

**W**elcome to the 4<sup>th</sup> issue of the IPROCOT newsletters! We hope you had a most joyful Christmas and a Happy New Year for 2016!

It has been a fantastic year with so many highlights across different aspects of IPROCOT consortium. Our interdisciplinary and cross sectoral collaboration has been going stronger and stronger. Fellows have been making impressive progress on their research projects, and building a collaborative culture! I am particularly pleased to see many high quality papers have now been published or submitted for publication from IPROCOT work! I have no doubt that with fellows' hard work and supervisors' dedication, more interesting papers will be published in 2016.

It is also my great pleasure to share with you some great news on fellows' achievement in 2015: Miss Serena Schiano won the **1<sup>st</sup> prize** in the poster competition at the Compaction Simulation Forum (CSF) held in Copenhagen, Denmark. She has been given an opportunity to give an oral presentation at this year's Compaction Simulation Forum to be held in Boston, USA, in June. Mr Alon Mazor won **2<sup>nd</sup> prize** in the Best Poster competition at the 7th International Granulation Workshop held in Sheffield in July. Mr Mohammad Hassan Khalid won the **Best paper award** at the 13th International Conference on Frontiers of Information Technology (FIT 2015).

Our 5<sup>th</sup> Advanced training course (i.e. ATC5) on "Complementary Skills for future S&T leaders" was successfully held at Babes Bolyai University, Romania, on 14- 16th September 2015. The objective of this training course is to provide training in generic and transferable skills, in particular in entrepreneurship, communicating the science and technology to the public, regulators, industry and the media. IPROCOT fellows gain the knowledge about interview skills, team working skills, and project management through preparing and delivering the lectures by themselves.

Our three experience researchers (ERs) have completed their research and training with IPROCOT in 2015 and started their new adventure in their career. We wish them all the best!

I would also like to inform you that we will run IPROCOT conference in conjunction with PARTEC 2016 in Nuremberg, Germany on 19-21st April 2016. On 19th April 2016, dedicated IPROCOT sessions will take place to showcase our fellows' collaborative work. I look forward to meeting you there!

Prof. Charley Wu  
IPROCOT coordinator

## Inside this issue

- A glimpse of IPROCOT research reported by Raphael Schubert
- A brief report of the 5<sup>th</sup> IPROCOT advanced training course
- Dissemination activities
- Outreach activities
- Secondment experience shared by Simone Loreti
- Fellow highlights



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## Crack formation in die filling processes

Raphael Schubert



On IPROCOT projects, we aim to find out how the properties of tablets are affected by manufacturing conditions and material properties. In particular, part of my project focuses on cracking of tablets during the process of die compaction. We firstly examine granules produced by roll compaction: the fine grained raw materials are pre-compacted between two rotating rolls to produce ribbons - large scale agglomerates of comparatively low tensile strength. These are then milled to produce the granules, which are the feedstock for die compaction. The individual granule is now much larger than the original grains, making the granules much easier to handle with improved flowability and thus increasing the productivity.

In die compaction, a predefined amount of granules is placed inside a cavity formed by a fixed side wall and two movable punches, then compacted uniaxially between the punches and finally ejected by raising the lower punch.

During this process, high pressures are applied to the material, and the tablet experiences complex anisotropy as well as inhomogeneous stress states. This may lead to immediate fracturing of the tablets, or to a structural weakening, which causes breakage during subsequent production and handling stages.

I aim to gain insight into the behavior of compacted

granular materials by performing numerical simulations at the particle scale using the discrete element method (DEM). The DEM solver integrates Newton's equations of motion for a large number of distinct spherical particles. There is a number of force models describing the interaction of a pair of particles in contact. During die compaction, particles sustain large plastic deformations; which needs to be considered with the DEM force model. Otherwise, unphysical behavior may be obtained.

Because of the high computational effort required for DEM simulations, one cannot simulate a whole tablet with particles of the actual sizes. Hence, I focus on a representative volume element which is meant to represent a small portion of the whole tablet. To understand the effect that different stresses have on the structural properties of the particle assembly, I first need to prescribe a certain macroscopic stress state inside the sample.

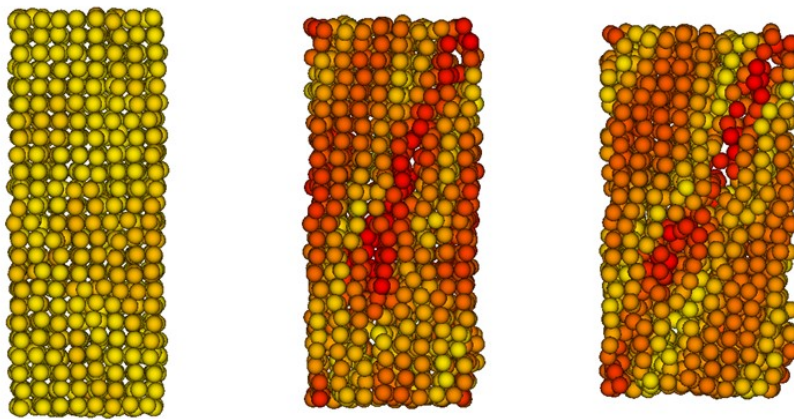
This is achieved by placing the particles in a periodic box and changing the size of the box. Decreasing the length of one side increases the stress in this direction, and vice versa. By carefully (and dynamically) adjusting the size according to the current stress state, a desired state will be reached after some relaxation. Deviatoric moments could be dealt with using non-orthogonal boxes and adjusting the skew, which, I believe, will not be necessary beyond simple shear.

When the desired stress state is realized in the sample, small perturbations are deliberately applied and the response is measured. This allows me to obtain a yield surface and describe the granular assembly as a continuous plastic material. Crack formation is very natural in that particles under strong tensile or shear stress will lose contact with some of their neighbors, so that a crack has formed.

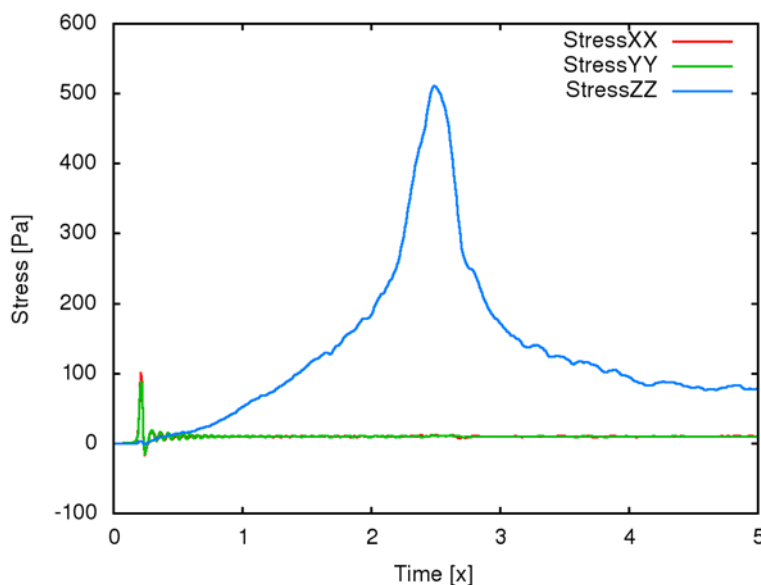
## Crack formation in die filling processes

Raphael Schubert

Using this data and my developed methods, I hope to contribute to future efforts to refine failure models used in finite element simulations of compaction and ejection, eventually leading to computational models that are able to predict the likelihood of tablet fracture during manufacture and transport.



**Figure 1** Crack formation in triaxial compression. A constant strain rate is applied along the vertical direction while the stress is kept constant for the two other directions. If the inter-particle friction is high enough, a crack will form. Particles are colored by local shear intensity.



**Figure 2:** Stress evolution in the triaxial compression test. Once cracks are formed, the powders lose their load bearing capacity, so the axial stress (ZZ) reduces sharply while the radial stresses (XX and YY) are kept constant. The snapshots correspond to the indicated times.

## The 5<sup>th</sup> IPROCOTM Advance Training Course

Hossam M. Zawbaa

Babes-Bolyai University, Cluj-Napoca, Romania hosted the 5<sup>th</sup> IPROCOTM advanced training course (ATC5) and the project meeting on 14-16th September 2015. During the project meeting (the first two days), the IPROCOTM fellows presented their project progress so far. From presentations and discussions, a good progress of their work was observed, covering the experimental study of manufacturing processes, the development of the mechanistic, statistical and computational intelligent models for process understanding. As IPROCOTM consortium is a multi-disciplinary network, it facilitates the interactions and collaborations across disciplinary in order to link different modelling techniques and develop multi-scale models. This meeting was a great opportunity for fellows to discuss their collaborations and plan their future secondments, as well as to create a tight network of friendships.

The focus of the 5th IPROCOTM ATC is on “Complementary skills for future S&T leaders”. Its objective is to provide training in generic and transferable skills, in particular in entrepreneurship, communicating the science and technology to the public, regulators, industry, and the media. The training’s topics are the following:

- Ethics in research and development;
- Team working skills;
- Project managements;
- IPR: management and exploitation;
- Time management skills;
- Interview skills: what to expect and how to prepare;
- Entrepreneurship.



IPROCOTM fellows gained the knowledge of interview skills, team working skills, project management and other transferable skills. All these skills are important for future career of the young scientists so they can thrive in a competitive industrial or academic environment that requires excellence in management, communication and regulatory knowledge.

The IPROCOTM events at Babes-Bolyai University were a great success and a good opportunity for IPROCOTM fellows that are coming from 11 academic institutes and industrial companies. This will enable the IPROCOTM fellows to continue with their research work even more successfully based on an enhanced understanding of the processes and to consolidate their collaborations within IPROCOTM network.





## The 5<sup>th</sup> IPROCOM Advance Training Course

Hossam M. Zawbaa

In what it concerned myself, I can say that I gained a lot of experience, from organizing such events (logistics, negotiation, communication, resource planning and leadership), to a better understanding of the project processes.

In conclusion, I believe that the main objectives of the project meeting and the 5th advanced training course (observing all work progress of the fellows and providing transferable skills training) have been achieved. According to the feedback from the participants, this meeting was a great success and it seems that everyone has enjoyed their stay in Romania. We all were very impressed by the excursion to Turda Salt Mine!



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Here is a selection of feedback and comments from the participants on ATC5:

*"The excursion to Turda salt mine was great and the most fun for me. However, it wasn't just that, I enjoyed meeting everyone once again and having in depth discussion on our projects."*

*"Everything was good generally but the things which I liked the most were the food and the excursion."*

*"I liked the WP discussions a lot, because it was very helpful for fellows and also for different work packages to corporate more with each other."*

*"Salina Turda was awesome, I love the sightseeing opportunity given by the ATCs."*

*"In general, I enjoyed the whole meeting, but specially the excursion because it was something new and very interesting, and it was great to have the opportunity of doing this activity in our last ATC."*

*"The programme was divided in a very good rhythm. I think the salt mine was a pretty nice excursion for all of us. Supervisors and fellows enjoyed it very much!"*

*"The project meeting met my expectations because I got lots of feedbacks about my presentation that included the results I have collected in the last few months. I learnt a lot on how to continue with the experiments and how to evaluate my results."*

*"At first I thought it would be better to receive trainings from experts, but once I attended to the presentations I realized there was a wonderful work behind. I found it an interesting activity to work on a presentation on a topic outside our field of expertise."*

## Participation at PARTICLES 2015 conference

Luca Orefice

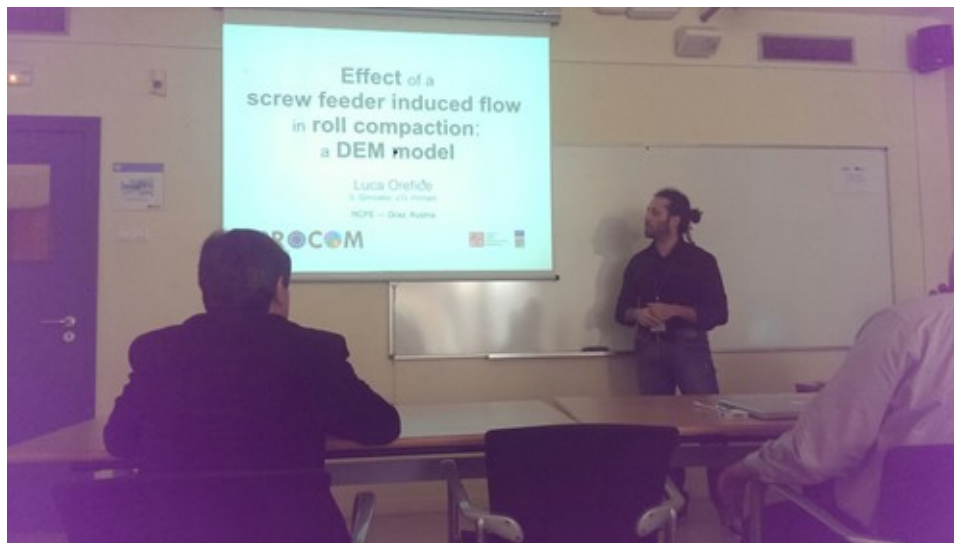
I was participating at the “IV Conference on Particle-Based Methods: PARTICLES 2015” held in Barcelona from the 28th to the 30th of September 2015.

There I was taking part in the granulation session, where I gave a presentation on “Effect of a screw feeder induced flow in roll compaction: a DEM model”. The main focus of my study was the analysis of the packing fraction and flow profiles in the transition zone between the feeding and the compaction regions. In collaboration with Alon Mazor, we aim to examine what impact the flow profile obtained from the DEM simulations will have on the compacted ribbon modelled using FEM. We will discuss our research in a “tandem presentation” at the upcoming PARTEC 2016 conference in Nuremberg, Germany.

The conference has been particularly stimulating

because I had the opportunity to meet many researchers I encountered during my various trainings and visits in this first half of my PhD program. In particular, I had the opportunity to brainstorm with the Multi-Scale Mechanics group from the University of Twente, where I aim to carry out my next secondment.

Last but not least I had the opportunity to attend to many interesting lectures, which gave me new ideas on the topic that I am studying, and which bolstered my interest on Physics of Complex Systems. I found some interesting analogies between some systems studied in the latter and the granular materials showed in some of the presentations. Therefore, I will try to apply my previous knowledge to better understand some peculiar behaviours of granular systems.



## IPROC fellow won the Best paper award at the FIT 2015 conference



The 13th International Conference on Frontiers of Information Technology (FIT 2015) was held at Islamabad, Pakistan, on 14-16th December 2015. Mr Mohammad Hassan Khalid presented a paper titled "From black-box to transparent computational intelligence models: A pharmaceutical case study". He also won the Best paper award. **Congratulations!**

## IPROCOT members at the 7th International Granulation Workshop

The 7th International Granulation Workshop was held on 1st-3rd July 2015 in Sheffield (UK). Several IPROCOT members attended the conference and presented their work.

Lucia Perez Gandarillas (ESR6) presented her recent work in an oral presentation entitled "Impact of milling process conditions on the granule's properties: effect of milling speed and rotation". The main objective of this work was to analyse the effect of different roll compaction conditions (sealing system and roll-compaction force) and milling parameters (mill type, angle of rotation and speed) on the properties of ribbons, granules and tablets.

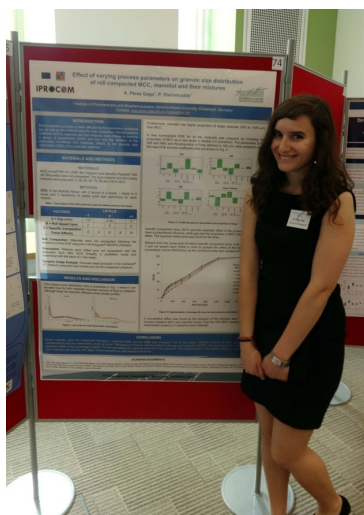
Lucia also had the opportunity to have some in-depth scientific discussions with others IPROCOT members attending the conference and with other researchers working in similar fields.

Alon Mazor (ESR 6) presented his poster entitled "FEM study of different roll compactor sealing system design", which won the 2<sup>nd</sup> prize in the AstraZeneca Most Pharmaceutically Relevant Poster Competition!



Ana Pérez Gago (ESR 3) presented a poster entitled "Effect of varying process parameters on granule size distributions of roll compacted MCC, mannitol and their mixtures". Kitti Csordas and Andreja Mirtic also presented their posters "Roll compaction of spray-dried mannitol using different" and "Influence of process parameters and mechanical properties of pharmaceutical materials on milling of roller compacted ribbons" respectively.

IPROCOT supervisors, Drs G Reynolds and A Michrafy, Profs C Wu and P Kleinebudde also attended the conference.





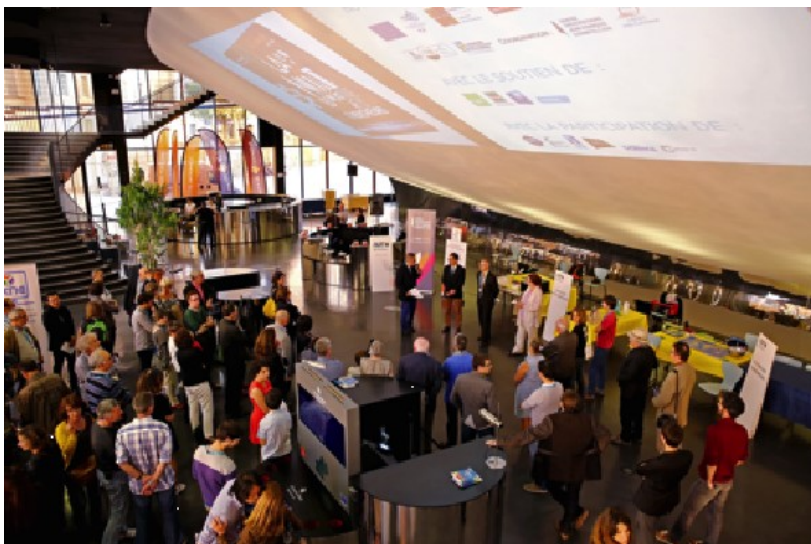
## European Researchers' Night

Lucia Perez-Gandarillas & Alon Mazor

European Researchers' night is a Marie Skłodowska-Curie (MSCA) action, under the Horizon 2020 specific programme "Excellent science". Its objective, as described in the Work Programme for 2014-2015, consists of: "Bringing the researchers closer to the general public and increasing awareness of the research and innovation activities with a view to supporting the public recognition of researchers, creating an understanding of the impact of researchers' work on daily life and encouraging young people to embark on scientific careers" [1].

The European Researchers' Night has celebrated its 10th anniversary with simultaneous events in 280 cities across Europe during the night of the 25th September 2015, offering visitors an opportunity to meet researchers and their work and take part in science activities.

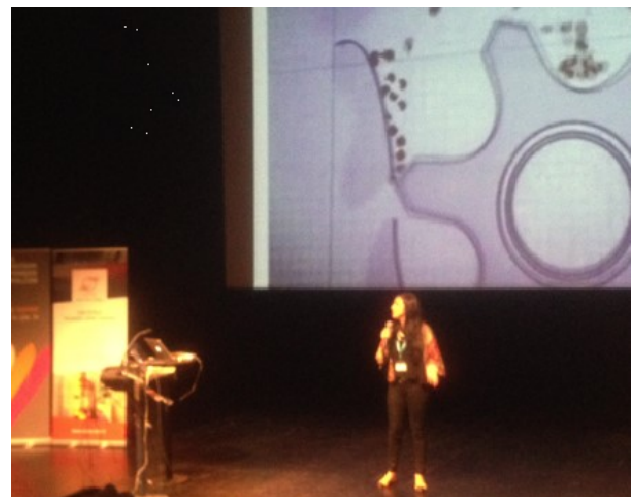
As many other cities, the city of Albi participated in this event, which was jointly organized by the University Jean-François Champollion, the Ecole des Mines d'Albi and the University of Toulouse. The event included lectures, face-to-face talks and experimental exhibitions. It had been a great success, receiving in total more than 1,000 visitors [2].



European Researches' night at Grand Theatre in Albi

### Top Chrono for my thesis

**Lucia Perez-Gandarillas** (ESR4) participated actively in the European Researchers' night through the activity "Top Chrono for my thesis". Lucia had 180 seconds to present an overview of her research activities. To prepare this activity, she had received a one-day training together with other 9 PhDs. After the presentation, she found that this exercise was a real challenge due to the short limit of time and the need to deliver the speech to a non-scientific audience.





## European Researchers' Night

Lucia Perez-Gandarillas & Alon Mazor

### Speed searching

Mr. Alon Mazor (ESR6) took part in the activity called “Speed Searching”. This activity is based on the speed dating (each meeting lasts 10 minutes), where the public can have a one-on-one interaction with the researcher. Alon had the chance to explain about pharmaceutical engineering and his own personal experience as an early stage researcher in the Marie Skłodowska-Curie action through IPROCUM. The visitors were very enthusiastic in learning about the on-going research activities and asked many interesting questions that were happily answered.



Mr Alon Mazor is giving talk to the visitors

### References

[1] [http://ec.europa.eu/research/researchersnight/index\\_en.htm](http://ec.europa.eu/research/researchersnight/index_en.htm)

[2] <http://www.ladepeche.fr/article/2015/09/27/2185621-nuit-blanche-pour-les-chercheurs.html>

## VISITING THE PHARMACY FACULTY OF THE HHU: *FROM COLOMBIA TO GERMANY*

Ana Perez Gago

On 15th April 2015, the faculty of Pharmacy from the Heinrich-Heine Universität welcomed the visit of undergraduate pharmacy students and their teacher from the Universidad del Atlántico, located in Barranquilla, Colombia. This group of 15 students supervised by MSc. Gina Domínguez were awarded with a scholarship for visiting several universities in Germany in order to learn how the education system for studying Pharmacy in this country works. Düsseldorf was their first stop.

As Spanish is my native language, I offered to take care of this group during their visit. The visit to our university started with an introduction of the Colombian students in which they explained how the education in Pharmacy is organized in their country, they also shared pictures of the campus with us and they even delighted us with a traditional dance with the traditional costumes as can be seen in the picture. After a lovely lunch in the cantina of the university, the session continued with several presentations describing the institutes which compound our university, given by the heads of the four departments: "Pharmaceutical Biology and Biotechnology", "Pharmaceutical and Medicinal Chemistry", "Pharmaceutics and Biopharmaceutics" and "Clinical Pharmacy and Pharmacotherapy". After these introductions, a lab tour was carried out, including our laboratories which I guided in Spanish. The day finished with a pleasant dinner in one of the classical brewery in Düsseldorf, where the traditional "Altbier" can be tasted.

The day was a highly interesting succession of presentations useful for both parties to understand how to study Pharmacy differs from one country to another, or even from Latin-American to Europe .



**Group photo with the Colombians students and several PhD and Professors from Heinrich-Heine university**

## First Secondment Experience in Spain

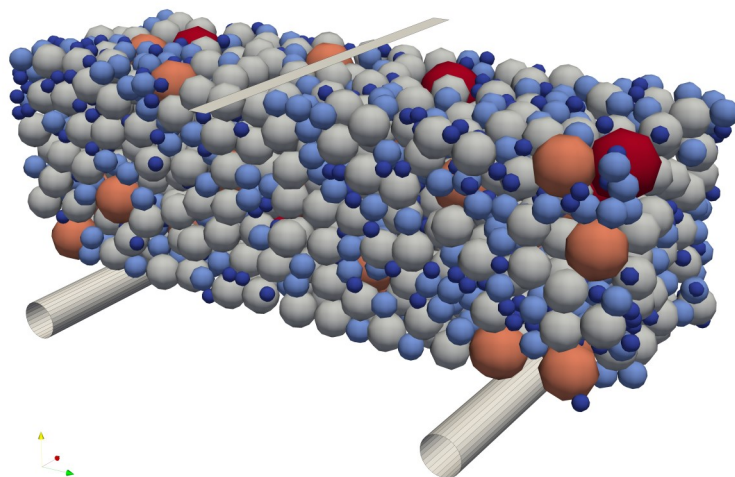
Simone Loreti

My first secondment was held at the Institute for Cross-Disciplinary Physics and Complex Systems (IFISC) in Spain in May 2015, in collaboration with the physicist, Enrico Ser Giacomo, under the supervision of Prof. Emilio Hernández-García.

The idea of this collaboration was to study a particular aspect of the breakage of particles' agglomerates during impacts with flat surfaces: the relation between the formation of fragments and the initial spatial distribution of particles. The micro-mechanics of breakage of agglomerates impacting with a target wall was performed numerically, using the discrete element method (DEM), in which three dimensional agglomerates of 3000-to-5000 polydisperse auto-adhesive elastic spheres with an average diameter of 20  $\mu\text{m}$  were considered.

These agglomerates were composed of spherical particles that can be described as three-dimensional networks, in which the particles corresponds to the nodes, and the contact between particles are the link, which makes the contact's strength represent the link's weight. Hence it was a weighted network.

Since we were studying the impact of agglomerates towards flat surfaces we were interested in the temporal evolution of this phenomenon, especially at the initial stage of the impact, i.e. the temporal evolution of a weighted network. The idea was to calculate a feature of dynamic weighted networks, i.e. a quantity called "most probable path" (MPP) for the propagation of the impact force, and explore the patterns. Another quantity called "betweenness" was also investigated. The main activity during the secondment was to clarify the temporal nature of these paths and the relation with the other network approaches reported in the literature.





## Fellow of this issue



# Kitti

**Csordas** is from Hódmezővásárhely, Hungary. She obtained her first degree after 5 meaningful years in June 2013 from Faculty of Pharmacy, University of Szeged. She is now a PhD student in the Heinrich-Heine University in Düsseldorf (HHUD), Germany.

She had an internship as a pharmacy student for 4 semesters in the Institute of Pharmaceutical Technology. She also wrote her dissertation (“Application of Quality by Design principles in the development of lysozyme contained solid dosage forms”) in this Institute. During her time in Düsseldorf, she became highly interested in doing a PhD abroad. The Institute of Pharmaceutical Technology has established a fruitful collaboration with Professor Dr. Dr.h.c. Peter Kleinebudde from the Institute of Pharmaceutics and Biopharmaceutics, HHUD, Germany for 14 years. She had the chance to build up on this collaboration and to study for her PhD in the Institute of Pharmaceutics and Biopharmaceutics within the framework of the IPROCOT Project funded by the European Commission.

Her project is on “Impact of powder properties and system design on roller compaction”. She is investigating how the different system designs influence the ribbon and granule properties. She is working with small-scale roll compactors. As a part of the project, she spent a few months on secondments to expose herself to the life in industry, and to use different types of roll compactors in companies, including AstraZeneca, located in Macclesfield, United Kingdom and L.B. BOHLE Maschinen + Verfahren GmbH, Ennigerloh, Germany.

She feels very lucky and happy to be a member in such a great and international project that teaches her how to work with scientists from different fields. So participation in the IPROCOT Project will help her to become a good researcher. She is very grateful to her supervisor, Prof. Dr. Dr.h.c. Peter Kleinebudde, for his support, supervision, advice and encouragement.



## Key Dates

19 - 21 April 2016

IPROCOT Session and PARTEC 2016, Nuremberg, Germany

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