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SCS Swiss Chemical Society Flow Chemistry

Flow Chemistry Highlights

A CHIMIA Column

Review of Recent Literature on Flow Chemistry. Selected Topic: Scalability

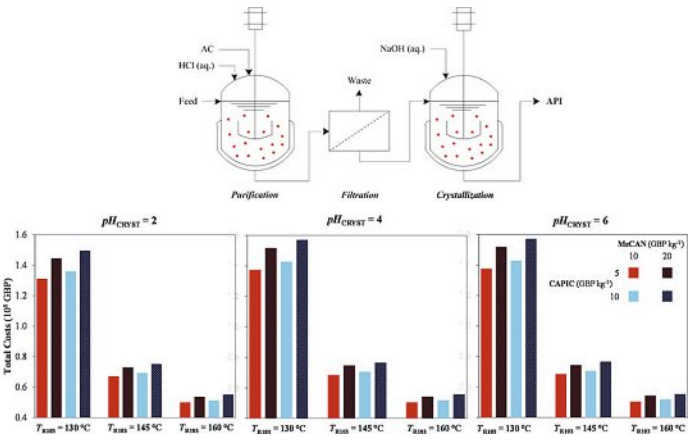
Process Design and Optimization for the Continuous Manufacturing of Nevirapine, an Active Pharmaceutical Ingredient for HIV Treatment

Samir Diab, D. Tyler McQuade, B. Frank Gupton, Dimitrios I. Gerogiorgis*, *Org. Process Res. Dev.* **2019**, *23*, 320. https://doi.org/10.1021/acs.oprd.8b00381

The cost-estimation of a chemical process is essential prior to any scale-up. But how does one do this without the final process in hand, and what should be the process design for maximal reliability, sustainability and cost-effectiveness? Gerogiorgis and team consider the technoeconomic optimization of the continuous manufacturing process to Nevirapine, a widely prescribed HIV medicine where cost-effectiveness is essential to the low- and middle-income countries most affected. Tackling different chemical routes to the small-molecule target as well as the extraction, filtration and crystallization, the authors use a combination of experimental kinetic data, Arrhenius parameter estimation, solubility modelling and process costing to seek out a minimum-cost design. Capital and operating expenditure (CapEx & OpEx) are estimated, and ranges of plant capacity and solvent recovery are mapped against the total costs. Both the total costs and the green-chemistry E-factor are positively affected by the selection of a fully continuous process compared to a process with flow chemistry followed by a batch crystallization.

Author's comments*:

"In this collaboration between process systems engineering and flow chemistry, we show how modelling can be used to realize improved costs and material efficiency (*e.g.* not reducing crystallization pH too far). Similar methodologies can be used for other drug manufacturing processes for deeper process understanding *in silico*".



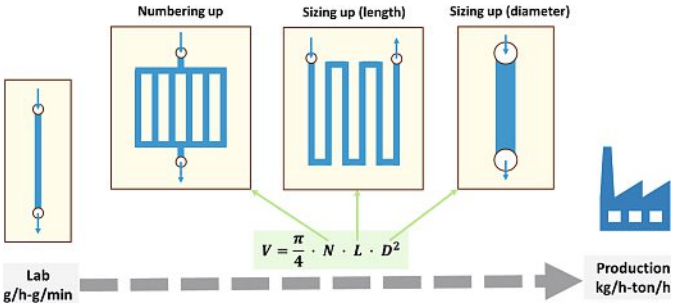
Scale-up of micro- and milli-reactors: An overview of strategies, design principles and applications

Zhengya Dong, Zhenghui Wen, Fang Zhao, Simon Kuhn*, Timothy Noël, *Chem. Eng. Sci.* **2021**, *10*, 100097. https://doi.org/10.1016/j.cesx.2021.100097

Microreaction technology offers many advantages for chemical synthesis: enhanced mass and heat transfer, ease of reaction control and inherent safety of small scale operations. However, adoption of continuous processing in industry is slowed down by the considerable effort needed to scale-up the lab-developed routes to the production levels. This thorough review of scaling-up strategies for micro- and milli-reactors by Dong *et al.* aims to assist the readers in this complex task. Scale-up methods are divided into two approaches: numbering-up, where individual reactors retain their size and thus the mass and heat transfer characteristics important for the synthesis but require a flow distribution strategy between single units; and sizing-up which may be realized either by increasing the reactor length, maintaining geometrical similarity (*e.g.* by scaling all dimensions by a constant factor) or by keeping a constant pressure drop across the reactor. While sizing-up approach benefits from uncomplicated flow delivery, it requires careful consideration of changes to residence time distribution, mixing and heat and mass transfer due to the change in reactor size. Different strategies are discussed and compared in detail, supported by comprehensive overview of literature on fundamental engineering aspects as well as examples of successful scale-ups with throughput up to kg/h.

Author's comments*:

"In this review we address the gap between academic and industrial use of micro- and milli-scale reactors by highlighting promising scale-up avenues."



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