Journal of Flow Chemistry (2019) 9:155–159
https://doi.org/10.1007/s41981-019-00045-w

Editorial

Timothy Noël [1]

Received: 31 July 2019 / Accepted: 2 August 2019 / Published online: 6 September 2019

Here we are with issue number 3 of this year and we have another collection of interesting flow chemistry papers for you. I hope you will enjoy the contributions of our authors as much as I did when I read them upon submission.

We have again some exciting news to share with you … our impact factor got a real boost and raised from 1.658 last year to a solid 2.277 this year. Obviously, credit goes to all our readers and authors who made sure that the published work got read and recognized. We hope that we can first consolidate this position and second keep growing in impact with our journal. So keep submitting your best flow chemistry work to the *Journal of Flow Chemistry*!

Also in this issue, we have two exciting "Meet the Flow Chemist" profiles, which are attached to this editorial. The first, academic one is from former IUPAC-ThalesNano Flow Chemistry Award-winner, Prof. Volker Hessel. Those of you who are familiar with the field know that Volker is one of the earliest adopters of microreactor technology and here you will read how he stumbled into it during his time at IMM. The second, industrial contributor is Dr. John Naber from Merck Sharpe & Dohme. John has always been passionate about flow chemistry and he learned the drill at MIT during his PhD. Salient detail is that he also got me acquainted with flow chemistry during my time at MIT as a postdoc! Needless to say, that this section will be again super interesting for you to read and to get inspired by these renowned experts.

Finally, we keep advertising flow chemistry via our twitter handle @JFlowChem. Notably, we got quite some new followers: from 265 in May, we have now 326 followers! So stay in touch with our journal or any interesting flow chemistry news via Twitter and do recommend us to your Twitter friends.

Enjoy the summer break and see you soon with issue #4!

Timothy Noël
August 2nd, 2019
Eindhoven

✉ Timothy Noël
T.Noel@tue.nl

1 Department of Chemical Engineering and Chemistry, Eindhoven University of Technology, Eindhoven, Netherlands

Meet the Flow Chemist

Name	John R. Naber
Date of Birth	12/12/1981
Position	Director of Flow Chemistry and Lab Automation Process Research & Development Merck & Co., Inc Rahway, NJ, USA
E-mail	john.naber@merck.com
Homepage	www.merck.com
Education	PhD – Chemistry – Massachusetts Institute of Technology (USA) Advisor: Prof. Stephen L. Buchwald BSc – Chemistry (honours) – University of Victoria (Canada) Advisor: Prof. Thomas Fyles

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

I was first introduced to flow chemistry in 2007 as a graduate student at MIT. I was in the 3rd year of my PhD and had just completed a project on Pd catalyzed Stille couplings when the MIT-Novartis Center for Continuous Manufacturing was launched. I felt that this "new" area of research would be something that I would really enjoy as I have always been a tinkerer and getting the chance to both build reactors and explore novel chemistry would be very exciting. Over the remaining 3 years of my PhD I was fortunate to be able to work closely with several talented coworkers from the Buchwald, Jensen and Jamison labs and to take advantage of the wonderful resources available at MIT to build a host of novel reactors, develop some of the first continuous flow methods for Buchwald-Hartwig aminations, and to learn about flow chemistry. Also, at the end of my time at MIT, I got the chance to introduce a young post-doctoral associate named Dr. Timothy Noel to flow chemistry and to the unique considerations of living in East Somerville, MA.

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

While there are many benefits of flow chemistry, my current role is in the Process Research & Development organization within a large pharmaceutical company, and as such, my work focuses on scale-up. In this regard, I think that the most important benefit of flow is the high surface area to volume ratio relative to batch. This high surface area allows for efficient mass transfer, efficient heat transfer, and the ability to add external reagents (injection points, light, etc.). This has allowed us to develop highly efficient processes for very fast, highly exothermic reactions without resorting to cryogenic reaction temperatures.

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

In my opinion, flow chemistry is still in its growth phase. Every year there are more academic groups focusing on flow and similarly, every year there are more pharmaceutical and biotech companies investing in implementing flow chemistry. This increased investment will inevitably lead to more use cases where flow has clear advantages over batch and I hope that this distinction will become clear in the future and that organic chemists will no longer view flow as a separate field but will view flow as the appropriate tool for performing certain types of chemistry.

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

Flow chemistry is best learned in the lab and best learned with a teacher. If you have never run a reaction in flow, the learning curve can be quite steep as you learn how to physically connect tubing, prime pumps, think about residence time, and unclog reactors. Having an experienced colleague or collaborator can dramatically accelerate this learning curve. Beyond that, it is also important to know that you don't always need fancy equipment to get started. There have been many great experiments run and methods developed with simple syringe pumps, fluoropolymer tubing and a handful of finger tight fittings.

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

1) John R. Naber and Stephen L. Buchwald, *"Packed-Bed Reactors for Continuous-Flow C-N Cross Coupling." Angew.Chem. Int. Ed.* **2010**, *49*, 9469.

This paper was the culmination of a lot of my graduate school work in continuous flow. It was grouped with a pair of papers on handling clogging via acoustic irritation and really epitomized the two different approaches of converting a batch reaction to flow. Engineering a reactor solution or using chemistry to modify the reaction to make it amenable to flow.

2) David Thaisrivongs*, John R. Naber* Nicholas J. Rogus, and Glenn Spencer, *"Development of an Organometallic Flow Chemistry Reaction at Pilot-Plant Scale for the Manufacture of Verubecestat" Org. Process Res. Dev.* **2018**, *22*, 403.

This was the first at-scale process that I was involved with developing. Taking a reaction from milliliter scale in the lab and seeing it run at liters per minute in a plant and successfully producing 100 s of kilograms of product was a significant milestone.

3) François Lévesque, Nicholas J. Rogus, Glenn Spencer, Plamen Grigorov, Jonathan P. McMullen, David A. Thaisrivongs, Ian W. Davies, and John R. Naber, *"Advancing Flow Chemistry Portability: A Simplified Approach to Scaling Up Flow Chemistry" Org. Process Res. Dev.* **2018**, *22*, 1015.

This is one of my favorite papers because it reads like a how-to guide for process chemists working in flow. While some of the principles are common place for chemical engineers, there was a significant gap in the chemistry literature around the quantification of mixing and hopefully future chemists will find this guide useful.

Meet The Flow Chemist

Name	Volker Hessel
Date of Birth	28 December 1964
Position	Since 2018 Deputy Dean (Research) & Professor
E-mail	Volker.hessel@adelaide.eu.au
Homepage	hessel-group.com.au
Education	1993 PhD in organic chemistry, Mainz University
Past Positions	1994 Researcher at Institut für Mikrotechnik Mainz GmbH (IMM) 1996 Group Leader Microreaction Technology at IMM 2002 Vice Director R&D at IMM 2005 Part-time Full Professor at Eindhoven University of Technology 2007 Director R&D at IMM 2011 Full Professor at Eindhoven University of Technology
Awards	2017 European Research Council Synergy Grant "SCOPE" 2017 European Research Council Proof of Concept Grant "PICASCO" 2016 FET OPEN Grant European Research Council "ONE-FLOW" 2016 IUPAC ThalesNano Flow Chemistry Award 2014 Chemical Engineering Science Award "Top Cited Paper 2011 and 2012" 2011 Advanced Research Grant of the European Research Council "Novel Process Windows" 2007 AIChE Award "Excellence in Process Development Research"

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

While I feel a glorious story is expected here from me, reality and life is more prosaic and soberly. I think John Lennon once said "Life happens when you are busy with other things". Early 1994 I simply searched for a job, after being PhD. I found it at the Institut fuer Mikrotechnik Mainz in Germany. I was hired for a project using self-assembly for gas separation membranes, following my PhD expertise. In my very first month, my boss came and said "From now on you make microreactors". Honestly, I have never regretted that 'forced future destination'. Yes since 25 years, "I am happy about and no worries", as the Australians would quote it. Realizing that only a very, very few researchers can state to have started flow chemistry as early as January 1994, I realize to be one of the fossils of that kind of research. My first true paper was to propose a mixing characterization approach to judge the performance of micromixers, published in 1999. It was the first of its kind and is still in my top-5 list of best cited papers.

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

As given, my first paper was on micromixers and micromixer research hold for about 10 years. Performing mixing (and heat transfer) at a time scale of about 1000 to 10,000 times faster than any conventional technology, deeply gave me the following this thing "microreactors/flow chemistry" is possibly different from all this other acclaimed future technologies. Safety was and is another key argument to use it. When we worked with UOP Company on the direct hydrogen peroxide synthesis, I realized what "freedom" in use of unconventional processing microreactors can offer. That led to the conception of 'Novel Process Windows', being ERC Advanced and ERC Proof of Concept-awarded. I will not forgot seeing a red glowing glass microreactor and the glass melting at a hot-spot, yet so "peaceful". This all motivated me to truly investigate novel process windows, and particularly what microreactors can do – and not can do.

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

I think the answer is very clear:

Photo chemistry and the use of sun light = following how nature does chemistry.

Making functional nanomaterials and any kind of complex soft matters such as four-fold microemulsions = as there is no other technology which can come even close to the performance of microfluidics.

Bio flow chemistry = as we already see now a pharmaceutical revolution toward 'biologics'.

Automation = computerized flow chemistry is reality; yet artificial intelligence and machine learning have not truly entered the field. However, it is sure they will.

Space flow chemistry = In-situ resource utilization (ISRU) is a major future business; off-earth and for earth. Space medicine is commercial already now. Space mining will be in the next years, and within a very few decades Space farming will be. There is common belief that flow chemistry is the key space manufacturing technology.

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

Not sure, if I should say never believe to old, fixed people, but rather get your own view ☺ Yet if someone listens to me, then I would say check if your technology is ready for industry transformations. Research that Shapes Future is one pillar of Uni Adelaide's strategy. Never make research without impact. Sounds trivial, yet still overlooked. Go for truly disruptive technologies, enabling functions, and innovation. Trivial, often overlooked. Do not do the 47th study of its kind, rather invent and impact. Include or be guided by early-bird cost and sustainability studies. Society (who pays you) expects you are strong enough to change the world. Give process design a key role, as only this is the way to a product. Do not invent a motor for which there is no car. Partner with industry from first moment and seek publicity to mirror your ideas to real life.

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

1) Borukhova, S., Noël, T., Metten, B., de Vos, B. & Hessel, V. (2016). From alcohol to 1,2,3,-triazole via multi-step continuous-flow synthesis of rufinamide precursor. Green Chemistry, 18, 4947–4953.

Paper with industrial co-authors which brings true process intensification (solvent-free processing) to multi-step flow chemistry. Meanwhile and it is all about this combination, this has been brought to pilot-scale and, with the aid of a business plan, we are underway to partner with industry.

2) Vural - Gürsel, I., Kurt, S.K., Wang, Q., Noël, T., Nigam, K.D.P., Kockmann, N. & Hessel, V. (2016). Utilization of milliscale coiled flow inverter in combination with phase separator for continuous flow liquid-liquid extraction processes. Chemical Engineering Journal, 283(1), 855–868.

Flow separation is not tackled as it should be, and reported concepts show proof of feasibility, yet hardly intensification; which desperately is needed. This paper is a good teamed approach, and keeps us busy with follow-up research until today.

3) Fu, Hui, Dencic, I., Tibhe, J, Sanchez Pedraza, C.A., Wang, Q., Noël, T., Meuldijk, J., Croon, M.H.J.M. de, Hessel, V., Weizenmann, N., Oeser, T., Kinkeade, T., Hyatt, D., Van Roy, S., Dejonghe, W. & Diels, L. (2012). Threonine aldolase immobilization on different supports for engineering of productive, cost-efficient enzymatic microreactors. Chemical Engineering Journal, 207–208, 564–576.

This study is truly holistic, combining bio-flow innovation with initial cost studies – fundamentals with impact – and the ambition is clearly to set a new tone. The topic is interdisciplinary, which explains the longer list of authors and institutions, including an innovative start-up company.