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Editorial

Timothy Noel[1]

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The year 2019 will always be a special year in the annals of the *Journal of Flow Chemistry*: It will be known as the year when Oliver Kappe stepped down as the founding Editor in Chief. Oliver led the journal between 2010 and 2018 and made the journal to what is now considered a relevant and well-respected platform for publishing cutting-edge work in the field of flow chemistry and continuous manufacturing. Personally, I am grateful and honored to be able to follow in the footsteps of Oliver and lead the journal in the coming years.

At the same time, we had a complete restructuring of the editorial board and both Paul Watts and Thomas Wirth will leave the journal as Associate Editors as well. Both merit significant credit for critically handling the manuscripts, selecting the appropriate referees and assessing the feedback in the past nine years. We welcome as new associate editors, Jean-Christophe Monbaliu (University of Liège), Shawn Collins (Université de Montréal) and Norbert Kockmann (TU Dortmund). I am confident that these new associate editors will ably assist authors and reviewers in the coming years, which will allow us to continue the success of Journal of Flow Chemistry.

I also would like to announce a new and exciting feature which will be added to this editorial. From now on, in every issue two author profiles will be published which we coin “Meet the Flow Chemist”. The goal of the “Meet the Flow Chemist” section is to get an overview of both academic and industrial flow chemists. In that way, we will be able to map the world of flow chemistry and see who the leading figures in the world are. We will ask the invited contributors to describe their reasons why flow chemistry makes a difference in their work along with some other revealing questions. Taken all the different contributions together, this section will provide an insightful testimony to newcomers in the field. The ultimate aim of this section is to showcase the importance of flow chemistry in a fun and accessible fashion. Every issue of J. Flow Chem., we will publish two featured researchers and will attach this to the editorial. Hence, the Meet the Flow Chemist contribution will be open access. I am very happy that the first two contributors are Oliver Kappe (University of Graz, and founding Editor in Chief of J Flow Chem) and Jesus Alcazar (Janssens Pharmaceuticals). Both have done exciting work in the past years, so do check out what they have to say on Flow Chemistry in this issue!

I am also happy to say that we keep working on our social media exposure. Some of you might have seen that we have a twitter account (@JFlowChem) and, at the moment, our account has 265 followers. Via this channel, we disseminate not only new papers that were published in our journal but also any relevant news related to flow chemistry. So if you like flow chemistry, be sure to follow our Twitter account.

Finally, I am happy to announce that we are working on an exciting special issue which will gather contributions from Emerging Investigators in the field of Flow Chemistry. This issue is led by two guest editors Milad Abolhasani (NC State University) and Jean-Christophe Monbaliu (University of Liège). Needless to say that you have to keep an eye on the journal to read the exciting work of these future leaders of the field!

With that, I would like to thank all our readers and authors for their continued support to make the *Journal of Flow Chemistry* a true success. Our primary objective remains to stimulate the development and advancement of flow chemistry for the benefit and progress of the chemistry community. We as editors will work hard to keep publishing the most exciting and interesting flow chemistry from around the globe.

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Eindhoven

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Meet The Flow Chemist – Prof. Dr. Oliver Kappe

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Awards	2004 Prous Science Award, European Federation of Medicinal Chemistry 2010 Dr. Wolfgang Houska Award, B&C Private Foundation, Austria 2018 IUPAC-ThalesNano Flow Chemistry Award

1) When did you start with flow chemistry? Describe the first paper or the first experiments.

We have started to work in the field of flow chemistry in earnest in 2008 when we were having trouble scaling our batch microwave chemistry experiments. Although microwave synthesis is very successful on laboratory scale, typically carried out in 10 mL sealed glass tubes, it cannot be easily implemented on production scale in batch owing to penetration depth issues. So it occurred to us that one can easily convert these sealed tube experiments to a flow system, i.e. a stainless steel capillary connected to a back pressure regulator and a pump. As heat transfer in a steel capillary is very rapid, one does not need to use microwaves for heating. We subsequently termed this the "microwave-to-flow" paradigm and today use small scale microwave batch experiments to optimize our high-temperature/pressure flow experiments.

2) What are the main benefits of flow that convinced you to use and implement this technology in your research?

Although there are many benefits associated to using flow chemistry principles, for us (and our industrial partners) the rapid scalability was a major driver that ultimately led the whole group to adopt flow chemistry very rapidly. In addition, you can just do so many more things in flow as opposed to batch, for example run experiments in supercritical acetonitrile at 350 °C with very little effort, or exquisitely control the temperature and reaction time of a highly exothermic organometallic transformation, that flow sometimes is the first choice. Of course, safety plays a major role and the fact that now many "forbidden" chemistries or reagents can be used again for organic synthesis speaks to the power of flow chemistry.

3) What do you think the future holds for flow chemistry?

One can clearly notice that many academic groups are starting out in flow chemistry right now across the globe. Some may use it only as a tool, for example to efficiently run photochemical or electrochemical transformations, others are attracted by the possibilities of continuous processing itself, in some cases from a chemical engineering or process chemistry standpoint. With flow chemistry now slowly entering the curriculum at Universities I suspect that there will be a stronger push in future years to adopt more flow chemistry principles also in the industrial sector, not only in pharmaceutical manufacturing where it is used today on an almost routine basis, but also in other industries.

4) Do you have any relevant tips for newcomers in the field?

Naturally, when we started in 2008 there were not that many synthetic organic chemistry groups doing flow. Today, the situation is different. On the other hand there is much more technology available today than it was 10 years ago. So new people in the field will have ample opportunity to try their ideas (not only in organic chemistry of course!). My only advice for young academics is: look out for the right type of graduate students or postdocs. As everybody in the field knows: depending on the specific project and technology you need not only chemistry skills but also the mindset of a mechanical engineer! A bit of knowledge in chemical engineering also helps.

Provide your three most relevant papers related to flow chemistry, and describe in one or two sentences why they are noteworthy.

1. Synthesis of 5-Substituted 1*H*-Tetrazoles from Nitriles and Hydrazoic Acid Using a Safe and Scalable High-Temperature Microreactor Approach. B. Gutmann, J.-P. Roduit, D. Roberge, C. O. Kappe, *Angew. Chem. Int. Ed.* **2010**, 49, 7101–7105 (*This paper – one of our first flow chemistry papers- demonstrates that extremely explosive and toxic hydrazoic acid can be handled safely in a microreactor environment at high temperature. In contrast to batch chemistry where the generation of hydrazoic acid is typically avoided, we have deliberately generated this reagent in flow).*

2. Continuous Flow Generation and Reactions of Anhydrous Diazomethane Using a Teflon AF 2400 Tube-in-Tube Reactor. F. Mastronardi, B. Gutmann, C. O. Kappe, *Org. Lett.* **2013**, *16*, 5590–5593 *(Herein we demonstrate the safe and distillation-free generation of anhydrous diazomethane using membrane technology, a protocol that since has been used in many academic and industrial labs).*

3. Integration of Bromine and Cyanogen Bromide Generators for the Telescoped Continuous Synthesis of Cyclic Guanidines, G. Glotz, R. Lebl, D. Dallinger, C. O. Kappe, *Angew. Chem. Int. Ed.* **2017**, *56*, 13,786–13,789 *(In this paper we have stressed the concept of on-site on-demand generation of a valuable chemical reagent,* i.e. *BrCN, which is then immediately consumed downstream to produce valuable products)*

Meet The Flow Chemist – Dr Jesus Alcazar

Name	Manuel Jesus Alcazar Vaca
Date of Birth	24-Dec-1967
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1) When did you start with flow chemistry? Describe the first paper or the first experiments.

My first contact with flow chemistry was through the H-Cube reactor back in 2007. We wanted to start our activities in flow with an established instrument to ensure reproducibility of our results. Moreover, this specific instrument allowed us to carry out hydrogenations in a straightforward and safe fashion. At that point, hydrogenation chemistry was underused in our laboratory. To our delight, the instrument proved its added value right away. After these first experiments, we decided to move forward and implemented throughout the years more flow chemistry in our Drug Discovery environment.

2) What are the main benefits of flow that convinced you to use and implement this technology in your research?

There are several benefits of flow chemistry that can be applicable to Drug Discovery Programs. Many people have reported in literature the ease of scalability to prepare multigram quantities of key intermediates. Others have reported the benefits of using hazardous reagents in flow, such as diazomethane. While these advantages were also observed in our activities, the main advantage for us has been the preparation and handling of unstable intermediates to perform chemistry that was underused in the lab. Moreover, flow chemistry allowed us to explore new chemical space to design and access those molecules which are hard to get with conventional synthetic techniques.

3) What do you think the future holds for flow chemistry?

According to me, there are two main directions for the field of flow chemistry:

- To continue the integration of new and challenging chemistry in flow, such as photochemistry, electrochemistry and supported biocatalysis. These are all niche synthetic methods which are very difficult to carry out in batch.
- Use of automation and automated screening technology. This is not only important for the preparation of a single compound (e.g. API applications), but also for the rapid and modular exploration of new chemical space around a certain hit molecule, which possesses some biological interest.

4) Do you have any relevant tips for newcomers in the field?

I would advise everyone to learn the technology through collaborations with some of the leading experts in the field. Learn from what is already established to avoid premature disappointments which would scare you away from the field. Once you feel comfortable enough with flow chemistry, integrate it as another, complementary tool for doing your chemistry. However, do not try to transfer everything done in batch into flow but use it only when it will really add value to your chemistry.

Provide your three most relevant papers related to flow chemistry and describe in one or two sentences why they are noteworthy.

- On-demand synthesis of organozinc halides under continuous flow conditions. *Nature Protocols*, **2018**, *13*, 324–334. *This methodology for preparing organozinc reagents in flow allowed us to access a completely new set of reagents, which has been of great value in our drug discovery programs.*

- Visible-Light-Induced Nickel-Catalyzed Negishi Cross-Couplings by Exogenous-Photosensitizer-Free Photocatalysis. *Angew. Chem. Int. Ed.* **2018**, *57*, 8473–8477. *This is the first article describing the application of bimetallic interactions in photochemistry. I am convinced that this article will open new chemistries in the future.*

- Reformatsky and Blaise reactions in flow as a tool for drug discovery. One pot diversity-oriented synthesis of valuable

intermediates and heterocycles. *Green Chem.,* **2017**, *19*, 1420–1424. *This article demonstrated how flow chemistry can be used for diversity-oriented synthesis (DOS). Herein, product diversification can be easily achieved through combination of flow and batch methodologies.*