Conference Report

The 15th Freiburg Symposium – A Short Review

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The 15th Freiburg Symposium was held on the 22nd and 23rd of April, 2021. The traditional, biennial Freiburger Symposium is organized by the DIAC, the Division for Industrial and Applied Chemistry of the Swiss Chemical Society. As is the case for so many other events, this year's symposium was for the first time held as a virtual conference. The 15th Anniversary edition of the Freiburg Symposium sailed under the theme of 'Industrial & Applied Chemistry 4.0 – Current and Future Trends'. – Industry 4.0, Plant of the Future, Smart Factory, Continuous Manufacturing, Big Data, Artificial Intelligence, Machine Learning, Virtual Reality, … all synonyms for the fast transformations we see everywhere, the chemical industry included. This fast-paced transformation of the chemical industry was the red thread of this year's symposium. The event attracted more than 120 participants, featured an attractive selection of presentations, a very interesting poster selection and for the first time two short talks by companies participating as exhibitors.

The program was split in several blocks, each comprising 2–3 presentations:

1. 'Flow chemistry and continuous manufacturing'
2. 'From Data to Information'
3. Keynote Lecture: 'Principles for Success in Digital Transformation'
4. The traditional lectures of the Sandmeyer Award winners of 2020 and 2021
5. 'Manufacturing Digitalization'
6. 'Industrial in-line, real-time Analysis & Data Processing'

The symposium started out with three presentations in the field of 'Flow Chemistry, Continuous Processing with integrated product isolation and purification'. Another headline of this section could have been, 'Beyond batch processing' which today still is very much the work horse of the Pharma, Agrochemicals and Fine Chemicals industries. This shift requires a whole range of new, 'fit for purpose' reactors much rather than 'fit for all' batch vessels. The three presentations of the first section nicely illustrated how 'Flow chemistry' in the lab is evolving towards continuous manufacturing on pilot and production scale. **Prof. C. Oliver Kappe** (University of Graz, Austria) presented a large selection of laboratory flow reactors that yielded a series of impressive results. In many cases these have been achieved exploiting processing conditions not accessible with standard laboratory equipment allowing to open new 'Processing Windows' and affording access to powerful route-enablers. The two industrial contributions illustrated two distinct strategies for the implementation of continuous manufacturing on pilot and production scale:

Development of continuous processes right from the laboratory discovery linked to a toolbox approach at Novartis (**Dr. Serena Mostarda**) or as in the case of Firmenich (**Dr. Harvey Randall**), the development of a continuous process for the further optimization and capacity expansion of a successful, industrial batch production process. The presented examples nicely illustrated how low volume fine chemical and pharmaceutical production can take advantage of continuous, intensified processing to be competitive in spite of a lot of existing multipurpose infrastructure.

The second section of the program focused on data mining. In the chemical industry, longstanding efforts in process monitoring and automation have allowed over the years to collect enormous quantities of data on laboratory, pilot, and production scale. But extracting information and therefore value from this 'ocean of data' remains a challenge.

Several commercial tools provide support for the visualization of data, process trends and modelling. In a tandem presentation **Joseph Reckamp** (Seeq, software developer) and **Dr. Helge Engelking** (Lonza, application) showed some compelling illustrations of the potential of such tools including examples of early process deviation detection as well as numerous possibilities of data mining as a process optimization enabler.

The application of analytical tools comprising Artificial Intelligence and Machine Learning applied in the context of chemical production processes has been presented by **Dr. Silvie Roussel** (Ondalys, France). Examples of in-line product discrimination (quality control) and process monitoring/ prediction in conjunction with Process Analytical Technology (PAT) illustrated the potential gain of Machine Learning tools for industry.

Another interesting approach which is often overlooked is 'hybrid modelling' – the integration of data mining and (process/expert) knowledge-driven approaches. **Dr. Michael Bortz** (Fraunhofer ITWM Kaiserslauten, Germany) presented several examples of how this path can be applied to production simulation and optimization but also for a model-based design of experiments in an R&D environment.

The first day was concluded with the key note lecture by **Philipp Karmires**, CDO – Chief Digital Officer of Linde, Germany. He shared how Linde is navigating the waters of the digital transformation and what he views as the principles of success in the digital transformation process. He presented how digitalization at Linde is in evolution, much rather then a revolution, advocating that the DNA and strength of the past are the best springboard into the Digital Age which includes at Linde many Virtual Reality applications.

The second day started with the traditional Sandmeyer lectures (award winners 2020: Dr. Andreas Schuster, Dr. Caroline Maierhofer, Dr. Stephan Bachmann, Dr. Hans Iding, Dr. Christian Lautz, Dr. Régis Mondière, Dr. Philipp Schmidt, Dr. Isabelle Thomé, from the Ipatasertib Team at F. Hoffmann La-Roche, and Dr. Christoph Strasser from Dottikon Exclusive Synthesis AG; 2021: Dr. Pierdomenico Biasi, John D'Alessandri, Ermanno Fillippi, Sergio Panza, Casale SA and Dr. René Eckert, Dr. Marvin Estenfelder, Dr. Stephan Reitmeier, Dr. Andreas Reitzmann from Clariant AG) bringing the symposium participants back to the very heart of the chemical industry, the chemistry itself. These talks were also very nice examples of successful and fruitful collaborations

between two companies with complementary expertise and capabilities.

The 'Manufacturing Digitalization' section' on the second day illustrated again well the increasing importance that mathematics and statistical modelling tools will play in future for process development and optimization. – *Dr. Edwin Kouratoun* from Syngenta presented an interesting approach consisting of the set-up of a 'Digital Twin'; developing a model of an entire production line using tools like Machine Learning or deep learning algorithms. These models are developed, trained, and tested on historical data allowing then their application in the field of process optimization and the development of 'golden batch' models.

As illustrated by *Prof. Clemence Corminboeuf* from the EPFL, Machine Learning tools are also finding their way into the optimization of homogeneous catalyst screenings and catalyst development in the lab. Combining quantum chemical expertise and machine learning tools allows to mine big libraries of metal/ligand combinations to identify the most promising homogeneous catalytic systems.

The last section of the symposium looked at the field of Process Analytical Technology (PAT). PAT is allowing to better understand, monitor as well as control processes in real time. It is very likely to become a critical enabler for the Industry 4.0 age. The two presentations in this section looked at two different applications in the field of (bio)pharmaceutical production. *Dr. Oliver Steinhof* from Biogen presented how PAT is playing a critical role in the commercial manufacturing of biologicals for the real time process control and the automatic in-line product release. It is a key element of the Biogen's 'Next Generation Manufacturing approach at their new plant in Luterbach, SO. Similarly, *Dr. Hans-Peter Nirmeier* from Lonza showed examples of how PAT and advanced data analysis are indispens-

able tools to increase the process understanding, to efficiently control manufacturing processes and its potential as an enabler to reduce cost and increase operational efficiency. However, the considerable PAT implementation costs and above all the GMP compliance efforts call for a systematic upfront analysis of the potential benefits.

The lecture program was complemented by two short talks, first by *Alain Georg* (Fluitec) presenting a continuous reaction calorimeter and a method of calculating process safety parameters for a continuous set up. In the second short talk by *Dr. Alexander Barroso* (Bruker Analytics) showcased the potential of FT-NIR as a real-time, on-line analytical tool in the field of process development as well as production process monitoring and advance process control.

The poster session has also seen a very good turn out with 15 posters, covering a very wide range of subjects including advanced process control, continuous reactor technology, on-line, real time process optimization of reactions as well as product isolation and purification processes. The best poster awards went to:
- 'From batch to continuous technology: The journey from laboratory to pilot scale' Dainis Kaldre *et al.,* F. Hoffmann-La Roche Ltd. Basel
- 'Cipargamin – Development of a new antimalarial drug', Thomas Ruch, Novartis Pharma AG

The two-day symposium featured many relevant aspects for the future of the chemical industry and elements helping it to stay competitive. It also showcased how the combination of the knowhow of chemists and process engineers with the capabilities of mathematicians and computer scientists can allow us to access yet mostly untapped potential and to collaboratively develop more efficient and sustainable processes.

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Fig. 1. Collage with symposium speakers and the President of the SCS during the live online symposium event. (Photo by SCS Head Office during the Zoom-Session).