Viscometer for liquids.

The Coaxial-Cylinder-Viscometer is a well-known device used to evaluate the physical characteristics of fluids. This instrument consists of an inner cylinder and the outer cylinder; the fluid, to be sheared, is placed in the annular gap between the two cylinders. The apparent torque, which can be measured during the rotation of the inner cylinder, can be converted to dynamic viscosity and to shear stress [3]. In our study, we sized and developed the FBR (Fluidised-Bed-Rheometer- Ruhr-Universität Bochum) which is based on the same measurement principle of the Coaxial-Cylinder-Viscometer. Indeed, the FBR is composed with two 450mm and 600mm length cylinders: the inner rotating one (80mm diameter made of carbon fibre) and the outer steady one (109mm diameter made of glass), respectively. A fluidised bed is generated in the 14.5mm gap between the cylinders and the torque needed to rotate the outer cylinder is determined and converted to the apparent viscosity and to the shear stress. To evaluate the momentum transfer in a fluidised bed, particles are fixed on the surface of the carbon fibre pipe. The interaction between particles and the wall can be evaluated by replacing the carbon fibre pipe with an aluminium one with different roughness.

In order to validate the FBR, we compare our measurements with the Freeman FT4 Powder Rheometer for aerated spherical particles (diameter ranging from 63 to 500 µm) in use at Heriot-Watt University. For the basic comparison of the different state of aeration in the fluidised bed, the FT4 48mm rotating impeller is used at different bed heights. Moreover, we are building a new cylindrical geometry for the FT4 Rheometer that makes it possible to have a direct comparison of the shear stress and the apparent viscosity in the fluidised bed. Once the Fluidised bed Rheometer is calibrated and validated, the measurements will be extended for a wider range of particles with different size and shape.

[1] M. S. Ray, “Chemical Engineering, Volume 2: Particle Technology and Separation Processes, 4th edn, by J.M. Coulson and J.F. Richardson. Pergamon Press, Oxford, UK. 1991. 968 pp. ISBN 0-08-037957-5,” *Dev. Chem. Eng. Miner. Process.*, vol. 1, no. 2–3, pp. 172–172.

[2] R. Borghi and F. Anselmet, *Turbulent Multiphase Flows with Heat and Mass Transfer*. John Wiley & Sons, 2013.

[3] D. S. Viswanath, T. Ghosh, D. H. L. Prasad, N. V. K. Dutt, and K. Y. Rani, *Viscosity of Liquids: Theory, Estimation, Experiment, and Data*. Springer Netherlands, 2007.

UNDERSTANDING THE FINE GRINDING OF CALCIUM CARBONATE IN STIRRED MEDIA MILLS

Sophie Rimmer[A] , Dr Andy Ingram[A], Dr Federico Alberini[A], Dr Richard Tamblyn[B]

[A:] Chemical Engineering, University of Birmingham, Edgbaston, B15 2TT
[B:] Imerys, Par Moor Centre, Par Moor Road, Par, PL24 2SQ

Calcium carbonate is a naturally occurring material that comprises around 4% of the world's crust and has many uses, including being the most widely used mineral in the paint and paper industries, where it is used as a filler or extender [1]. These applications require particles to be in the micron size range, which can be achieved by fine grinding in a stirred media mill. Stirred media mills are comprised of a stationary chamber equipped with an agitator. The chamber is filled with grinding media and a calcium carbonate slurry with a sodium polyaccrylate dispersant. The grinding media collide and impart stress on the calcium carbonate particles, causing them to break. However, this fine grinding process has a very low energy efficiency due to heat, vibration and noise losses. It is thought that only around 3-5% of the input energy is actually used for grinding, leaving a lot of scope for improvements [2].

Both the overall energy consumption and the final product particle size distribution are affected by the power draw of the mill. The power during grinding can be monitored using a load cell. The slurry viscosity affects the power draw, as well as the grinding media, as is illustrated in figure 1. Separating the effects of the grinding media and slurry viscosity can provide a more detailed understanding of the power curve and hence the grinding process.

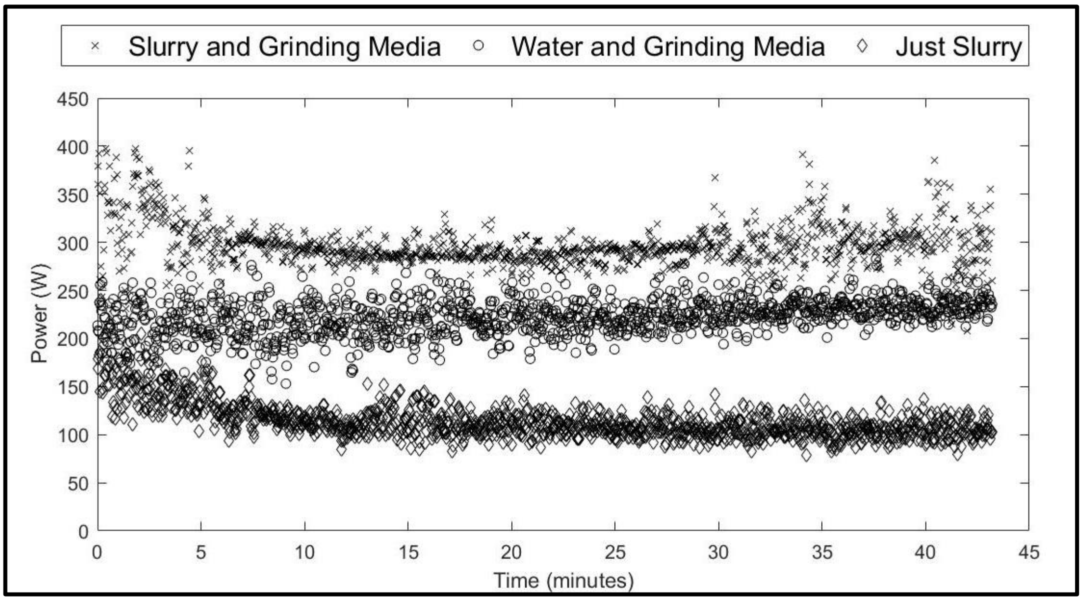

Figure 1: Power Curves in Stirred Mill

The slurry viscosity determines the velocity of the grinding media, which in turn has an effect on the amount of force imparted to particles during collisions and hence determines the final particle size distribution. This effect can be studied in more detail by observing flow patterns within the chamber. Flow visualisation studies are an important part of understanding the fine grinding process – the relative velocities of grinding media in different regions of the mill can be determined, which provides the potential for efficiency improvements to be made. All regions of the mill should ideally have a large amount of high impact collisions. Most previous flow visualisation experiments use PEPT (positron emission particle tracking), where the movement of one grinding media is tracked for a long period of time to gain information on flow in different regions of the vessel [3-5].

There is the potential for PIV (particle image velocimetry) to be used instead of PEPT for flow visualisation, providing the advantage that multiple particles can be observed, meaning that tests can be conducted in a much shorter amount of time. For PIV, a transparent set-up is required, meaning that a transparent mimic fluid for the calcium carbonate slurry needs to be found. If several mimic fluids are found for different points during the grind, the development of flow patterns during grinding can be studied and the process parameters that give the desired flow patterns can be determined.

References

[1] N.K. Mathur, S.R. Jakhar, R. Mathur, Calcium Carbonate and Derived Products, *International Journal of Science and Research,* 5, pp 2128-2133, 2013.
[2] P. Moore, Dust to Dust, *International Mining*, 3, pp 58-62, 2012
[3] R. Tamblyn, Analysis of Energy Requirements in Stirred Media Mills, PhD Thesis, University of Birmingham, 2009
[4] R.W. Barley, J. Conway-Baker, R.D. Pascoe, J. Kostuch, B. McLoughlin, D.J. Parker, Measurement of the Motion of Grinding Media in a Vertically Stirred Mill Using Positron Emission Particle Tracking (PEPT) Part II., *Minerals Engineering*, 17, pp 1179-1187, 2004
[5] Y. Yang, N.A. Rowson, R. Tamblyn, A. Ingram, Effect of Operating Parameters on Fine Particle Grinding in a Vertically Stirred Media Mill, *Separation Science and Technology,* 52, pp 1143-1152, 2017

Euler-Lagrange Simulations of Gas-Solid Flow in a Small-Scale Fluidised Bed

V. Solié, A. Angus, R. Maione, A. Ozel
Institute of Mechanical, Process & Energy Engineering, Heriot-Watt University

Introduction: Fluidised beds are widely used in chemical process industries, whether it be in the gasification of solid fuels, drying operations, or many more. The behaviour of such systems, however, has complex multi-scale features and requires further understanding. Euler-Lagrange methods have been developed for two decades to simulate hydrodynamics of gas-solid flow within fluidised beds, but what differentiates these methods is the treatment of particle-particle interactions, as well as the simulation of individual particles versus parcels of particles. In this study, we have performed simulations of gas-solid flow in a small scale fluidised bed with OpenFOAM utilising both 'computational fluid dynamics - discrete element method' (CFD-DEM) and 'course-grain particle method' (CGPM). These are collision resolved methods simulated for individual particles and parcels, respectively [1].

Methodology: Simulations of the fluidised bed system were carried out with the DPMFoam solver of OpenFOAM. This solver utilises a Euler-Lagrange approach, where the locally averaged equations of motion for the fluid phase are solved in a Eulerian framework (often denoted simply as CFD of the gas phase) and the particles are tracked in a Lagrangian fashion by solving Newton's equations of motion [2]. The flow configuration is a fluidised bed of identical specifications as the one used by Gopalan et al [3]. Collisions are modelled with a soft sphere approach using the Hertzian spring-dashpot collision model and the drag force is modelled by using the Wen-Yu drag model. When using the CGPM method particles were grouped into parcels of eight particles with double the diameter of the basic particles, and flow parameters were modified based on dimensional analysis using the statistical weight.

Results: Time-averaged Eulerian solid velocity and gas pressure profiles predicted with CFD-DEM and CGPM are compared with those of Lu et al [1] and experimental data of Gopalan et al [3]. Simulation results with CFD-DEM show better agreement but, as expected, the CGPM method performed much more efficiently at the cost of lost accuracy.

References:

[1] Liqiang Lu, Balaji Gopalan, Sofiane Benyahia (2017). Assessment of Different Discrete Particle Methods Ability To Predict Gas-Particle Flow in a Small-Scale Fluidized Bed. *Industrial & Engineering Chemistry Research, 56,* 7865-7876.
[2] Z. Y. Zhou, S. B. Kuang, K. W. Chu, A. B. Yu (2010). Discrete particle simulation of particle-fluid flow: model formulations and their applicability. *J. Fluid Mech., 661,* 482-510.
[3] Gopalan, B., Shahnam, M.; Panday, R., Tucker, J., Shaffer, F., Shadle, L., Mei, J., Rogers, W., Guenther, C., Syamlal, M. Measurements of pressure drop and particle velocity in a pseudo 2-D rectangular bed with Geldart Group D particles. Powder Technol. 2016, 291, 299−310.

Characterising dynamic powder flowability by the ball indentation method

M. Tirapelle, C. Hare

Department of Chemical and Process Engineering, University of Surrey, Guildford, GU2 7XH, UK

Abstract

Unreliable powder flow is a major problem during processing of powders, and as such there are a number of methods available for powder flow characterisation. The shear cell is the most widely used, particularly for powders subjected to moderate or high stresses, and under quasi-static conditions, with established methods for designing large bins and hoppers based on the measurement. However, this method is not suitable for measuring the flowability of dynamic systems, such as powder mixing. The classification of the flow regimes is based on dimensionless strain rate. At low dimensionless shear rates ($\gamma^*<0.15$) the 'quasi-static' flow regime exists, where behaviour is dominated by frictional interactions and shear stress is independent of flow rate. Whereas at very high shear rates ($\gamma^*>3$) powders are in the 'rapid granular flow regime', where behaviour is dominated by collisions. In between there is the intermediate regime where both collisional and frictional interactions between particles must be considered [1]. Beyond the quasi-static regime the shear stress increases with strain rate, though the relationship between shear stress and strain rate is material dependent.

The ball indentation method directly measures hardness, which is related to the unconfined yield stress by the constrain factor [2]. Here we investigate dynamic indentation, which simply consists of dropping a ball onto a cylindrical bed of previously consolidated powder. The impact of the ball on the bed is recorded with a high speed camera, to determine velocity and penetration depth. The strain rate is varied by using a range of indenter materials and sizes, and a range of drop heights. The variation of hardness with strain rate is considered for several materials, and compared to flow energy measurements in the FT4 Powder Rheometer in the same strain rate range.

The indenter size is shown to have no effect on the hardness measurement, and the obtained results are consistent with the flowability evaluation achieved with the rheometer.

Acknowledgements

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References

[1] G. I. Tardos, S. McNamara, I. Talu, Slow and intermediate flow of a frictional bulk powder in the Couette geometry, Powder Technology, 131 (2003) 23–39.

[2] A. Hassanpour, M. Ghadiri, Characterisation of Flowability of Loosely Compacted Cohesive Powders by Indentation, Particle & Particle Systems Characterisation, 24 (2007) 117–123.

Title: Measuring the Tablet-Punch Separation Force During Tablet Compaction Using an Instrumented Adhesion Punch

Authors: Henrietta Tsosie (hrt32@drexel.edu) & Dr. Antonios Zavaliangos (zaval@drexel.edu), Drexel University, Philadelphia, PA 19104

Purpose:

One of the most difficult problems encountered during pharmaceutical formulation development is the propensity of powder to adhere to the tooling, a phenomenon known as *sticking*. The instrumented adhesion punch is a relatively new approach to measuring adhesion forces and a new design was implemented for this study. This design by Huxley-Bertram contains a LVDT core to measure the displacement of the upper punch tip upon separation from the tablet surface. The punch surface includes a tapered edge which reduces the flashing effect through lower powder densification at the outer diameter during compaction. The purpose of this work was to evaluate the adhesion behavior using this instrumented punch during the unloading phase of tablet compaction for sorbitol (Parteck SI 150 and Sigma-Aldrich), mannitol (SD100 and SD200), and microcrystalline cellulose (PH102) at a range of compaction pressures.

Methods:

All materials were stored in a humidity chamber set to 32% RH for 36 hours prior to testing. All surfaces which contacted powder were cleaned with wipes that had been pre-soaked in a 70/30% isopropyl alcohol/deionized water. The bottom punch and inner diameter of the die were swabbed with magnesium stearate. Mass fills required for final in-die relative density were pre-measured prior to testing. An initial die fill height of 10 mm was used. The tablet was manually removed after each run and weighed and a photograph of the upper punch tip was taken. The dimensions of the tablet were measured using a thickness gage (Mitutoyo). The punch surfaces were inspected and compressed air was blown through the punch cavity to release any loose material that may have remained between the punch tip and the body. The upper punch tip was cleaned once again using pre-soaked wipes and compressed air was blown through the punch cavity. This process was repeated for two additional compactions, with the exception of sorbitol (Sigma-Aldrich) where a single compaction was completed. The maximum separation force between the punch and tablet was measured for each sample.

Results:

For all materials tested, with the exception of PH102, there was a general increasing trend with maximum separation forces reported up to 65% RD. The maximum force versus compaction pressure shows an increase in the adhesion force ranging from 1-30 N for mannitol. Maximum separation forces for the two sorbitol materials measured between 2-40 N with the Sigma-Aldrich sorbitol displaying a lower separation force overall. No adhesion forces were recorded for PH102. Visual inspection confirmed that material had adhered to the punch surface for both mannitol and sorbitol materials but none for PH102.

Conclusions:

Initial evaluation of the adhesion punch results show an increase in the adhesion force at increasing RD up to 65% RD with visual confirmation of the upper punch surface. Adhesion forces were measured for mannitol and sorbitol while no adhesion force was measured for PH102, a non-sticking material. More studies are required to determine how changes in tablet height, relative density, testing speeds, and punch surface roughness can affect the maximum separation forces reported in this study. In addition, other materials with a different material behavior (i.e. brittle) may display a different response.

IFPRI Project Abstract

Die filling of aerated powders

Prof. Chuan-Yu (Charley) Wu, Anastasiya Zakhvatayeva
Department of Chemical and Process Engineering, University of Surrey, Guildford, GU2 7XH, UK
16 October 2017
Abstract Date: 04 May 2018

Project Objective:

1. To investigate gravity die filling of common pharmaceutical excipients, using linear and rotary die filling devices.
2. To investigate suction die filling of common pharmaceutical excipients, suing linear die filling device.
3. To compare the die filling mechanism in suction and gravity filling and investigate potential correlations between powder properties and the die filling efficiency

Approach:

An experimental investigation of the following aspects is carried out:

1. Gravity die filling on the linear and rotary systems: die filling experiments are carried out systematically using seven common pharmaceutical powders. The die filling efficiency is compared with a set of powder properties, like particle size distribution, cohesion, flowability.
2. Suction die filling on the linear system: the device is upgraded with a vertical drive, connected to a piston, positioned inside the die. The downward movement of the piston creates a suction effect that aids the powder flow inside the die. The assembled system mimics therefore the process occurring inside the filling shoe of an industrial tableting machine. The study of suction die filling is carried out systematically, along with a full factorial DOE approach. The results are compared with the gravity filling.

Recent Results:

A rotary die filling system was used for the first part of the experiment (Fig.1). Its performance was compared with that of the linear die filling device. It was shown that the efficiency of the rotary die filling is higher than that of the linear one (Fig.2).

An extensive characterization of powder properties was performed and the results of die filling were analyzed in terms of such powder characteristics as particle size distribution (Fig.3), flow index, cohesion, flow function, air permeability.

The linear die filling device, equipped with pneumatic horizontal drive, was complemented with a vertical electromechanical drive (Fig.4) so that a fully controlled suction die filling system is developed. Special dies were manufactured, equipped with a removable piston (Fig.5).

The efficiency of suction filling at different suction speeds was compared with the gravity filling process. It was shown that the die filling efficiency is dramtically improved with suction filling and the variation of fill ratio with the shoe speed is linear rather than exponential (Fig.6).

Fig. 1. Rotary die filling system, top view.

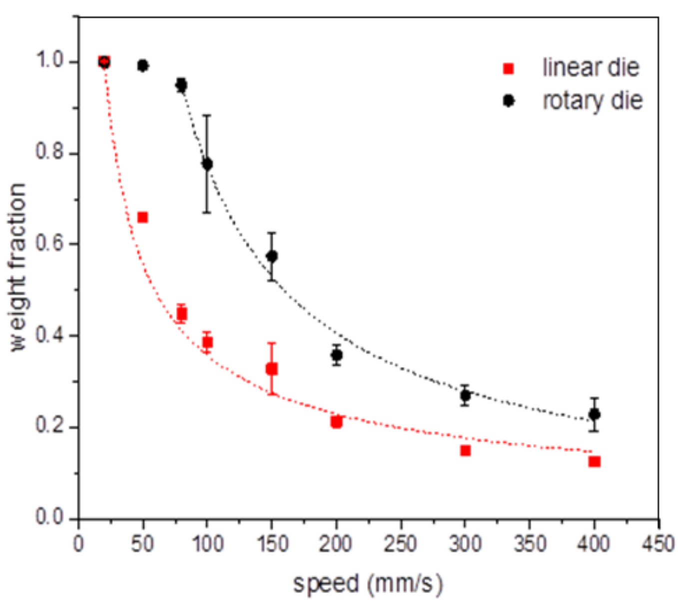

Fig. 2: Comparison of die filling efficiency of mannitol in linear (red line) and rotary (black line) systems.

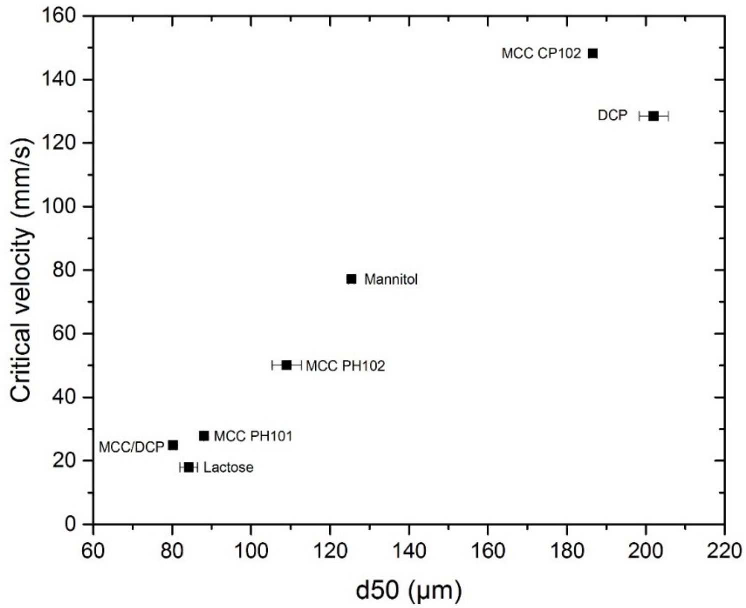

Fig. 3: Correlation between the particle size (d50) and die filling efficiency (fill ratio) for different powders.

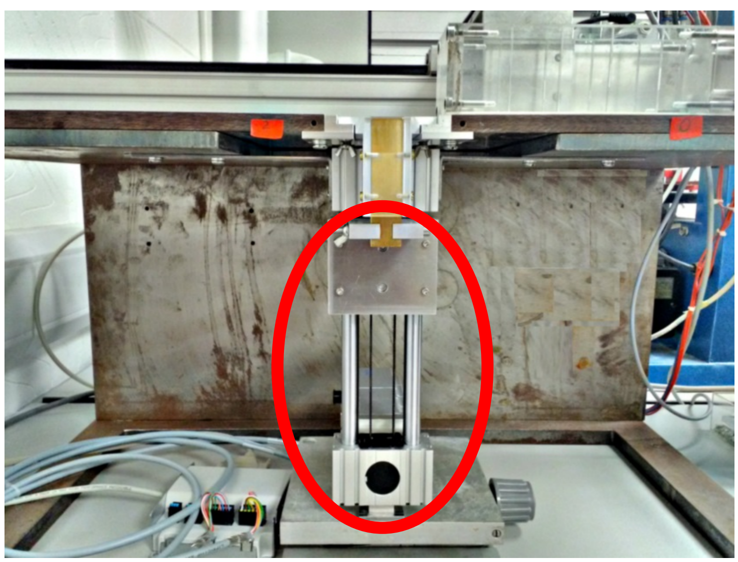

Fig. 4. The linear die filling device with the vertical electromechanical drive (circled in red)

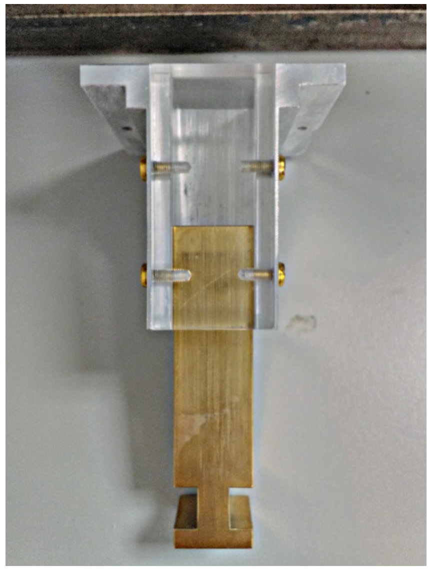

Fig. 5. Square die with a removable piston

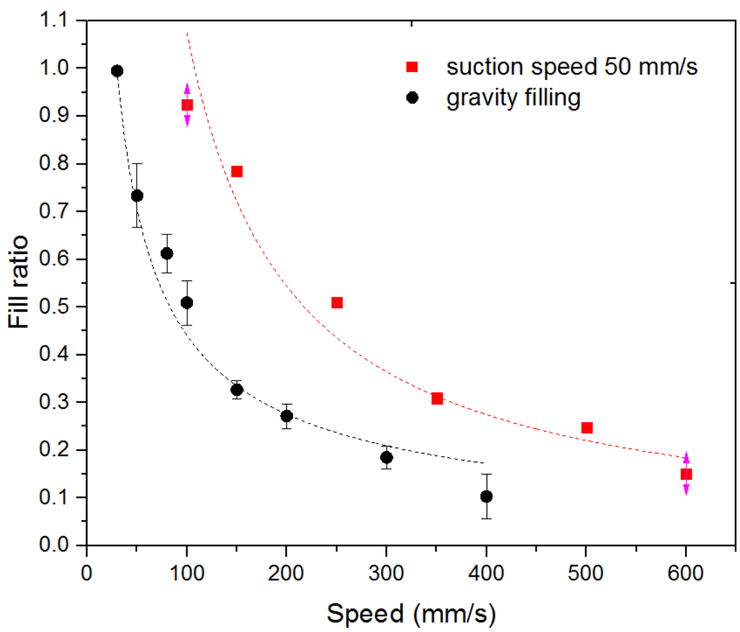

Fig. 6. Comparison of die filling efficiency of MCC PH102 on a linear die filling system: gravity fill (in black) and suction fill (in red).

Next Steps:

Further investigation on the topic is needed, specifically:

- Study of suction die filling of blends: investigation of blend uniformity under different suctions speeds.
- Die filling with a paddle die filling system: study of forced feeding mechanism.

Granule Growth And Internal Microsturcture Of Wetting And Non-Wetting Powder Belends

Duaa Al-aaraj, University of Sheffield

Wet granulation is a size enlargement process, commonly found in food, fertilizer, pharmaceutical and detergent industries. Granulation of non-wetting powder is a common problem in the pharmaceutical industry, which compromises a uniform distribution of drugs in the granulation batch. The effects of hydrophobic powder in wet granulation has been investigated by some studies, including observing the formation and stability of liquid marbles, liquid marbles morphology, examining the driving force of liquid marbles formation, and looking at hydrophobic powder distribution for different ranges of formulation wettability. The granulation growth behaviour of pure hydrophilic powder is becoming established but an understanding of the effect of heterogeneous- wetting components on the granule growth mechanism in high shear granulation remains relatively unknown, and this forms the motivation of this study.

In this study, the effect of hydrophobicity, mixing time and liquid viscosity on granule structure and size is investigated. Mixtures of hydrophilic and hydrophobic of pharmaceutical powder were granulated with dextran solutions in a tumbling drum and high shear. The results show that granule size increased with an increasing binder viscosity and mixing time, and decreasing with contact angle. Hollow granules were obtained with high binder viscosity, and the occurrence of granule coalescence was increased at lower binder viscosity and prolonged mixing time.

High-shear granulation: Experimental investigation and modelling of layered growth

Stefan de Koster

University of Sheffield

High-shear granulation, the production of agglomerates called granules by agitation of wet powders in heavy mixers, is widely used in many industries. Despite its wide application, the key mechanisms of the granulation process, i.e., wetting and nucleation, consolidation and growth, and breakage and attrition, are not fully understood. This lack of knowledge makes the design of granulated products a laborious process.

The aim of this work is to elucidate the kinetics of consolidation and layered growth in high-shear mixers and use these kinetics to develop a growth kernel for population balance modelling (PBM). In order to achieve this, a novel consolidation-only granulator (COG) has been developed to isolate growth and consolidation behaviour of granules. The obtained kinetics are then compared to an existing kinetic model in the literature, based on surface tension-driven growth. Although this model has been shown to predict static growth behaviour correctly, it has not been validated for dynamic situations.

For the investigation of dynamic growth kinetics, both the newly developed COG and a high-shear mixer with a flat blade impeller were used. Prenucleated granules were consolidated in the granulators, extracted and weighed. In this way, the growth of the granules could be monitored over time. For the COG, nuclei were produced with drop nucleation on static powder beds, whereas nuclei for the high-shear mixer were produced from paste in order to increase their survivability. True and envelope densities of the granules were determined using helium and powder pycnometry, respectively. The structure of a select number of granules was also investigated with X-ray tomography.

Four different powder-binder systems were investigated: lactose-silicone oil, lactose-polyethylene glycol (PEG), glass beads-silicone oil and glass beads-PEG. The binder viscosity was expected to have a significant effect on the growth rate. Therefore, binder viscosities were varied to investigate this dependency by using different grades of silicone oil and PEG.

Our work shows that the COG is a new, reliable tool for generating layered growth and consolidation. Furthermore, the kinetics obtained from the studies with the COG reveal that growth behaviour is linear with the square root of time, as predicted by the surface tension-driven growth model found in literature. This finding showed that consolidation behaviour has predictable kinetics, which made it possible to develop a model for layered growth. This developed model was evaluated using Mathematica software, and a comparison with experimental data showed that the model described the experimental growth behaviour well. In this way, this study has contributed to increasing our understanding of granule layering, and the development of more mechanistic and reliable models for population balance modelling.

FlowCam Nano

Camilo DenBrok

Fluid Imaging

The quantification and characterization of suspended solids in a variety of fluids has long been a challenge to industry. Emulsions, water and hydraulic fluids have specific quality specifications regarding the presence or absence of particles. Particulate matter in the sub-visible and sub-micron range often serve as reliable predictors of overall particle concentrations and therefore present the opportunity to predict or prevent problems within a process.

In this study, Her et al. assess the ability of the FlowCam Nano, a nano-flow imaging instrument by Fluid Imaging Technologies, Inc. to enumerate and characterize nano- and microparticles in a liquid sample. The nano-flow imaging instrument simultaneously imaged, counted, and characterized the nano- and microparticles present in the liquid.

This study showed how the nano-flow imaging instrument can generate highly resolved images of nano- and microparticulates ranging in size from 300 nm to 30 µm. The ability to enumerate nano- and microparticulates while simultaneously characterizing morphology enables improved identification of the particulates in the liquid and their origin.

The oil-immersion, blue LED-equipped nano-flow imaging instrument has shown capabilities in assessing particulates in many fluids. This technology could improve the detection and identification of nano- and microparticulate in source water and assess the efficacy of nano- and microparticulate removal in water treatment processes

Breakage of Carbamazepine Dihydrate Crystals under Impact

W. Goh, F. Muller, K. Sinha, N. Nere, R. Ho, S. Bordawekar and A. Sheikh

University of Leeds

Carbamazepine dihydrate crystals are acicular in shape with a very large ratio of length to width. The crystals are very weak and hence frangible and readily undergo extensive attrition during isolation and drying after crystallisation. We explore and evaluate a simple and rapid method of assessing the breakage extent by the use of the aerodynamic disperser of 'Malvern G3 Morphologi'. The shift in the crystal aspect ratio as a result of the impact breakage is quantified for various dispersion pressures using image analysis software of the instrument. The breakage extent obtained by the method is analysed and the mode of failure is identified. The results are compared with other more established impact-based method and will be presented. Disclosures: Data were generated by University of Leeds. AbbVie Inc., North Chicago, USA, provided financial support for a studentship of Wei-Pin Goh. Kushal Sinha, Nandkishor Nere, Raimundo Ho, Shailendra Bordawekar and Ahmad Sheikh are present employees of AbbVie Inc.

Characterising powder flow in dynamic processes

Marvellous Khala, Colin Hare, Chuan-Yu Wu, Martin Murtagh, Navin Venugopal, and Tim Freeman

University of Surrey

Prediction of flow performance in industrial processes is often challenging, particularly for cohesive powders due to their flow inconsistency. Many quantitative and qualitative flow measurement techniques exist that can characterise flow performance in quasi-static processes. However, there are few available techniques capable of assessing powder flowability under dynamic conditions. The FT4 Powder Rheometer (Freeman Technology), which drives a rotating blade along the vertical axis through a column of powder contained within a cylindrical vessel, is one of the few available devices that is capable of measuring powder flow in a dynamic state. The flow resistance of the rotating blade as it penetrates the powder bed is characterised by the flow energy, however, there is lack of understanding in how to relate this measurement to process design.

This work focuses on developing the relationship between the flow energy and shear stress in the FT4 rheometer. The effect of particle size and blade tip speed on flow energy has been measured experimentally for glass beads. The material investigated shows a decrease in downward specific flow energy with increasing particle size; indicating that the increased shear resistance in the bulk for smaller particle sizes exists under dynamic conditions. For smaller particles (< 300 μm) the flow energy decreases with increasing blade tip speed, however, for larger particles (> 1.7 mm) the flow energy increases with increasing blade tip speed. Numerical simulations are carried out using the Discrete Element Method (DEM) for 1.7-2.0 mm spherical particles to estimate the prevailing stresses and strains in the powder bed in relation to flow energy, particle properties, blade velocity and direction. Particle Image Velocimetry (PIV) is used to obtain the particle velocity distribution on the wall boundary surface which is compared to the numerical simulations for validation of the model.

Cohesive Powder Flow of Faceted Particles in Screw Feeders

Alejandro López, Vincenzino Vivacqua , Robert Hammond, Mojtaba Ghadiri

University of Leeds

Powder flow in screw feeders is of great interest to a wide range of industries, particularly for continuous manufacturing of pharmaceutical powders. However, analysis of flow of cohesive powders with sharp corners and edges presents a great challenge and is not yet well understood. In the present work, an in-depth analysis of cohesive powder flow of faceted particles in a screw feeder is carried out by Discrete Element Method. The influence of fundamental parameters (physical properties) and phenomena such as cohesive arching in the hopper and pitches of the screw feeder are analysed and their influence on the outlet mass flow rate is evaluated. Cohesive arching takes place when the surface energy of the particles goes above certain values and its onset is also affected by the particle geometry. Parameters for the simulations are carefully calibrated through different test methods such as Drop Test Method for surface energy and high speed camera footage for the coefficient of restitution. Cohesive arching and flow irregularities are studied and the parameters leading to their formation are analysed, for which Rocky DEM software package is used. The computational results are compared with experiments in the FT4 rheometer showing a good correlation between them.

Flowability assessment of titania at low stresses

Azza Mahmoud, Colin Hare, Chuan-Yu Wu, Ali Hassanpour

University of Surrey

Fluidised bed technology is largely employed in the process industries. Despite their various applications, such as fluidised bed -reactors, -combustion or -dryers [1], there is still no accurate method to calculate the momentum transfer in fluidised beds [2]. Against this background, the central question that motivates this research project is whether it is possible to characterise the particles momentum transfer in fluidised beds using the same measurement principle as the one used in a Coaxial-Cylinder-Viscometer for liquids.

The Coaxial-Cylinder-Viscometer is a well-known device used to evaluate the physical characteristics of fluids. This instrument consists of an inner cylinder and the outer cylinder; the fluid, to be sheared, is placed in the annular gap between the two cylinders. The apparent torque, which can be measured during the rotation of the inner cylinder, can be converted to dynamic viscosity and to shear stress [3]. In our study, we sized and developed the FBR (Fluidised-Bed-Rheometer- Ruhr-Universität Bochum) which is based on the same measurement principle of the Coaxial-Cylinder-Viscometer. Indeed, the FBR is composed with two 450mm and 600mm length cylinders: the inner rotating one (80mm diameter made of carbon fibre) and the outer steady one (109mm diameter made of glass), respectively. A fluidised bed is generated in the 14.5mm gap between the cylinders and the torque needed to rotate the outer cylinder is determined and converted to the apparent viscosity and to the shear stress. To evaluate the momentum transfer in a fluidised bed, particles are fixed on the surface of the carbon fibre pipe. The interaction between particles and the wall can be evaluated by replacing the carbon fibre pipe with an aluminium one with different roughness.

In order to validate the FBR, we compare our measurements with the Freeman FT4 Powder Rheometer for aerated spherical particles (diameter ranging from 63 to 500 µm) in use at Heriot-Watt University. For the basic comparison of the different state of aeration in the fluidised bed, the FT4 48mm rotating impeller is used at different bed heights. Moreover, we are building a new cylindrical geometry for the FT4 Rheometer that makes it possible to have a direct comparison of the shear stress and the apparent viscosity in the fluidised bed. Once the Fluidised bed Rheometer is calibrated and validated, the measurements will be extended for a wider range of particles with different size and shape.

Development of powder flow characterisation methodology for Additive manufacturing process

Mozhdeh Mehrabi, Jabbar Gardy, Ali Hassanpour, Andrew Bayly

University of Leeds

Additive manufacturing (AM) process is an official industry term to describe the recent technology that build an object by adding layer upon layer of powdered materials such as metal, plastic, etc.

The important aspect of AM is to provide low energy, low cost and, low waste manufacturing routes for high value products. This requires control and in depth understanding of the process and powder characteristics for specific application and certain machine. One of the major characteristics of the feed powder for the manufacturing is their flowability and its the assessment is crucial in order to create good-quality powder layer for AM.

Particle shape, size and surface properties such as roughness and adhesion/cohesion are major factors that influence the bulk flow behaviour of powders.

The aim of this study is to fully characterise the aforementioned particles properties for a number of metal powders and correlate these properties to their bulk flow behaviour e.g. powder spreading, in order to create good quality powder layers in additive manufacturing process.

The particles single properties (size, shape and surface properties) as well as their bulk flowability have been assessed using different techniques (such as angle of repose, shear cell and ball indentation) and the correlation between the bulk properties and single particle characteristics will be reported.

Spherical agglomeration: an investigation of the breakage mechanism using a contracting nozzle

Siti Norfarahin Mohd Yusoff

University of Sheffield

Spherical agglomeration is a size enlargement process, where crystals are grown into agglomerates through the addition of immiscible bridging liquid in-situ in a crystalliser. The advantages of this process include the potential to improve flowability, solubility and compactibility of crystalline drug particles. The spherical agglomeration process shows particular promise in improving the flow and down-stream processing of needle-like crystalline drug particles. In this work, three primary rate processes for spherical agglomeration are proposed: wetting and nucleation; growth and consolidation; attrition and breakage.

The aim of this study is to investigate and quantify the breakage rate process in spherical agglomeration process by isolating the breakage mechanism. Spherical agglomerates were produced using D4,3 86 µm polystyrene beads as model particles, with kerosene as the bridging liquid and water as the liquid suspension. A microfluidic system was used to deliver a controlled bridging liquid drop size.

Here we present the results from novel agglomerate breakage experiments. In these experiments, a suspension of spherical agglomerates were passed through a contracting nozzle placed in between two syringes. This contracting nozzle produces a well-defined shear field, which can be modified by changing the syringe discharge rate and the contracting nozzle aperture. Wet sieving analysis was used to measure the particle size distribution before and after the agglomerates were broken. The effect of varying shear rate on agglomerate size and shape was studied. It was found that agglomerate breakage increased with increasing shear rate. The number of passes through the contracting nozzle also had an effect on the agglomerate breakage; breakage was seen to increase with number of passes through the nozzle.

The Role of Glidants in Interparticle Friction

Sadegh Nadimi, Mingwen Bai, Beverley Inkson, Anne Neville & Mojtaba Ghadiri

University of Leeds

Manipulating friction in particle engineering is of great interest in a wide range of manufacturing processes, but its characterisation is very challenging due to measurement difficulties. In bulk shear deformation, the interparticle interactions are directly affected by surface characteristics, including shape, roughness and adhesion. It is common practice to add a glidant to reduce friction and manipulate adhesion in order to improve the powder flow and compaction. For example in pharmaceutical industry, this improves the drug delivery, in particular for the pulmonary route, but also in tabletting. However, the role of glidant as shape, roughness and adhesion modifier is not well understood. In this study, model carrier particles, with their shape, roughness and adhesion fully characterised, are coated with magnesium stearate (MgSt) using a high shear mixer. The spatial distribution of the glidant coating on the particle surfaces is quantified using Energy-Dispersive X-ray spectroscopy (EDX) under scanning electron microscopy (SEM) and X-ray Photoelectron Spectroscopy (XPS). The adhesion of the coated particles is quantified using the Drop-Test Method and the bulk shear strength is measured using the Schulze shear tester. The insight into the role of glidant is fundamental for better understanding and control of particulate solids processes in many manufacturing operations.

Particle Characterisation and Analysis of Jamming in Particle Spreading in Additive Manufacturing

Wenguang Nan, Mehrdad Pasha, Tina Bonakdar, Alejandro Lopez, Umair Zafar,

Sadegh Nadimi, Mojtaba Ghadiri

University of Leeds

Wet granulation is a size enlargement process, commonly found in food, fertilizer, pharmaceutical and detergent industries. Granulation of non-wetting powder is a common problem in the pharmaceutical industry, which compromises a uniform distribution of drugs in the granulation batch. The effects of hydrophobic powder in wet granulation has been investigated by some studies, including observing the formation and stability of liquid marbles, liquid marbles morphology, examining the driving force of liquid marbles formation, and looking at hydrophobic powder distribution for different ranges of formulation wettability. The granulation growth behaviour of pure hydrophilic powder is becoming established but an understanding of the effect of heterogeneous- wetting components on the granule growth mechanism in high shear granulation remains relatively unknown, and this forms the motivation of this study.

In this study, the effect of hydrophobicity, mixing time and liquid viscosity on granule structure and size is investigated. Mixtures of hydrophilic and hydrophobic of pharmaceutical powder were granulated with dextran solutions in a tumbling drum and high shear. The results show that granule size increased with an increasing binder viscosity and mixing time, and decreasing with contact angle. Hollow granules were obtained with high binder viscosity, and the occurrence of granule coalescence was increased at lower binder viscosity and prolonged mixing time.

Liquid migration during extrusion of concentrated shear thickening suspensions

Rory O'Neill, John Royer and Wilson Poon

University of Edinburgh

Extrusion of concentrated suspensions through a constriction in a die is ubiquitous in industrial applications. However, due to suspensions' inherent heterogeneity separation of the solid and liquid components, liquid migration, can occur decreasing the concentration of the extruded material. Although the occurrence of liquid migration can have catastrophic consequences, the mechanism behind it is not fully understood.

We investigate liquid migration during the extrusion of a model shear thickening suspension (corn starch particles suspended in glycerol/water) in the context of recent advances in understanding shear thickening. In these suspensions, the formation of frictional contacts under shear [1] results in an increased viscosity that diverges at a volume fraction ϕm substantially below random close packing [2], so that flow in simple shear becomes unsteady at high stresses [3]. We demonstrate the onset of this unsteady flow in simple shear can be connected to the onset of liquid migration, gaining a deeper insight into the mechanism behind liquid migration during the extrusion of shear thickening suspensions.

Flow of Formulated Powders

Mehrdad Pasha, Xiaodong Jia, and Mojtaba Ghadiri

University of Leeds

In the manufacturing of formulated powders and granules several types of particulate solids are often mixed to prepare the final products with certain specifications. Stability, content uniformity, ease of manufacturing and product performance are some of the critical attributes, which are always under consideration. The physical, chemical and surface properties of individual components play a strong role in influencing the product attributes. There is therefore a need to develop a predictive tool for the performance and behVirtual Formulation Laboratory (VFL) is a collaborative project with participation of groups from the University of Leeds, University of Leicester, University of Greenwich, and Imperial College of London, addressing the formulation science of dry powders. The ultimate aim is to develop a software tool for prediction and optimisation of manufacturability and stability of advanced solids-based formulations, especially for evaluation of their flow, segregation, mixing, caking and tabletting. The objectives are: (a) to characterise physical, chemical and mechanical and surface properties and structures, and (b) to incorporate these into a software tool (VFL) which could predict the bulk behaviour. This would enable the formulator to test the effects of formulation changes in virtual space and address potential problems in flow, mixing, caking, and tabletting.aviour of formulated products at the early stages of product and process development. Our current work on the prediction of flow of binary mixtures under dynamic conditions using Discrete Element Method is presented. The FT4 rheometer of Freeman Technology, Tewkesbury, UK, is used as the dynamic powder tester, evaluating the work required to penetrate a rotating impeller into a bed of solids. The effect of particle size distribution and interfacial surface energy of binary mixtures on the expended work is analysed and reported.

dry granulation with a new mass-based breakage function

S. Pillitteri, M. Marck, G. Lumay, E. Opsomer & N. Vandewalle

Université de Liège

Shaking a granular medium increases its packing fraction. While extensively studied, this phenomenon, called compaction, remains puzzling. Indeed, the compaction dynamics is determined by many parameters like the grain shapes, the grain sizes and the type of vibration. In the present study, we focus on the distribution of grain sizes. In particular, we present an experimental investigation of the packing fraction of various mixtures of spherical grains with different sizes. The compaction dynamics is also analyzed for different vibration strengths and orientations. Finally, a theoretical model is presented to fit the experimental data. This study is conducted in the framework of the “PowderReg” project, funded by the European programme Interreg VA GR within the priority axis 4 "Strengthen the competitiveness and the attractiveness of the Grande Région / Großregion."

Population balance modelling of ribbon milling process in

Pozza Filippoa, Chuan-Yu Wu, L.X. Liu

University of Padua

Abstract: Die compaction followed by milling is one of the methods for dry granulation. The material properties of the powder and the conditions in the compactor a ect the strength of the tablets, and subsequently a ect the size distribution of milled ribbons. A good prediction of milled granule size distribution is essential for ensuring table quality. The population balance model (PBM) approach is widely adopted to model breakage, crystallization and settling processes in various industries, such as mining, food, chemical and pharmaceutical industries. Modelling breakage processes with PBM requires the formulation of a breakage kernel that represents the breakage phenomenon. The strength of the population balance model is its capability to predict the particle size distribution of the milled product as a function of the material properties and the design and operational variables of the mill. Therefore, a mass-based population balance model coupled with a new mass-based breakage kernel based on the Weibull function is developed in this study to simulate the batch milling process. Both model parameter estimation and sensitivity are performed. The model shows good agreement with the experimental data and it is particularly suitable for modelling bi-modal distribution. A sensitivity analysis leads to a simplied model with only one variable as a function of porosity and the accuracy is experimentally validated.

Effect of External Load on the Evolution of Post-Compaction Properties of Sodium Chloride Compacts and its Mixtures

Jovana Radojevic and Antonios Zavaliangos

Drexel University

Purpose:

The purpose of this work is to deepen the understanding of the room-temperature sintering mechanism responsible for strengthening of sodium chloride (NaCl) compacts during post-compaction storage. A mechanistic consideration of factors that lead to disruption of this mechanism is offered as well.

Methods:

As received NaCl powder was ball milled for 18 hours to reduce particle size. Prior to compaction, powders were stored in a controlled environment at 20°C and 60% relative humidity (RH) for at least 4 days. Compacts were made from both as received and milled NaCl powders. Compaction was done using Instron 5800R IUTM (Norwood, MA) at five different pressures to obtain compacts of different relative densities. One group of compacts was tested immediately after compaction while the other group was stored under the same conditions for 24 hours prior to tensile strength testing. Diametrical compression testing was done on a CT5 (Engineering Systems NOTTM) desktop mechanical testing machine and Hertz formula was used to calculate tensile strengths of compacts. Scanning electron microscopy (SEM) images were obtained on the ZEISS Surpa HV50 SEM machine.

Milled NaCl powders were mixed with 3 different excipients: potato starch (Avebe), microcrystalline cellulose (MCC Avicel PH102) and dicalcium phosphate (Emcompress) in 50/50 v/v % ratios. Mixing was performed on a rotating mixer for 12 hours. After mixing the same compaction and testing procedures were followed for mixtures.

Results:

Compacts made of milled NaCl powders exhibited higher strengths and a larger increase in strength than compacts made of as-received powders. SEM images reveal significant differences in samples tested immediately after compaction and after a 24h storage. Fracture surfaces of the former show detached particles of NaCl indicating that fracture separated the particles. Surfaces of samples tested 24 hours after compaction reveal noticeably more cleavage planes which indicate that fracture went through the particle rather than around it. This strongly suggests that contacts between particles strengthened during storage (via the sintering mechanism) and it was easier for the crack to propagate through the particle than to separate the neighboring particles.

Experiments with diametrically loaded specimens revealed that the strengths of NaCl compacts decrease with an increase in induced tensile stresses. Mixtures of NaCl with starch and MCC show a decrease in strength after 24h storage while a mixture of NaCl with Emcompress experiences an increase in strength under the same conditions.

Conclusions:

Dissolution reprecipitation mechanism responsible for strengthening of NaCl compacts was described in more detail. SEM images support the claim that post-compaction storage of NaCl compacts at 20°C and 60%RH strengthens particle contacts. The strengthening mechanism can be delayed or completely inhibited if large enough tensile stresses are imposed on compacted NaCl particles. Compaction of a mixture of NaCl with a material of a different elastic modulus leads to development of residual stresses in each of the phases, where the stiffer material experiences tensile stresses. In cases when NaCl is the stiffer phase the strength of mixtures decreases during storage while mixtures of NaCl with a material of a higher elastic modulus lead to an increase of mixtures' strengths.

Understanding and improving powders spreadability for a recoater process in Additive Manufacturing

Filip Francquia, Geoffroy Lumayb and Quentin Ribeyrea

Granutools

Introduction

Granular materials and fine powders are widely used in several Additive Manufacturing (AM) applications. For example, in SLS (Selective Laser Sintering), SLM (Selective Laser Melting) and EBM (Electron Beam Melting) techniques, successive thin layers of powders are created with a ruler or with a rotating cylinder. Each layer is partially sintered or melted with and energy beam (laser or electron beam). The layer thickness defines a vertical resolution. Therefore, a thin-layer leads to a better resolution.

In order to obtain this effect, the powder is as fine as possible. Unfortunately, when the grain size decreases, the cohesiveness increases and the flowability decreases. Moreover, the powder becomes more and more sensitive to moisture. Thus, a compromise between grains size and flowability must be found. The quality of the part build with Additive Manufacturing is directly related to the powder flowing properties. The flowability must be good enough to obtain homogeneous successive powder layers.

Problematic

Different recent publications have evidencing that the classical flowmeters are unable to give pertinent information about powder flow behaviour in powder-bed-based AM. In shear cell tested and classical rheometers, the existence of a compressive load is incompatible with the free surface flow used in AM devices. However, the measurement method based on the rotating drum is a good candidate because the powder flow is analysed precisely at the powder/air interface without any compressive load. Moreover, the rotating drum geometry allows studying the natural aeration of the powder during the flow.

In this paper we will show that the probability to obtain waves during the layer formation is proportional to the Cohesive Index measured by the GranuDrum instrument. Therefore, four differents titanium powders will be presented. Finally, we will show how this measurement technique can predict the optimal ruler (recoater) speed to obtain a homogeneous powder layer.

Understanding the Fine Grinding of Calcium Carbonate in Stirred Media Mills

Sophie Rimmer, Dr Andy Ingram, Dr Federico Alberini, Dr Richard Tamblyn

University of Birmingham

Calcium carbonate is a naturally occurring material that comprises around 4% of the world's crust and has many uses, including being the most widely used mineral in the paint and paper industries, where it is used as a filler or extender [1]. These applications require particles to be in the micron size range, which can be achieved by fine grinding in a stirred media mill. Stirred media mills are comprised of a stationary chamber equipped with an agitator. The chamber is filled with grinding media and a calcium carbonate slurry with a sodium polyaccrylate dispersant. The grinding media collide and impart stress on the calcium carbonate particles, causing them to break. However, this fine grinding process has a very low energy efficiency due to heat, vibration and noise losses. It is thought that only around 3-5% of the input energy is actually used for grinding, leaving a lot of scope for improvements [2].

Both the overall energy consumption and the final product particle size distribution are affected by the power draw of the mill. The power during grinding can be monitored using a load cell. The slurry viscosity affects the power draw, as well as the grinding media, as is illustrated in figure 1. Separating the effects of the grinding media and slurry viscosity can provide a more detailed understanding of the power curve and hence the grinding process.

Figure 1: Power Curves in Stirred Mill

The slurry viscosity determines the velocity of the grinding media, which in turn has an effect on the amount of force imparted to particles during collisions and hence determines the final particle size distribution. This effect can be studied in more detail by observing flow patterns within the chamber. Flow visualisation studies are an important part of understanding the fine grinding process – the relative velocities of

grinding media in different regions of the mill can be determined, which provides the potential for efficiency improvements to be made. All regions of the mill should ideally have a large amount of high impact collisions. Most previous flow visualisation experiments use PEPT (positron emission particle tracking), where the movement of one grinding media is tracked for a long period of time to gain information on flow in different regions of the vessel [3-5].

There is the potential for PIV (particle image velocimetry) to be used instead of PEPT for flow visualisation, providing the advantage that multiple particles can be observed, meaning that tests can be conducted in a much shorter amount of time. For PIV, a transparent set-up is required, meaning that a transparent mimic fluid for the calcium carbonate slurry needs to be found. If several mimic fluids are found for different points during the grind, the development of flow patterns during grinding can be studied and the process parameters that give the desired flow patterns can be determined.

CFD-DEM Modelling of Spiral Jet Milling

Lewis Scott, Antonia Borissova, Mojtaba Ghadiri

University of Leeds

The spiral jet mill is widely used for applications requiring a narrow particle size distribution in the micron range. Size reduction is brought about by fluid energy, causing inter-particle and particle-wall collisions in a rapidly shearing bed under a centrifugal force field. The forced-vortex fluid flow field prevents large particles leaving the mill, unless their size reduces to the extent that the radial fluid velocity can drag them out of the mill. It is mechanically a simple system, but its analysis is highly challenging, as the particles move with a velocity gradient in a dense phase state near the wall and in a lean phase state towards the central exit port. This is obviously driven by the high nozzle velocity inducing tangential acceleration of the particles, but also, in turn, the particle motion with great radial void fraction gradients, ranging from dense to lean phases, has a strong influence over the fluid flow field. To make the situation even more intractable, particles undergo size reduction and change the rheology of the moving bed. Clearly, this is a complex fluid dynamics situation for which current deterministic modelling tools are unable to tackle it rigorously. In this work, we consider a simpler case of particles not undergoing size reduction and analyse the solids-fluid motion by the use of CFD-DEM approach. A spiral jet mill (Hosokawa Micron 50AS) is simulated and the particle collision behaviour (frequency and velocity) is analysed as a function of gas pressure and particle loading rate. This will then be combined with a semi-empirical model of breakage by impact to predict the extent of size reduction as a function of the feed material properties of the operating conditions. The approach has the potential to identify the method for scaling up of such mills and optimising the energy utilisation.

Granule Characterisation After Twin Screw Granulation

Rachael Shinebaum, Andrew Ingram, Hannah Batchelor, Gavin K. Reynolds, Ian Gabbott, Elaine H. Stone, Catherine J. Howe, Natasha Mudhar

University of Birmingham

Wet granulation is a commonly used process within a wide range of industries and improves the performance of particulate products via their structure, properties and attributes before future processing. Within the pharmaceutical industry, a shift towards continuous processing of granules via wet granulation, away from traditional batch-wise techniques is underway. Continuous manufacturing reduces plant footprint, reduces process development costs and allows ease of scale-up to full production (Seem, et al., 2015). Twin Screw Granulation (TSG) is a continuous process which, in recent years, has been the subject of much research to increase knowledge in its role within solid oral dosage form manufacturing. Within the TSG process there are a large number of variable process parameters including: screw element configuration, screw speed, liquid feed quantity and powder feed rate (Lute, et al., 2016). Further work is required to gain a deep understanding of the mechanisms and process factors required to predict the characteristics and quality of the resulting granules required by the FDA regulations, for example Quality by Design (QbD) and Process Analytical Technology (PAT) (Dhenge, et al., 2012).

This study presents the key properties of granules produced via TSG including particle size distribution, shape, internal porosity, strength and tabletabilty. Granules of pure mannitol and two varieties of lactose were produced using TSG with water as a liquid binder. The TSG set-up was varied from conveying only elements, one kneading zone and finally two kneading zones.

Figure 1. The effect of increasing granulating fluid and TSG kneading zones on granule size.

Granule size was found using sieve analysis and increased dramatically with increasing liquid content and kneading zones used within the TSG barrel. Utilising bulk uniaxial compaction and micro X-ray computer tomography as characterisation techniques, the granules produced at a high liquid to solid ratio were found to be stronger and less porous than those with low liquid content across all three materials. A hydraulic Compaction Simulator was used to assess the granule tabletability and results showed that the compressive nature of granules varied between all materials and manufacturing conditions. It is hoped that a greater understanding of the pore shape and size within granules will aid the prediction of granule performance in tabletability.

Computational suspension rheology: Tuning viscosity and shear thickening

Julien Sindt

University of Edinburgh

Sudden increases in suspension viscosities at high flow rates due to shear thickening is a cause of great grievance within many industries. Recent experimental and theoretical work has shown that shear thickening occurs when the particles within a dense-particle suspension reach frictional contact. Here, we show three examples of ongoing simulation work attempting to get a handle on tuning the viscosity and shear thickening of dense-particle suspensions. The projects shown demonstrate the ability of simulations to link well with theory and experiment."

Photoelastic rheological study of slow, dense, free-surface granular flows

Amalia Thomas, Nathalie M Vriend

University of Sheffield

A novel experimental setup was constructed in which steady 2D avalanches of photoelastic discs are maintained in a narrow, inclined chute over smooth and rough bases. The dry granular flows produced are in the extreme of the slow, dense and thin regime, and in some experiments the transition between solid- and fluid-like behaviours is observable. Constant density and quasi-linear velocity profiles were measured through particle tracking at several downstream locations along the chute. Inter-particle interactions were quantified applying the photoelastic technique and modelled by drawing statistics from the discrete force measurements and by calculating coarse-grained profiles of all stress tensor components. The results are the first obtained experimentally that combine flow kinematic and dynamic measurements for an important but little explored regime. As such, the conclusions drawn offer experimental validation of existing models, and new insight on the distribution of forces within slow, dense and thin flows, on the effect of topography, and on the transition between solid and fluid-like states.

Optimising the Study of Granular Media Through a Combined Experimental-Numerical Approach

Kit Windows-Yule

University of Birmingham

The experimental imaging and/or numerical modelling of granular and particulate media is crucial to our understanding of these important systems. However, all contemporary experimental and numerical techniques used in the study of granular and particulate media possess limitations - be it in terms of resolution, reliability, range or various other factors - meaning that there exists no single technique capable of providing full information regarding a given system. However, by combining multiple techniques, it is possible to build up a complete picture. Using the specific example of combined experimental imaging using Positron Emission Particle Tracking and Discrete Element Method simulation, we illustrate the power of adopting such a hybrid approach.

Self-Assembled Monolayers as Nucleating Surfaces to Study Early Formation Pathways of Crystal Polymorphs

Ulrich Wiesner

Cornell University

Long abstract with images - Project Objective:

IFPRI is interested in understanding and controlling crystallinity, polymorphism, and particle morphology in the early formation stages of crystals. High level objective of this project is therefore to identify appropriate model systems to study, adapt, and apply characterization techniques to describe early particle formation states, and to collect data that is relevant for the development of molecular dynamics simulations or other models of assembly of molecules into nascent crystals. Focus should be on identifying possible early non-classical crystallization pathways, including amorphous states and oriented attachment of clusters to growing particles.

Approach:

Self-assembled monolayers (SAMs) will be used to identify model systems for studies of the relationship between surface chemistry, solution conditions, and nucleation and growth of particular crystal polymorphs. Interesting early particle/crystal formation stages will be identified using synchrotron-based in-situ x-ray experiments. In final stages of this project cryo-(scanning) electron microscopy will be used to study the morphology of such early particles/crystals.

An investigation of particle coating behaviour via contact spreading in a small scale fluidised bed coating system

Norzaida Yusof

University of Sheffield

Spray coating in fluidised bed systems is of importance in many industries, such as food and pharmaceuticals. The bulk of research in these systems considers the interaction between liquid sprays and particles, however the effect of liquid transfer between particles via contact spreading is usually assumed to be insignificant.

This study was designed to investigate the role of liquid spreading in small-scale fluidised bed systems via the contact spreading mechanism. Alumina beads (mean size 1 mm) were used as model material and aqueous solutions of Hydroxypropyl methylcellulose (HPMC) with different molecular weights (16000, 35600 and 60000) were used to vary the viscosity of the coating liquids. The coating liquids were dyed to quantify the inter-particle coating variability in terms of coefficient of variation (CoV) based on the red intensity on coated particles by colorimetric analysis. The experiments were also carried out at varying fluidisation velocity (1.2-1.8 times the minimum superficial fluidisation velocity).

For all experimental conditions, coating uniformity increased with mixing time. This emphasises the importance of the contact spreading mechanism in fluidised bed coating.

Assessment of Triboelectric Charging Propensity of Powders by Aerodynamic Dispersion

Umair Zafar and Mojtaba Ghadiri

University of Leeds

Powder handling and processing can give rise to tribo-electrification of particles. The resulting electrostatic force can induce segregation and agglomeration of particle as well as undesirable adhesion to the walls of the processing equipment. This can have deleterious effects on product quality and smooth operation of the process. Current methods for assessing tribo-electric charging propensity of powders are unsuitable for testing small sample quantities. This is an area of great interest in pharmaceutical applications as in the early stages of a new drug development the quantity of powder available for testing is usually very small. In this work, the dispersion unit of the Malvern Morphologi G3® is adapted for dispersing particles by a pressure pulse of compressed gas. This causes inter-particle and particle-wall collisions leading to charge transfer, which is measured immediately downstream of the dispersion unit by an electrometer connected to a Faraday cup. The effect of a number of factors such as sample volume, dispersion pressure, test material functional group and wall material on the extent of tribo-electric charging is investigated for organic crystalline particles, such as aspirin, α-lactose monohydrate, paracetamol, metacetamol, urea, etc. The methodology is highly sensitive to variations of surface characteristics and can pick up differences in crystallisation conditions and manufacturing processes.