IPROCOM Newsletter

Issue No. 3 **June 2015**

Welcome to the 3rd issue of the IPROCOM newsletters! I hope you have a fantastic summer wherever you are!

The 3nd Advanced Training Course (ATC3) on "Intelligent modelling: principles & applications" was successfully held in Jagiellonian University, Krakow, Poland in October 2014. We all had a wonderful and rewarding time! In addition, the 4th Advanced Training Course (ATC4) on "Regulations, legislation and good manufacture practice" was also successfully held in AstraZeneca plc, Macclesfield, in March 2015. I'd like to express my appreciation to the organisers of both events, and to all invited speakers and IPROCOM supervisors and international advisory board members for their contributions. You can find more information on IPROCOM ATC3 & ATC4 in this newsletter.

IPROCOM members at ATC3, Krakow, Poland

IPROCOM members at ATC4, Macclesfield, UK

The mid-term review meeting organized in Krakow, Poland on 17th October 2014 went well. Professor Karen Hapgood (Monash University, Australia) in her capacity of the expert reviewer appointed by REA commented that "The project is making good progress, the project has achieved most of its objectives and technical goals for the period with relatively minor deviations". I'd like to express my gratitude to all IPROCOM members for your hard work and great achievement during the first half of the project!

Dr Sebastian Gonzalez completed his project with IPROCOM and became the first IPROCOM alumnus. We wish him every success for the future! I am also very pleased to know that several journal papers have been published based upon IPROCOM work, and Serena Schiano has won the first prize in the poster competition at the Compaction Simulation Forum 2015. Well done, fellows, keep it up!

Finally, ATC5 is fast approaching. I look forward to meeting you all in Cluj-Napoca, Romania soon.

Prof. Charley Wu, IPROCOM coordinator

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This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement No. 316555.

Particle flow in roll compaction: a DEM model

Luca Orefice

Introduction

Despite a roll compactor being mechanically simple, the system is still a "black box" since it is difficult to obtain any experimental data about the powder either in the feeding or in the compaction regions, besides the particles' behaviour. The latter can be monitored with simple particle tracking [1], but gives no information about either the density of the powder or its velocity field.

DEM models can be useful to better understand the process at the particle level. Not only the powder components are resolved, which naturally introduces finite size effects due to the rearrangement of the particle while "competing" for free space, but physical quantities such as density and velocity can be directly computed in any region of the bulk. In a memory-dependent system such as granular matter, most of the information about the system is lost after the compaction, thus the necessity to compute those quantities directly in the compaction region. On the other side, the experimental data gathered from the compaction can be used to validate the model.

Results

Figure 1 shows the trajectories of 16 particles while travelling from the feeding region and subsequently crossing the roll gap.

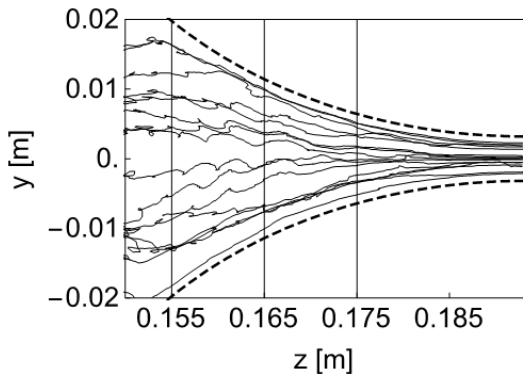


Figure 1 Snapshot of the system in the segregated state for a vertical cut along the rotation axis.

The oscillatory behaviour due to the flow is induced by the rotation of the screw, and is in qualitative agreement with the experimental results obtained by particle tracking [1].

Figure 2 shows coarse grained averages of mass density and particles' velocity along the feeding direction.

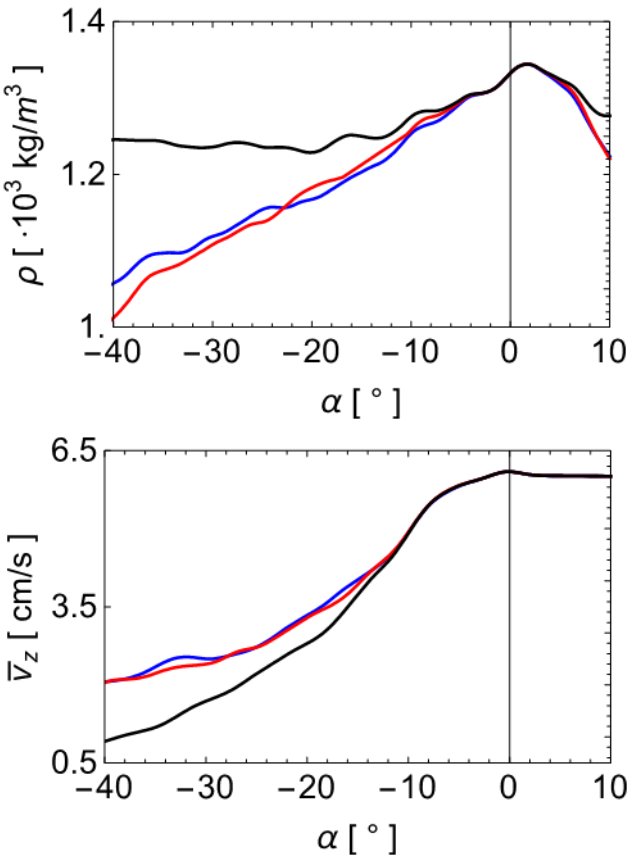


Figure 2: coarse grained mass density (top) and axial velocity (bottom) for different angular positions with respect to the rollers' gap. The three curves are referring to the three different surfaces: middle plane (black), top roll (red) and bottom roll (blue)

The density is higher around the middle plane due to a pre-compression of the powder starting in the feeding region as a result of the screw motion, while the peak of the density is reached in the compaction gap.

Particle flow in rolling compaction: a DEM model

Luca Orefice

For the velocity along the feeding direction two regions can be identified: for α < 10° the particles dragged by the rollers have a higher velocity than the ones at the middle plane. Having different velocities means that the particles are still rearranging with respect to one another. However, for α > 10° the velocity profiles become identical, which means that the particles are almost interlocked and arranged in layers, moving collectively as a bulk at the same velocity toward the gap.

When the steady state of the system is reached the particles initially loaded into the screw manage to fill the compaction region and the mass throughput becomes constant in time. However, the particles are fed into the system by a screw feeder, whose output is not constant in time but periodic with a period of TS=2/3 s. This means that, in the neighbourhood of the feeding region, the particles' flow is periodic as well.

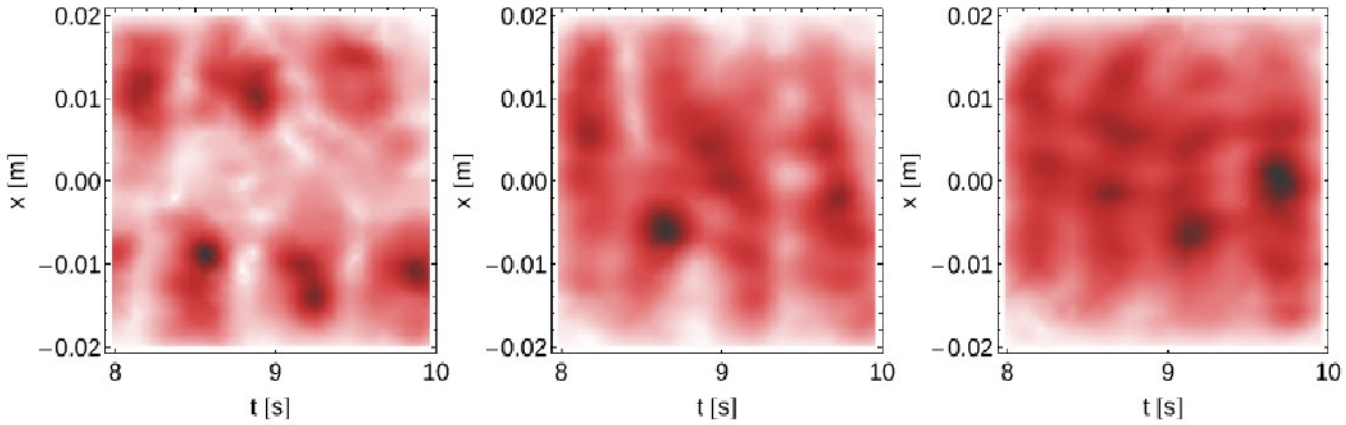


Figure 3 coarse grained space-time plots of particle's speed at three different axial positions (from left to right: z=0.155, 0.165, 0.175 m). Its magnitude in the stagnant center region around the centerline is considerably lower than its mean for z=0.155 m, while oscillates in the edges with a period equal to the screw's period.

The spatial distribution of the mass density, besides being anisotropic in space as showed earlier, is homogeneous in time. The speed of the particles, however, oscillates in time with a period TS as can be seen in Figure 3.

Conclusions

The model does not exhibit any nip angle in the strict meaning of the term, i.e. a region where there is a collective motion along the feeding direction due to the particles sticking to the rollers, moving with their tangential velocity toward the gap. Here the collective uniform motion is found, but the particles still slip upon the rollers' surfaces, having a velocity lower than the tangential one. This might be due to the cohesiveness nature of the particles; further investigations in this direction will be a topic for future studies.

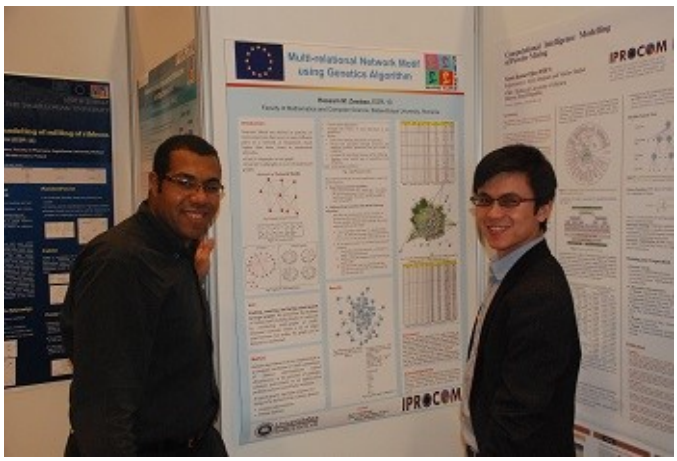
Finally, gravity seems not to be influential for both density and velocity: the screw feeding force and the rollers' compaction force are the ones dominating the process, as expected.

References

[1] Guigon P. and Simon O., Roll press design — influence of force feed systems on compaction, Powder Technology, 130:41-48 (2003)

The 3rd IPROCOM Advance Training Course

The Third IPROCOM advanced training course (ATC 3) on "Intelligent modelling: principles & applications" was successfully held in Jagiellonian University (JU), Krakow, Poland, on 21st-23rd October 2014. The training course provide training on various approaches available to design, plan and optimize experiments and to analyse and represent complex dataset. Lectures were given by 8 international experts from Poland, UK, Germany, Romania, Australia and Czech Republic. IPROCOM ATC3 was reported in local internet-based press *"Polski".*



The ATC3 was well received with some encouraging comments from the participants including:

"*It was very interesting to appreciate the part of intelligent modelling in IPROCOM. Drs Aleksander Mendyk and Crina Grosan were eager to teach some fundamentals in computer science and computational algorithms that might be useful to most of the IPROCOM projects. The keynote lectures of Profs Kleinebudde and Hapgood were excellent in my opinion. Both presented an interesting insight of pharmaceutical manufacturing from an academic point of view.*"

"*I liked the dinners and I loved the museum. The catering was as far as now the best, even though there was no time for guided tour of the city that I found very beautiful*."

"The contents of the ATC3 was very different from previous training and it was interesting for me to find out how broad applications intelligence modelling have (Google, weather forecast, ...)."

The 4th IPROCOM Advance Training Course

Andreja Mirtic

From 23th to 27th March 2015, AstraZeneca hosted the 4th IPROCOM advance training course (ATC) for IPROCOM fellows, in addition to the project meeting. During the project meeting the IPROCOM fellows presented their work-in-progress. From their presentations, a good progress of their work was observed, covering the experimental study of manufacturing processes, developing the mechanistic models with various numerical and computational techniques, and using statistical and computational intelligent models for process understanding. IPROCOM consortium is very multidisciplinary and encourages the interactions and collaborations across disciplinary in order to link different modelling techniques and develop a multi-scale models. This meeting was a great opportunity for fellows to discuss their collaborations and plan their secondments, as well as to create a tight network of friendships.

The 4th IPROCOM ATC was on "Regulations, legislation and good manufacturing practice" for various industrial sectors and transferable skills. Fellows gain the knowledge about technical writing, interview skills, communicational skills and were trained how to give an interview in front of the camera. All these skills are important for future career of young scientists to be able to thrive in a competitive industrial or research environment that requires excellence in management and communication and also regulatory knowledge.

The IPROCOM events at AstraZeneca were a great success and a good opportunity for IPROCOM fellows that are coming from academic institutions to see activities in the industry. The fellows had also a unique opportunity to visit the manufacturing plant TPF/TXF, where they saw the whole manufacturing process, from the powder to the tablets. This will enable the IPROCOM fellows to continue with their work even more successfully based on the strong understanding of the processes and established collaborations within IPROCOM network.

Here is a selection of comments from the participants on ATC4:

"The lectures were very interesting, especially if you work in industry, these topics are very important."

"I really liked the plant tour. It was really useful for us to see how the real production works and the difference between lab scale and industrial scale."

"It was useful to get all this knowledge again and also to have the possibility to complete my knowledge in this area. I think there are many fellows they did not hear about this topics in their PhD studies, so it was the perfect occasion and location to give them an introduction ."

"It was interesting to see that in all the presentations, presenters tend to mention variables and modelling aspect of the process. Good to know about the drug license."

Dissemination activities

Varun Kumar Ojha

As a Marie Curie research fellow, I had the opportunity to connect with researchers across the world. I spent 2014 Christmas holidays in India (my home country). I discovered opportunities to discuss the research work I am doing as a Marie Skłodowska-Curie Fellow with some students, Ph.D Scholars, and researchers from various universities and institutes across the country (India). Eventually, it has turned out to be an exciting opportunity for me to encourage and motivate undergraduates, postgraduates, PhD students, and researchers to various research opportunities offered by the Marie Skłodowska-Curie actions - Research Fellowship Programme.

I had the opportunity to discuss the IPROCOM project in detail. I also received constructive feedback from the researchers and professors for further improving my ongoing research work, which may also help me to improve my research further. I attended two International Conferences: International Conference on Computational Intelligence and Data Mining, on December 20, 2015 Veer Surender Sai University, Burla India and IEEE International Conference on High Performance Computing and Applications on December 22 at Bhubaneswar, India.

On January 10, 2015, I presented a seminar “Advances in Computational Intelligence and Future Research Scope at Visva-Bharati University, India. I actively participated with a team from VSB-Technical University of Ostrava, Czech Republic and organized international Workshops on “Big Data Analytics” in Saintgits College of Engineering (Mahatma Gandhi University) and Cochin University of Science and Technology, India on January 19 and 21, 2015, respectively. On January 21, 2015, we also organized a Technical Seminar on “Big Data Analytics” at Toc-H Institute of Science and Technology, Cochin.

During the course of my research work, I have developed a software tools for feature selection and predictive modelling. In March 2015, I had the opportunity to present "A computational intelligence Perspective of Modelling and Data Analysis" at the department of Chemical and Process Engineering , and "Flexible Neural Tree as an Effective Tool for the Function Approximation and Feature Selection" at the Department of Computing at the University of Surrey.

Recently, I had the opportunity to participate in Marie Curie Alumni Association (MCAA) event in Brno, Czech Republic. My participation included a poster presentation on my research activity, achievements so far as a Marie Curie Fellow. The MCAA events program includes two interesting workshops: 1) a workshop how to present “Your research in 3 minutes: the FameLab competition”, it was organized by FameLab; 2) a comprehensive information on “MSCA: Funding schemes” for future research opportunities.

I am enjoying the Marie Curie research fellowship and keen to continue good quality research!

Research seminar at University of Cantabria

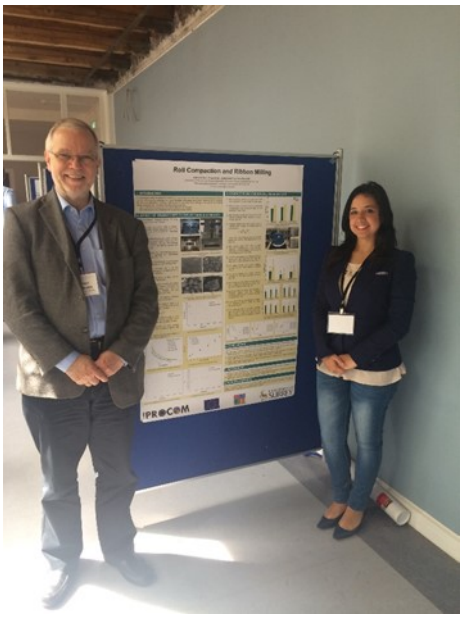
Lucia Perez Gandarillas (ESR4) had the opportunity to present an overview of her research activities at University of Cantabria (Spain) on 13th March 2015. The presentation was entitled "Improvement of mechanical processes in the pharmaceutical industry" and it took place in the framework of Master and Doctoral programs in Industrial Engineering. Research seminars are organized periodically by the research group GER (Green Engineering and Resources) from the Department of Chemistry and Process & Resource Engineering of University of Cantabria. The research seminars are oriented towards final-year master students and PhDs with the main goal of approaching a wide range of research activities to students.

The research work of the GER group (http://www.geruc.es) is focused on four major areas: waste valorization, weight of evidence, environmental information management and decision support tools and process systems.

Lucia's seminar had two main objectives: on one hand, to discuss R&D opportunities in general; on the other hand, to present the research activities of the research group RAPSODEE-Ecole des Mines d'Albi, in particular, IPROCOM research activities (http://www.surrey.ac.uk/iprocom/). During the seminar, Lucia had the opportunity to discuss with students and professors, receiving challenging questions and constructive feedbacks.

IPROCOM at the Compaction Simulation Forum (CSF) 2015

The Compaction Simulation Forum (CSF) was held on 16-17th June 2015, in Copenhagen, Denmark. The forum had a principal theme on "The connection between scientists and compression technology", so pharmaceutical compression processes, like tabletting and roll compaction, were the main areas of interest. In this forum, a series of oral presentations on powder characterization, crystallography, roll compaction behaviour and multiscale modelling of powder compaction were held, in addition there was a well organised poster session providing excellent opportunity for networking and discussion. The forum also attracted a number of companies, including Advantest, Freeman Technology, Norlab, Huxley Bertram, Medel'Pharm and Gamlen Tableting, in addition to academic participants.



"This conference was a great experience in my scientific career, as it gave me the opportunities to share my opinions with experienced scientists in the same field and I learnt a lot from the discussions. Furthermore discussing directly with people from the industry helped me in the understanding of the actual challenges and problems in the pharmaceutical industry deserving further study to achieve a better understanding and optimization of the process." said Serena Schiano.

Serena was also delighted to win the first prize in the poster competition, and to see so many participants interested in her research. This motivates her to work even hard in this challenging but exciting field. It was a great and fun experience!!!

A special and unforgettable experience: a secondment at AstraZeneca

Kitti Csordas

As in all fellows' life, after spending several months in the institute or company, there is a moment, when we should decide, where to spend our first secondment in the IPROCOM project. This decision is an important one in our work, because it gives us a special and unique opportunity to produce more data and results. I am working on the topic "Effect of material properties and system designs on roll compaction" at the Institute of Pharmaceutics and Biopharmaceutics in Duesseldorf, Germany. To fulfill the aims of my topic, it is necessary to work with different types of small scale roll compactors.

We have a Gerteis Minipactor roll compactor at our institute (Figure 1), that I have already used for the production of mannitol ribbons. It has an inclined feeding system and consists of two screws. One is for feeding and the second screw is responsible for powder tamping. As the feeding system, also the two counter-rotating rolls are obliquely positioned. It is a unique design among roll compactors on the market. Nevertheless, roll parameters play an important role in roll compaction. Rolls of Gerteis Minipactor are 25 cm in diameter and 2.5 cm wide. The roll surface can also be varied with the choice of smooth and knurled surfaces. On the other hand the design of roll compaction can be examined through the used sealing system, where Gerteis offers two possibilities: rim-rolls and side-seal. The set parameters during manufacturing were the following: specific compaction force was 2 kN/cm, 4 kN/cm, 6 kN/cm, 8 kN/cm and 10 kN/cm, in combination with 1.5mm and 3 mm roll gap. The roll speed was set at 2 rpm and 4 rpm. According to my project plan, I need to transfer the set process parameter combinations to other type of roll compactors. AlexanderWerk BT 120 roll compactor (Figure 2) has similar parameters to the Gerteis Minipactor: it has a roll diameter 12 cm and a roll width 2.5 mm, however it has a horizontal feeding system and vertically positioned rolls. Knurled (kn) and smooth (sm) roll surfaces are available too, however AlexanderWerk provides only one type of sealing system, called side-sealing (SS). This type of roll compactor is available in AstraZeneca, one of IPROCOM partners. Thus, I have decided to spend six weeks in AstraZeneca, Macclesfield, UK.

Figure 1 Gerteis Minipactor roll compactor

Figure 2 AlexanderWerk roll compactor

The first and biggest challenge was to keep the aforementioned process parameter combinations as similar as possible. To succeed, the limitations of AlexanderWerk BT 120 roll compactor had to be tested using mannitol (Pearlitol 200 SD) (Mann), microcrystalline cellulose (Avicel PH 101) (MCC) and 1:1 mixture of mannitol and MCC (MIX). After several trial tests, the parameter combinations could be defined. It was important to have process parameter settings for both materials as follows: hydraulic pressure was set at

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5 levels: 18 bars (3 kN/cm), 24 bars (4 kN/cm), 36 bars (6 kN/cm), 48 bars (8 kN/cm) and 60 bars (10 kN/cm). Ribbons were produced with a roll gap of 1.5 mm and 2.3 mm. The roll speed was kept at 3 rpm for all experiments. Above 3 rpm roll speed, the material could not be transported by the screw with a proper velocity, so the desired roll gap has never been achieved. After manufacturing 13 batches three times, the produced ribbons were analyzed utilizing GeoPyc 1360 Envelope Density Analyzer. Based on the porosity results, it can be observed that, the higher the hydraulic pressure is exerted on the material, the lower the ribbon porosity. The measured ribbon porosities are presented in Figures 3 and 4. Ribbon porosity is higher at larger roll gaps .

Knurled MCC ribbons produced with 18 bars hydraulic pressure with a 1.5 mm roll gap resulted in the highest porosity (44.2%), although the same parameter combination and design compacting mannitol resulted in 24.4% porosity. It can be explained by the plastic-elastic deformation behavior of MCC. Compacting mannitol using smooth rolls at 24 bar hydraulic pressure and 1.5 mm roll gap led to the lowest porosity (8.7%). This unusual value of porosity is the result of the brittleness of mannitol and the low surface friction between the material and roll compactor.

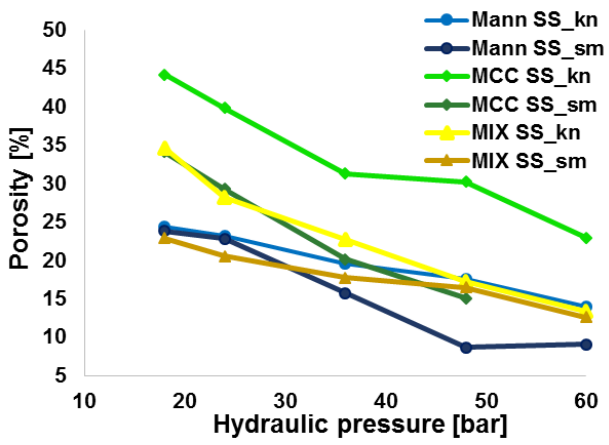

Figure 3 Correlation between ribbon porosity and hydraulic pressure at a roll gap of 1.5 mm.

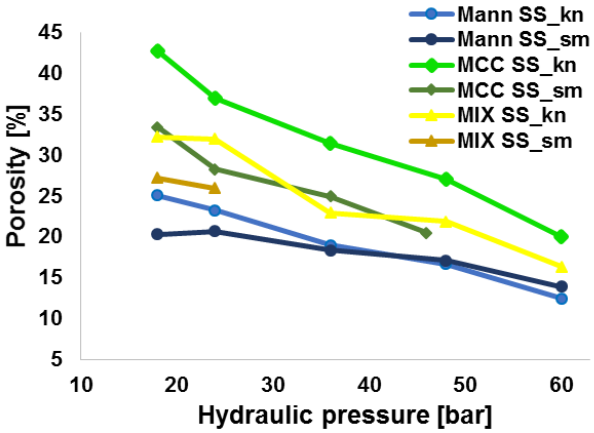

Figure 4 Correlation between ribbon porosity and hydraulic pressure at a roll gap of 2.3 mm

The goals of the first secondment were achieved. It was a very rewarding experience to work with a horizontal fed roll compactor that improved my understanding of roll compaction. Measuring the ribbon porosity using GeoPyc opened an interesting and useful area in my work on IPROCOM.

Last but not least I would like to express my gratitude to Dr. Gavin Reynolds and Dr. Andreja Mirtic, who supervised and helped my work with their suggestions and advices. We had a sucessful cooperation. I would also like to thank the support of AstraZeneca, which made it possible for me to use the necessary amount of materials and equipment during my secondment. I would like to thank to Jeff Perry, Dr. Phil Plumb and Dr. Farhan Alhusban, who gave me trainings and helped me in the practical work, Kevin Haye and Robert Perry, who provided me boxes of materials for roller compaction. I thank all the AstraZeneca co-workers from Gawsworth for the enjoyable time. I hope we will meet soon at conferences, where we can discuss our future collaboration in the field of granulation.

Fellow of this issue

Zilin Yan is from China and obtained his first degree from Huazhong University of Science and Technology (China) in materials science and engineering. He worked on the design of functionally graded coatings using finite element methods for his master's thesis. He obtained his Master's degree from the University of Chinese Academy of Sciences in nuclear energy science and engineering. He was then granted an 'Erasmus Mundus PhD fellowship' to pursue his PhD degree in University of Grenoble (France) and Technical University of Darmstadt (Germany). He explored microstructure evolution during sintering of the multilayer ceramic capacitors using DEM in conjunction with tomography, such as 3D X-ray CT and FIB-SEM 3D reconstruction. He was awarded PhD degrees in materials science from both universities in October 2013.

Dr. Zilin Yan is an author of 13 peer-reviewed journal articles and 10 conference papers. He serves as a peer reviewer for the international journals: Materials Letters and Fusion Engineering and Design. He won a travel grant to attend a winter school in Japan (2009), a Best Poster Award at International Conference on Sintering (2011) and a Chinese Government Award for Outstanding Self-financed Student Abroad (2013).

He has equal interest in numerical modelling and experimental studies on particulate materials (powder flow, compaction, forming and sintering). He has research experience in numerical methods, mainly finite/discrete element modelling, and material characterization, such as using powder rheometers, conventional microscopes, and 3D tomography.

He is now working as a Marie Curie experienced researchers (postdoc) based at Johnson Matthey Technology Centre Chilton site, Billingham, UK. He develops models to examine powder properties such as flowability and compressibility using the discrete element method. He also works on DEM calibration and validation. He is working with other researchers to develop a multi-scale modelling platform for powder compaction. He volunteers for the 'Children Challenge Industry' programme operated on Chilton site.

He enjoys this IPROCOM training network and he already accomplished his secondments to the University of Surrey (UK) and Fraunhofer IWM (Germany). He attended 12th UK Particle Forum 2014 (Manchester) and Powder Flow 2015 (Leeds) to disseminate his research outcomes and promote the IPROCOM project.

Key Dates

13 - 16 September 2015	IPROCOM ATC5, Cluj-Napoca, Romania
19 - 21 April 2016	IPROCOM conference & PARTEC 2016, Nuremberg, Germany

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- Kitti Csordas
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