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Flow Chemistry Highlights

Flow Chemistry Network

Review of Recent Literature on Flow Chemistry. Selected Topic: Self-Optimization

Rxn Rover: automation of chemical reactions with user-friendly, modular software

Zachery Crandall, Kevin Basemann, Long Qi, and Teresa L. Windus*
React. Chem. Eng. **2022**, *7*, 416,
https://doi.org/10.1039/D1RE00265A

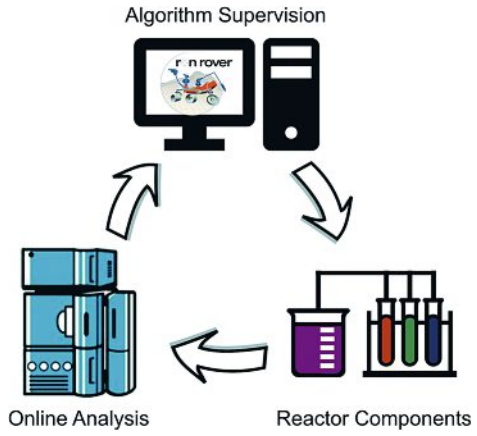
Reaction optimization is a time- and resource-consuming endeavor and a necessary part of the development of any chemical process. Automating optimization efforts could reduce cost and improve the reliability of generated data. Flow chemistry is intrinsically predisposed to automation, as flow equipment consists of automatable pumps, sensors etc., an advantage exploited by the authors of this paper.

Crandall *et al.* constructed an automated flow reactor for closed-loop reaction optimization. The system comprises three pumps, a heated tubular reactor and a UPLC for reaction analysis. Two optimization methods were tested: SQSnobFit global optimization algorithm and Deep Reaction Optimizer, a deep reinforcement learning algorithm. Authors optimized a reduction of imine to amine in 68 experiments, achieving 70% yield and 95% selectivity. The whole run took 62 hours.

Major focus of the paper lies on the software the authors developed to automate the lab hardware. Rxn Rover is written in LabView and enables users to flexibly add hardware by implementing relevant plugins. The entire Rxn Rover, with the plugins as well as documentation on the software are openly available on the team's GitHub page to aid other researchers in lab automation efforts.

Author's comments:*

"We saw that labs needed automated reaction optimization/discovery tools that were inexpensive, intuitively operated, and powered by the fast-emerging machine intelligence algorithms. Our solution was to build a free, general software framework that would allow experimentalists to easily connect their flow reactors, online analytical instrumentation, and optimization algorithms to automate reaction optimization/discovery."



Simultaneous self-optimisation of yield and purity through successive combination of inline FT-IR spectroscopy and online mass spectrometry in flow reactions

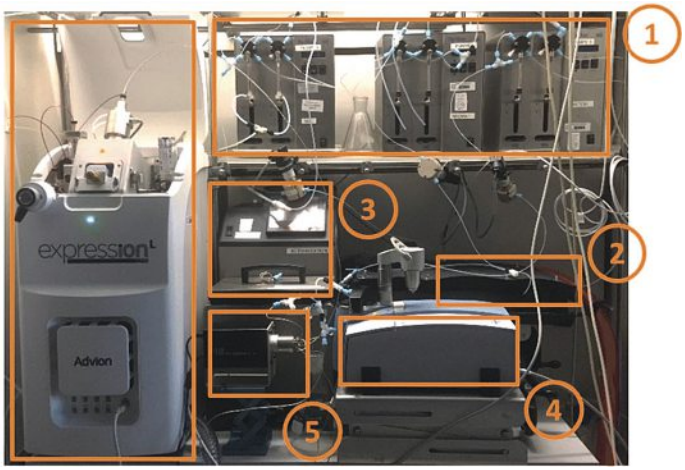
Verena Fath, Philipp Lau, Christoph Greve, Philipp Weller, Norbert Kochmann and Thorsten Roeder*
J. Flow Chem. **2021**, *11*, 285,
https://doi.org/10.1007/s41981-021-00140-x

An optimized chemical process produces less waste and places less demands on the work-up and isolation of product. The authors tackle two reactions with organolithium reagents, and uniquely employ both inline FT-IR and online mass-spectroscopy to track in real-time both the main-reaction and byproducts respectively. Accordingly, both yield and purity can be optimized, and this is done with a modified Simplex algorithm as well as Design of Experiment with a Central Composite Design.

An automated microreactor system enables sequential experiments without the need for a human operator, and on changing the reaction conditions such as flow-rates and reaction temperature, an IR spectrum could be obtained from the outlet of the reactor in less than a second, and an MS result every minute.
In conclusion, both an epoxide formation from *in situ* formed bromomethyl lithium, and a 1,2-addition of an aryl-lithium to a ketone could be optimized within a working day, taking less than 20 experiments each.

Author's comments:*

"The progress in online analytics in the last decades is very impressive. This enables online control loops for autonomous process optimization. It is always astounding that chemical intuition and algorithms come to comparable results."



Would you like to propose a Flow Chemistry Highlight topic here?
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