

The 10th Symposium on Continuous Flow Reactor Technology for Industrial Applications

November 13-15, 2018 Milano, Italy

The 10th Symposium on Continuous Flow Reactor Technology for Industrial Applications, has been successfully organized, also this year, by *Chimica oggi/Chemistry Today* journal, TKS Publisher, in Milano. This Symposium, as in the past editions, respectively held in Madrid, Paris, Como, Pisa, Lisbon, Budapest, Delft and Barcelona, has given the opportunity to all the participants to verify the most relevant progress in the industrial application of flow reactor technology thanks to 32 different speeches, presented by speakers from both industry and academia and coming from many different countries, 15 posters and the description of many equipments and techniques by the 25 exhibitors. In particular, the Symposium was organized in 5 Sessions chaired by Prof. **Mimi Hii** of the Imperial College London and an interesting final Roundtable on "How Flow Chemistry has had an impact on Chemistry in the last 10 years" that was moderated by Prof. **Oliver Kappe** of the University of Graz. Coffee and lunch breaks allowed participants to have a look at and discuss posters and to contact the vendors, at the exhibition booths, for information and explanation about their equipments and techniques. The networking cocktail at the Hotel Ramada Plaza – on the first day - and business dinner at the "Casa dei Ciliegi" – on the second day – helped people to get more comfortable and created an informal atmosphere which lingered during the whole event.

Two Keynotes were presented respectively by Prof. Florence Alastair of the Strathclyde University and by Prof. King Kuok (Mimi Hi) of Imperial College London. Examples of continuous crystallization as unit operation of pharmaceutical production with predictive design and monitoring technique were described in the first presentation. The second keynote was related to different examples of catalysis in flow, considering in particular catalytic oxidations studied by the team "Catalysis in Flow" of the Imperial College of London. Three different types of oxidations were studied: using oxygen as oxidant for converting alcohols to aldehydes and ketones, using electrons (and water) for redox processes with direct process or indirect, this last mediated by the use of inorganic salts.

On the first day, after the keynote of Prof. **Florence Alastair**, different interesting speeches were presented facing different aspect of the Continuous Flow Reactor Technology such as: the evolution of flow technologies until today, the analysis of the economic driven technology for a developing process and the economic perspective of micro and millireactors. At this purpose, **Laurent Pichon** of MEPI presented a review of 10 years of flow chemistry development with a brief description of the innovations made from different groups in different countries. **Gerardo de Leon Izeppi** of Microinnova described how to

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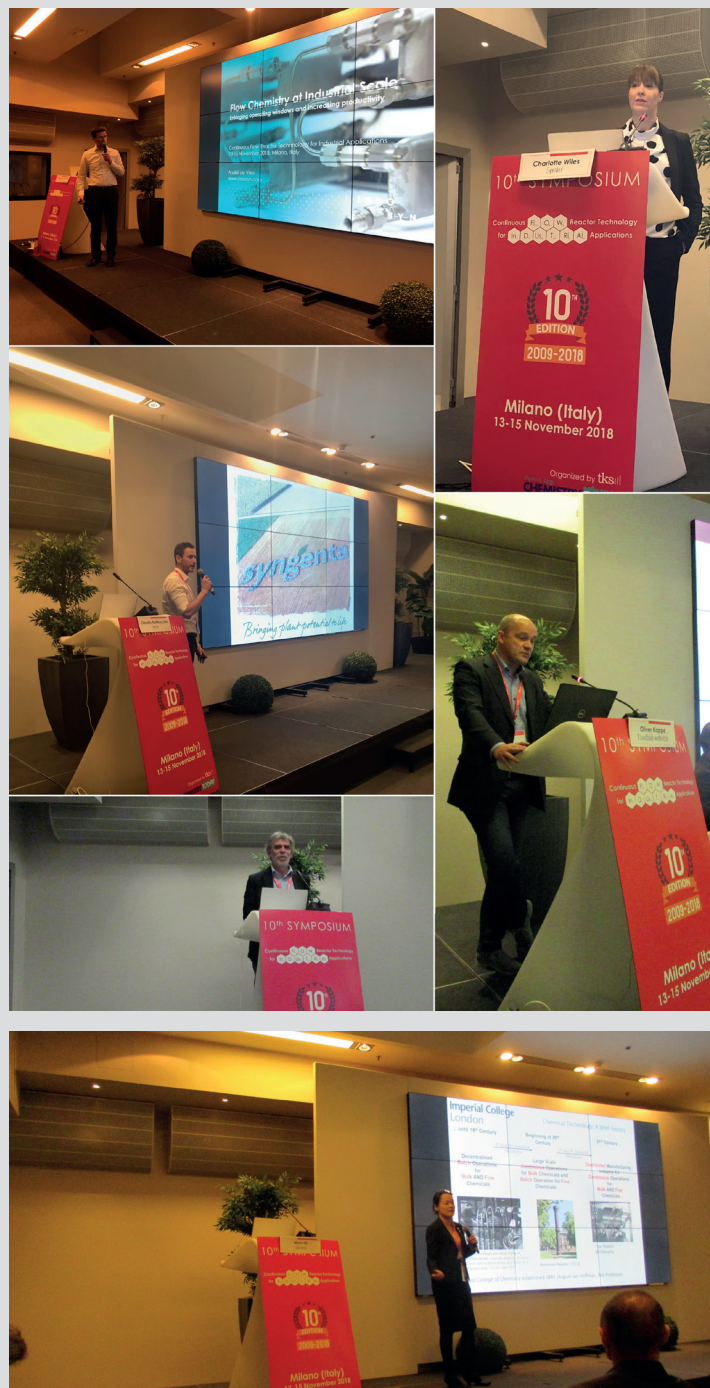
approach the economical evaluation of convenience for passing from batch to a continuous process giving some examples. **Anne Kaaden** of the EHRFELD Mikrotechnik described the history of the microreactors developed by their company starting from the pioneering works of Prof. Ehrfeld and concluded suggesting the economic perspectives of micro and millireactors.

After this Economic Session, 5 brief Posters Oral communications from Academia chosen for their potential Industrial Applications were presented. The second day started with the speech presented by **Charlotte Wiles** of the Chemtrix on "10 years of Flow Chemistry" considering some examples of process implementation (nitration and fluorination) starting from the R&D concept to the industrial realization of the mentioned company. Then, a commercial presentation from **Hiroaki Yasukouchi** of the Kaneka Corporation followed with different examples of pharmaceutical reactions, involving phosgene, made in flow microreactors.

An interesting speech was presented by **Matthew M. Bio** of the Snapdragon Chemistry that focused his intervention on the role of the automation in flow chemistry technology reporting details on the Matteson reaction as an example. According to this speaker in a process design we have to consider that in the batch process we design the chemistry to fit the reactor, while, in the flow process we design the reactor to fit the chemistry. The successive presentation made by **Sebastian Härtner** of Merck KgaA, was devoted to the description of the approach developed in more than 20 years by Merck to the flow chemistry, considering not only the reactor but also the other process units in a vision of smart factory and developing intelligent process based on a new modular automation concept. Three further presentations completed the Session of the morning. The first of these three lectures, presented by **Flavien Susanne** of the GlaxoSmithKline pointed out the importance of the process modeling and simulation in the development of continuous pharmaceutical processes. The second speech (commercial) by **Massimo Bertoldi** (La Mesta) showed the advantage of using a reactor like Raptor, described in detail by the speaker, for achieving the process intensification at different scale of production. Different processes realized by La Mesta using this type of reactor were described and the performances respectively obtained with batch and flow reactor were compared. The last presentation of the session given by **Elizabeth Farrant** of New Path Molecular was related to the automated continuous flow peptide synthesis.

The afternoon Session started with the previously mentioned Keynote Lecture taken by Prof. Mimi Hii on catalysis in flow followed by three further speeches and after the interval by other three. The first speech presented by **Claudio Battilocchio** of Syngenta dealt with continuous multistep processes for the preparation of active chemical components, considering in particular the generation and consumption in situ of dangerous compounds to avoid their accumulation.

Elin Stridfeldt (EnginZyme) – commercial speech
- described different applications of enzymes immobilization on a solid support operating in packed bed flow reactors. The third speech was presented by **Frédéric Toussaint** (UCB Pharma) and dealt with the



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promotion of some thiol-mediated free radical reactions in flow reactors.

After the interval the Session continued and a coordinated work was presented by three different speakers of three different companies that worked together in order to realize integrated continuous processes considering all the occurring steps, that is: the reaction, the separation and the analysis. The work was presented by **Alessandra Vizza** of the Corning Reactor Technologies for what concerns the modular continuous reactors, by Andrea Adamo (Zaiput Flow Technology) for the description of the modules of continuous liquid-liquid extraction developed by Zaiput and by **Jurgen Kolz** of Magritek for the NMR in line analysis. The successive commercial speech, presented by **Wouter Debrouwer** (Creaflow) described the Hanu-reactor that is a continuous flow pulsating plate photoreactor, suitable for preparative photochemistry. Some examples of photochemical reactions performed with this type of reactor were described. The last lecture of the day was presented by **André de Vries** (Innosyn) describing the advantages of using micro-channels for a better mass and heat transfer. Microreactors and micromixers realized by devices realized by Innosyn were described and examples of applications to highly exothermic reactions or reactions involving hazardous reactants were presented.

The program of the third day was structured with a Session containing seven presentations followed by the Roundtable. The Session started with an interesting lecture given by **Jonathan Knight** of Cambrex that presented a case history describing the problems and advantages of moving from an industrial batch operation to an industrial continuous flow operation. The example reported was related in particular to the nitration of an aromatic ring. The second commercial speech by **Akira Matsuoka** of Kobe Steel dealt with the investigation about the lack of technology and strategy to convert the laboratory scale chemistry in actual production scale. At this purpose, Kobe Steel has developed a flow chemistry equipment called Stacked Multi-Channel Reactor (SMCR) that increases the reactor capacity by numbering-up of sub mm to mm order in diameter for actual production.

According to the speaker commercial process development can be easy and quick by adopting this strategy. Then, **John Tsanaksidis** of CSIRO described the Catalytic Static Mixers (CSM) developed by CSIRO and illustrated with some examples of hydrogenation the advantages of using the CSM technology in flow chemistry. In the successive speech **Wouter Stam** of Flowid described the benefits of using the reactor SpinPro developed by Flowid- characterized by the presence of a series of rotating disks - in promoting multiphase reactions and.

After a brief interval **Miguel Gonzales** of the Asymchem illustrated the advantages of the continuous processes with respect to the batch ones for the synthesis in different steps of some pharmaceutical specialties. A comparison of the two mentioned technologies was reported comparing in particular achieved performances and operation times.

Carsten Damerau of the HNP Mikrosystem described the pumps most suitable for enabling continuous flow chemistry.

At the end, **Ernie Hillier** of Waters concluded the Session by presenting the modalities of HPLC analysis dedicated to flow chemistry.

After this last Session and the lunch interval the Roundtable entitled: "How has Flow Chemistry Impacted on Chemistry" moderated by Oliver Kappe of the University of Graz and with the participation of part of the speakers and the audience started. The themes foreseen were: the technical aspects, the market aspects, the regulatory impact, the global uptake, outsourcing. Great discussion came up on the Technical aspects and the debate more or less focused on this topic. For sure the most important take home message is to change mentality and accept the risk. What we can see from this event is the birth of a Community: competition among companies is there but it is overtaken by the need to solve problems and to succeed in performing a reaction and obtaining a safe, green and optimal product. This Community, independently of the geographical barriers, nowadays looks at this Symposium as an occasion for exchanging information, updating the knowledge on flow chemistry, enlarging the horizon of the industrial perspectives and renewing friendships. In conclusion, considering the informative contents of the lectures and posters, giving new insights on the flow chemistry and the very exciting visit to the booths of the exhibitors presenting their updated equipments, this 10th edition of the Symposium on Continuous Flow Reactor Technology for Industrial Applications has been very useful for the scope of diffusing the knowledge in the field of process intensification and also for favoring the interpersonal contacts between people working on the subject contributing to the acceleration of the progress in the field. ■

ABOUT THE AUTHOR

*Prof. **Santacesaria** worked at the Polytechnic of Milano (1970-1986) developing researches in the fields of catalysis, kinetics, reactors design and simulation and separation science. In 1986 won the chair of Industrial Chemistry of the University of Naples. Santacesaria had been the Coordinator of the research on "Colloid, Interphase and Surfactants" in the National Program of Research "Progetto Finalizzato Chimica Fine" and had been the founder of GICI the Italian Group of Colloid and Interphase Science of the Italian Chemical Society. He had been organizer of many national and international Congresses, workshops and post-doctoral schools. He has been President of the Industrial Chemistry Division of the Italian Chemical Society (2004-2009). He has collaborated with many Italian chemical industries. He has published more than 250 scientific papers and more than 30 Patents. In 2011 has been awarded by the Italian Chemical Society with the Gold Medal entitled to "Emanuele Paternò". In 2012 retired from the University and becomes CEO of the Spin off company Eurochem Engineering. In 2016 was awarded by the Italian Group of Catalysis with the Giacomo Fauser silver plaque and related Conference.*



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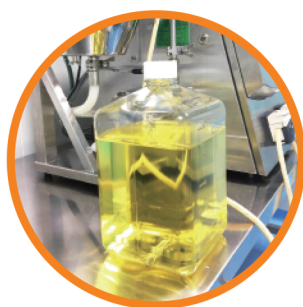
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