Seal-less pumping technology in handling slurry with accuracy and improving scalability for continuous reaction

Karan Mansukhani & Suhan Shetty, Wanner International

Abstract

Handling liquids with suspended, often abrasive, solids such as slurries in flow chemistry processes is problematic for several reasons, not least the ability to dose reactants accurately, particularly at low flow rates.

Inaccurate dosing can cause wrong stoichiometry, giving a lower yield or unwanted byproducts, inconsistent residence time (ditto and issues scaling up) that can make the process unsafe, especially in exothermic reactions where thermal runaway is a risk.

Low pulsation is the simplest and most cost-effective means of delivering high accuracy, eliminating the need for pulsation dampeners and fixing problems associated with pipe strain. Seal-less pumps with multiple pumping elements in a single head design achieves this and can work with a range of chemicals, including aluminium chloralhydrate and active pharmaceutical ingredients.

Pumps must deliver the liquid at the required pressure/backpressure without compromising on flow rate. Viscosity[6] is also a significant property, especially if it changes during the reaction. Careful consideration of valve set design becomes very important.

The use of suspended solid catalysts throughout a wide range of flow chemistry processes presents a significant barrier to scaling up quickly, efficiently, and effectively.

Importance of suspensions in modern flow chemistry

Slurries, or suspensions, are a fundamental part of much chemical processing, whether that's the requirement for solid catalysts or as products precipitate as reactions progress. They are especially useful in flow chemistry environments, from laboratory scale up to full production lines.

In slurry reactors, finely divided solid catalysts are dispersed in liquid to maximize surface area, improve mass and heat transfer, and facilitate catalytic reactions such as hydrogenation, Fischer–Tropsch synthesis, and hydrocracking. The finer the particle, the greater the surface area, giving quicker reaction times in most cases. However, it is the fineness of these particles that presents huge problems in processing. They can clog various parts of the process, including pumping the reactants around the process.

Problems with fine solids

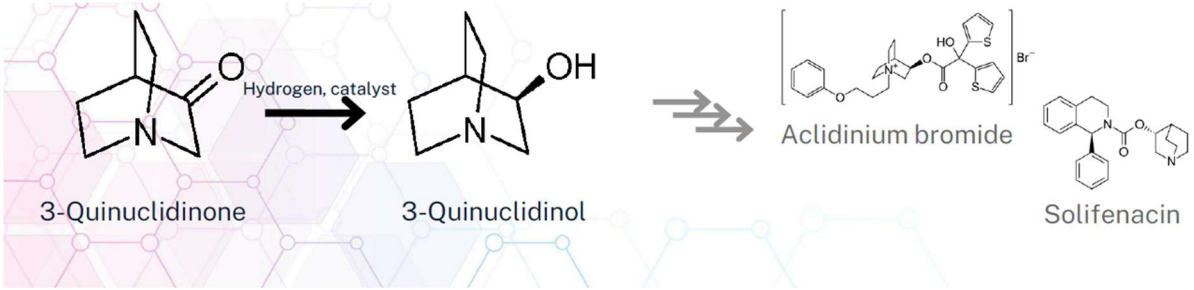
Fine solids can create problems with mixing[10], which is a significant barrier to high efficiency. Poor mixing can lead to precipitation or sedimentation, particularly with low flow rates. It can give uneven particle distribution, all of which can cause feed inconsistency, altered reaction stoichiometry, erratic yields, and potential equipment plugging.

Slurry handling is critical in both batch and continuous processes to ensure consistent suspension and reaction conditions. In continuous flow systems, designs must prevent solids from settling, bridging, or fouling, and ensure that solids flow smoothly through pipes and channels[5].

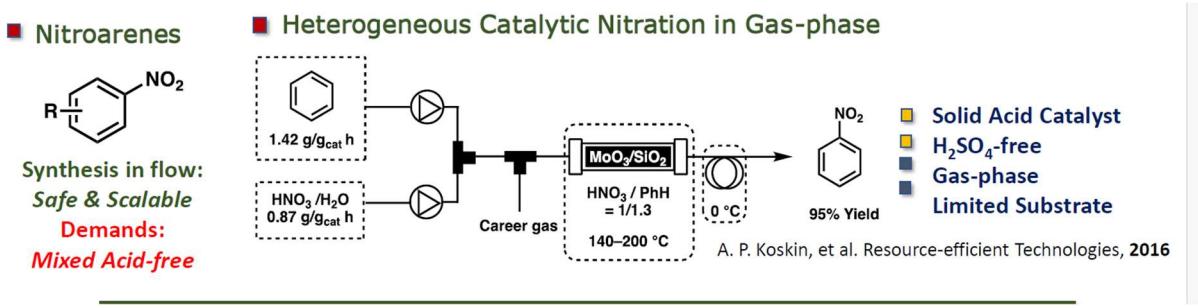
Uneven suspension can result in local reactant deficiencies or excesses, reducing yields and promoting undesired byproducts.

The challenges in batch processing of a halogen-lithium exchange and C-arylation reaction were highlighted in a paper at last year's conference by Mike Kenny[2]. In this exothermic reaction, unstable lithium intermediates were generated, and controlling the rate proved challenging, with thermal runaway posing a real risk.

While the unstable lithium intermediates were mitigated under cryogenic conditions, reactive species precipitated at these low temperatures, resulting in low yields. However, transferring to a flow process enabled milder process conditions (-78°C to -30°C), increased yield over batch (50% to 88%), and reduced process time from 3.5 hours to 6 seconds.

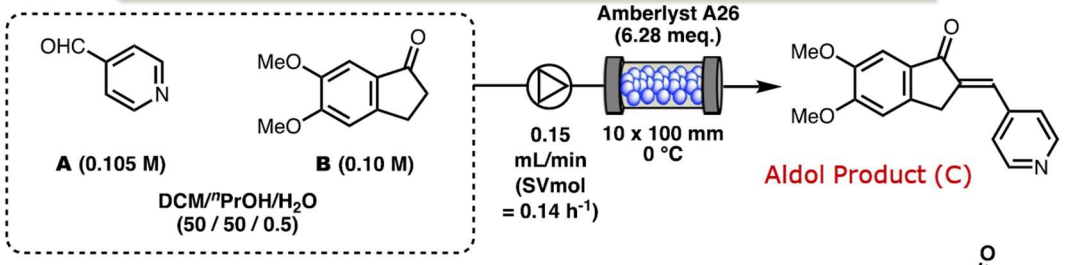


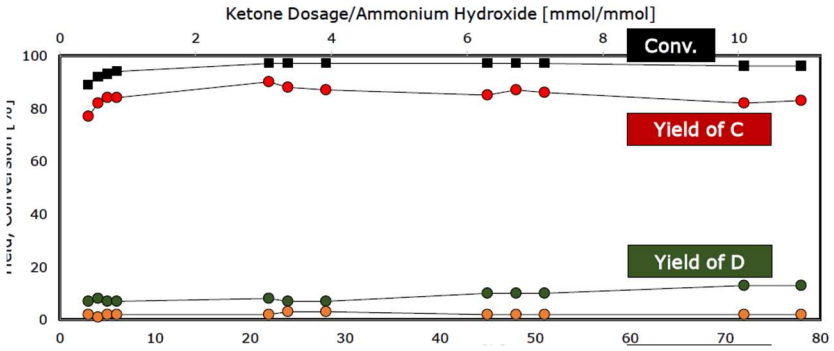
Haruro Ishitani showed the following pumping of a solid acid catalyst with a pH of 1-1.3:

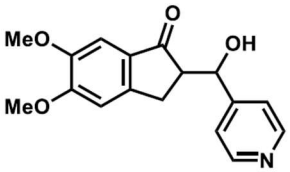


He also demonstrated pumping 70% nitric acid (pH = -1.2), slide 7, and very low pumping volumes (0.04mL/min) through a column on slide 8. This degree of causticity needs cautious handling.

Continuous-flow Aldol Condensation





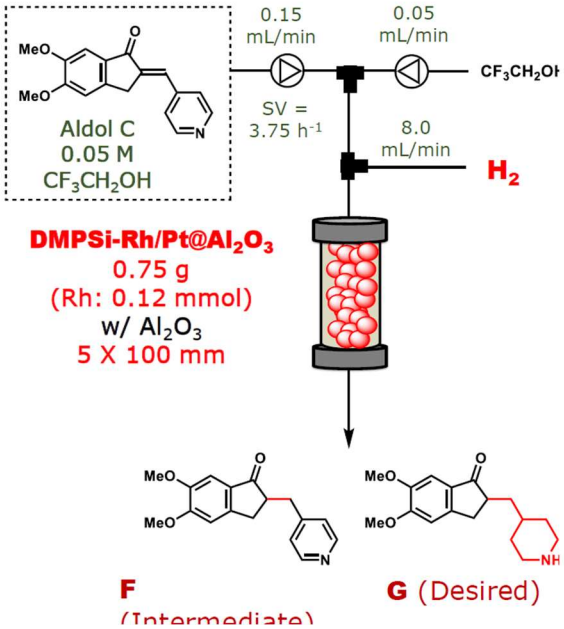


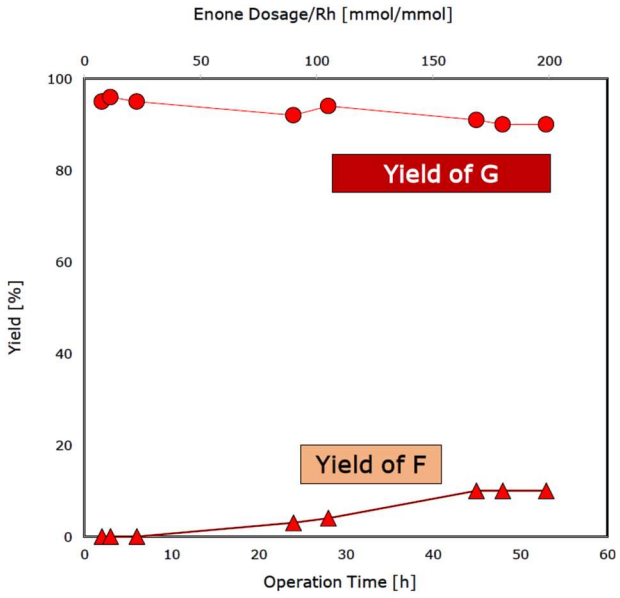
Intermediate (D)

+

Dimerization
(Over-reaction)
Product (E)

Continuous-flow Double Hydrogenation





For exothermic reactions, suspended solids pose a runaway risk. Slurry reactors (especially exothermic systems) require careful temperature control. Uneven mixing can create local hot spots, leading to thermal runaway or explosions.

These problems become exacerbated if the carrier liquid is caustic. Some examples of caustic, strongly alkaline environments include:

- Metal-phthalocyanine catalysts (e.g., cobalt, iron, manganese, vanadium phthalocyanines) supported on activated carbon, alumina, or silica, used to oxidize sulphides and mercaptans in refinery spent-caustic streams (high-pH waste containing NaOH and contaminants) — these catalysts enhance oxidation when combined with air/oxygen;
- γ-Alumina solid catalysts treated or used in the presence of liquid NaOH or KOH have been developed for oxidative desulfurization of fuels—showing the use of solid catalysts within strongly alkaline liquid environments.
- Merox process: In petroleum refining, caustic scrubbing with NaOH or KOH removes mercaptans. A solid-catalyst bed (Merox catalyst) in the alkaline medium promotes conversion of mercaptans to disulfides — a classic industrial process involving solid catalysts in caustic environments.

Such issues are experienced across the flow chemistry landscape, not least in pharmaceutical manufacture.

Wanner metering pumps are used in a spray drying process for tablet manufacture by one company. Operating at flow rates of up to 35 l/hr and pressures of up to 103 bar, the pump delivers a proprietary liquid with 15% solids in suspension to the spray dry orifice. The dry powder produced is then converted into tablets (in this case for control of patients' blood pressure).

These pumps replaced seal-reliant piston pumps previously used on the application. Any potential for seal wear was further exposed here by a tendency for the liquid to crystallise as temperature falls. Crystal accumulation at the seal caused premature wear, leading to leakage, irregular flow and pressure fluctuation – with accompanying noise and vibration.

With no dynamic seals in their design the Wanner pumps have experienced no problems on this application. The specially designed spring-loaded check valve sets were able to handle the abrasive solids with no leaks, delivering reliably constant flow and pressure with low vibration and noise. They exceed API675 and are used for APIs, eg, dosing solvents @80-100lph into the continuous flow reactors at a discharge pressure of 15 bar.

Caustic suspensions carry additional environmental, health, and safety risks if any part of the system leaks or if pipes are under strain.

Accuracy

Mixing[10] accuracy matters - poor mixing leads to sedimentation or uneven particle distribution, causing feed inconsistency, altered reaction stoichiometry, erratic yields, and potential equipment plugging.

And that particularly applies to HPLC within the flow chemistry landscape. Dr Smita Sandeep Kale[7], MD of Sanovaskale Technologies, highlights the importance of smooth flow. She reports:

“Many challenges are encountered while using these chromatographic systems during process development. These include less or no pulsation in flow, the ability of the pump system to pump the liquid at a required pressure/backpressure without compromising on flow rate, low shear (specifically in case of proteins, enzymes, peptides, etc.), accuracy of flow, dead volumes, and scalability from small to large scale, distinguishing industry practices.

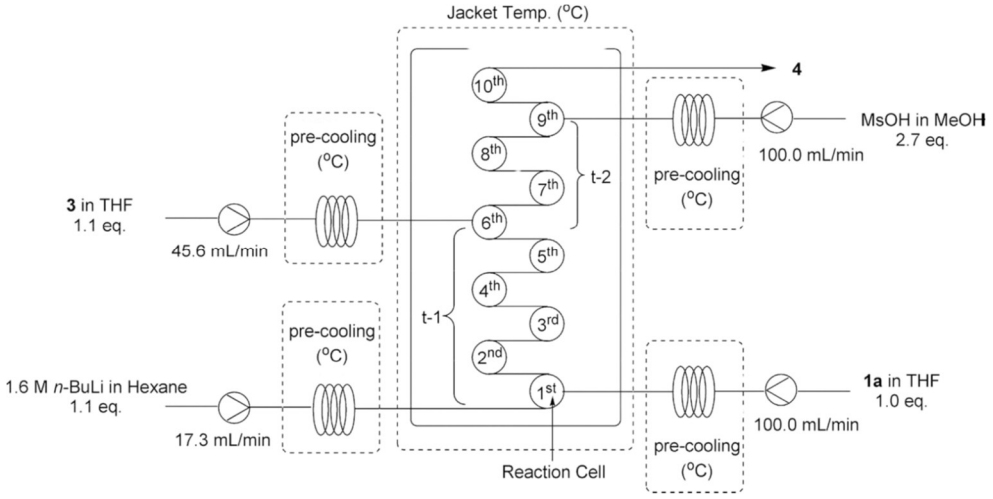
"A smooth liquid flow with minimal pulsation is critical in increasing efficiency, accuracy, and manufacturing consistency within preparative and process chromatography, preparative high-performance liquid chromatography (HPLC), etc., for pharmaceutical and other healthcare manufacturing processes.

“Pulsating liquid flow is proven to cause numerous problems, including reduced separation efficiencies, peak shape, peak profile disturbance leading to extra volume in effect during elution, pressure variations, and detection inaccuracies.

"The need for extremely low pulsation pumps for process chromatography and pre-HPLC systems has become crucial for pharmaceutical and even for allied industry applications, where legislation on chemical composition, reproducibility, and precision is highly stringent.”

The benefits of using a flow process over batch are shown in the halogen-lithium exchange and C-arylation reaction[2]. The flow process negates the risk of unstable lithium intermediates and difficulty controlling an exothermic runaway, as the batch requires cryogenic conditions needed to mitigate this risk of runaway, while at the same time increasing precipitation of reactive species at low temperatures and giving low yields.

The flow equivalent operates under milder conditions (-78°C to -30°C), increasing yield from 50% to 88% and reducing process time from 3.5 hours to 6 seconds per batch. The accuracy of mixing the ingredients is key, with the very low production volumes, as seen below[2]

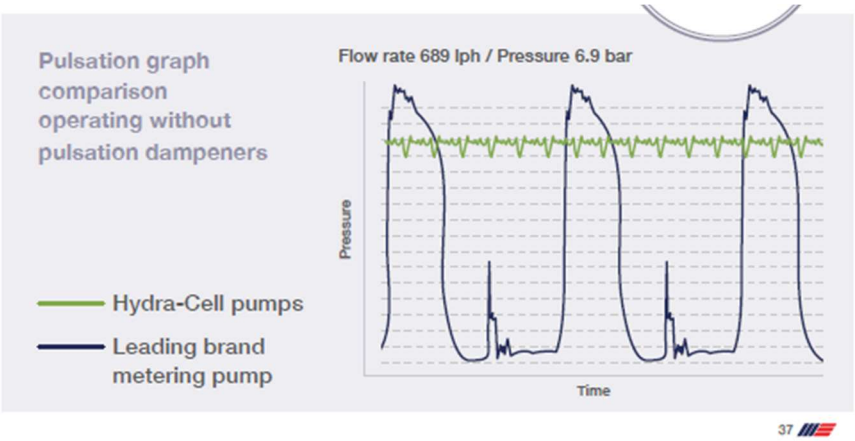


Pulsation

Critical for flow chemistry and HPLC applications, the Wanner ®Hydra-Cell Pro® pumps exceed API 675 performance standards and boasts extremely low pulse flow. This eliminates the need for pulsation dampeners, eliminates pipe strain due to pulsation, and delivers an accurate and smooth flow for flow chemistry dosing applications over a vast adjustable range of flow rates.

The degree of pulsation within a process is dependent on the pump technology used. A study (Wanner Pumps, unpublished, quoted in European Pharmaceutical Review[8]) showed the difference between two different pumping technologies.

The Wanner team ran a series of tests and graph below compares the pulsations delivered by a typical metering pump and a Hydra-Cell.



In another test, the Wanner pump was set at 467 Lph and varied by less than 1 Lph (< 0.2%), well within the API 675 standard, while a single diaphragm plunger operated within a range of 416-530 Lph (+/- 13%), clearly a huge increase in pulsation. The smooth, constant flow of the Wanner pump enabled controllable, consistent delivery of reactants to the process, and also makes using a calibration column much easier.

It achieves this by operating up to five diaphragms in sequence in a single pump head. It significantly reduces pressure pulsations to such a level that, in 99.9% of applications, no discharge pulsation dampener is required, thereby reducing installation costs and ensuring more consistent performance. This also eliminates pipe strain, delivering an accurate and smooth flow for flow chemistry dosing applications over a large adjustable range of flow rates.

Sanovaskale, a Pune-based specialist in scaling API, intermediates and biotech, was metering a solution with 50%v/v and 80%v/v isopropanol in water as the solvent for one of its processes[7]. This flammable material is dosed with aqueous hydrochloric acid (5% w/v) and sodium hydroxide (6% w/v) at flow rates ranging from 30 L/h to 7.5 m^3/h at a pressure in the range of 4 to 30 bar.

They required a smooth-flowing, high-accuracy, low-maintenance pumping solution with a minimal footprint that did not require pulsation dampeners. They utilised Wanner pumps to pump a range of water-based solutions, organic solvents, acids, and alkalis in various small and large-scale process chromatography systems.

Secondly, most detectors used in liquid chromatography systems are sensitive to the system's flow and pressure. As a result, a pulsating flow will yield an inconsistent detector/sensor signal, and thus a significant impact on the baseline, which in turn affects elution profiles, volumes, and quantitation.

Inconsistent signals caused by pulsating flow can be particularly problematic when looking for small peaks, such as known impurities, chromatographic concentration, and separation steps. A stable baseline/signal from sensors and detectors with no peaks is routinely part of the specifications required for a process and prep-HPLC chromatogram to be in accordance with GMP.

In column chromatography, sudden changes in flow can adversely affect column peak broadening and resolution between two closely migrating products, reduce separation efficiency shown by HETP, and affect the number of plates under such conditions, and column health, wherein column packing quality or chromatographic bed is affected.

This is particularly important in HPLC (both small and large scale), where columns and resins or adsorbents are often re-used and have significant replacement costs. Furthermore, changing columns mid-project can affect results, as a new column may change retention times and quantitation.

Inconsistent liquid flow caused by pulsation can compromise the integrity of chromatography system tubing or piping. Repeated compression and relaxation reduce the lifespan of the tubing material and will require more frequent replacement.

Furthermore, in a few cases, preparative and process chromatography require constant flow delivery at a specific backpressure, without which operation is not possible. Under such conditions, Wanner pumps have given excellent results and reproducibility at our site, both for small- and large-scale critical chromatographic separations.

In another case, the company switched to continuous production and implemented the Wanner pump, which reliably handles corrosive liquids with low pulse and requires minimal service and maintenance. It is now accurately dosing chlorinated mass in ethanol within a flow range of 30-80 LPH at a pressure of 10 bar.

Further, at Sanovaskale we also work on continuous processes of microreactor based synthesis, catalysis and biocatalysis from development to scale up. In these applications, a consistent flow at a particular constant pressure is also essential to achieve quality results.

Other examples we have worked on include the manufacture of insulin, with a process that has been running smoothly at 9 lpm and 80 bar for almost a decade, efficiently and reliably, with 24/7 operation, without any breakdowns. The Wanner pump technology addresses the problem of pulsation without dampeners, offers a smaller footprint, and facilitates rapid system installation and integration.

For the cosmetic industry, we pumped aluminium chlorohydrate into a spray dryer. $AlCl(H_2O)$ is used as an antiperspirant in the cosmetic industry and is highly abrasive and

corrosive in nature. The previous plunger pump was failing frequently, with leaks and operation downtime.

The multiple diaphragm pumping elements in a single pump head, which operate in sequence with short stroke lengths, reduce acceleration head losses on the suction side of the pump due to much lower changes in liquid velocity. This is especially the case when compared to hydraulically balanced plunger diaphragm pumps with one diaphragm in a single pump head.

Scale-up

The most crucial part of scaling up is maintaining running. Can the system be relied upon to run day in, day out with no breakdowns and minimise downtime, say for maintenance?

Scaling up means different things for different industries. For pharmaceutical manufacture this can be in the region of 100kg of product per year. For fine and specialist chemicals, the quantity can be in the region of 100 tonnes; for agrochemicals, it can be in the tens of thousands of tonnes per year. In contrast, for bulk chemicals such as petrochemicals, the quantities can be in the tens or hundreds of thousands of tonnes per year.

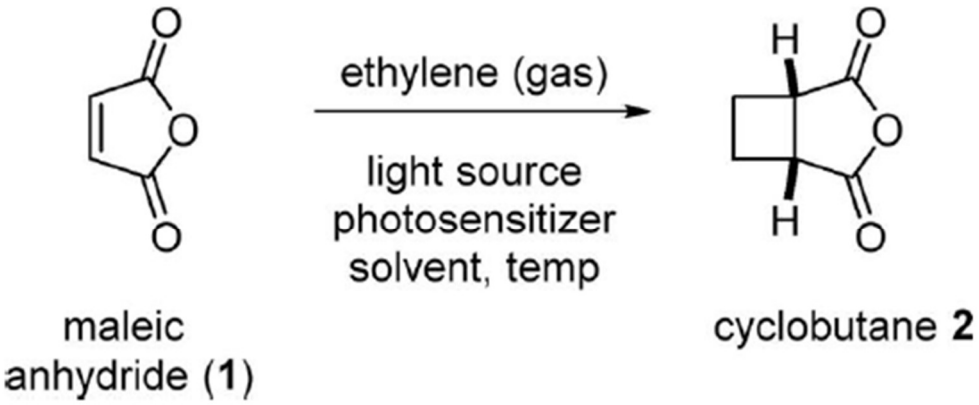
Lab-scale setups may simulate batch or continuous slurry behaviour and are used to assess rheology, settling, reaction kinetics, and equipment design before scaling up.

Scaling up from lab or development levels presents problems for reactions involving suspended solids presents its own challenges and obstacles. This challenge applies across many industries and scales, from very low-volume manufacturing processes to large-scale operations involving hundreds of kilograms.

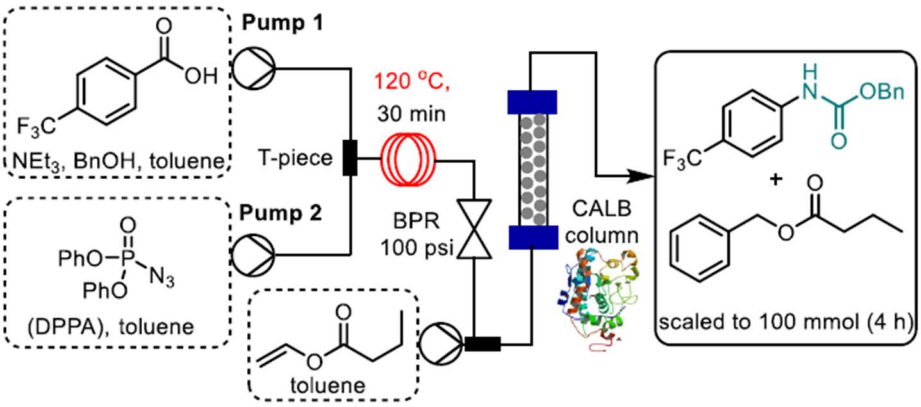
For any process across this spectrum, if a microchannel is involved, the challenge is to ensure that it isn't blocked.

Some reactions are more scalable in flow chemistry. Marcus Bauman[3] at last year's FCI summarised the general features included a high concentration and high solubility (substrate, reagents, product, byproducts); short residence times, ideally below 15 minutes; high chemical yield (>80%); and process robustness. Additionally, he noted the importance of complexity-generating reactions (additions in general) versus substitutions, emphasizing the importance of atom economy.

He gave an example of a photo-cycloaddition reaction, the manufacture of cyclobutene from maleic anhydride:



And how important is the pump, considering that these two reactants require highly accurate handling?



Marc Piepenbrock[9] of Erhfield Mikrotechnik explains lithiation of small chemicals for pharma production. He describes a reaction of 50-70mL/min @ 0 °C to -20 °C, producing 1.5kg of product each day, with a reaction time of 1-5 seconds. Batch scale-up is impossible.

This paper, again from last year's conference, shows the difference from lab to production of 1mL/minute up to 1m3 per hour.

There are different issues for low flow rates and high flow rates. For low flow rates, there is a risk of settling, bridging, and formation of slugs—especially with polydisperse or fine particles. Settling can occur in boundary layers, reducing transport efficiency[4,7].

High flow rates[5, 6] can improve suspension via turbulence but may cause erosion, catalyst attrition, or damage to reactor internals.

Flow rate extremes also affect heat and mass transfer, with very low rates failing to maintain uniform conditions and very high rates risking physical degradation or poor reactor control.

Conclusion

How effectively suspensions are processed can be a key determinant on efficiency or indeed whether a chemical process is scalable or not. If the particles are abrasive, this multiplies the problems, whether that's clogging processing equipment leading to breakdown, or accuracy of dosing or mixing, which can lead to the wrong products being produced, uncontrolled reactions or in the worst-case thermal runaway.

Pumping the suspended solids with minimised pulsation will deliver accuracy and seal-less pumps achieve this and work with a range of aggressive chemicals.

These pumps deliver the liquid at the required pressure/backpressure without compromising on flow rate.

Sources

1. Vankayala, Bhanu Kiran, AARTI Industries, "Process Intensification Using Micro Structured Reactors", 11th International Conference Flow Chemistry 2024
2. Dr Mike Kenny, AM Technology, Multiphasic flow chemistry: hydrogenation case study, 11th International Conference Flow Chemistry 2024
3. Assoc. Prof. Marcus Baumann, University College Dublin - Engineering Chemistry, “Scaling Continuous Flow Reactions: Case Studies from Academia and Industry”, 11th International Conference Flow Chemistry 2024
4. Haruro Ishitani, Tokyo University, “Heterogeneous Catalytic Flow Reactions”, 11th International Conference Flow Chemistry 2024
5. https://www.amt.uk/solids-in-flow
6. https://www.chemicalprocessing.com/processing-equipment/fluid-handling/article/11375813/process-engineering-avoid-trouble-with-slurries-chemical-processing
7. Dr Smita Kale, Sanovaskale Technologies, “Improving scalability and efficiency of production in process chromatography”, Laboratory Talk https://laboratorytalk.com/article/2096245/improving-scalability-and-efficiency-of-production-in-process-chromatography
8. Paul David and Jai MacIntosh, “Oil and Gas Technology for Continuous Bio Processing in Pharma”, European Pharmaceutical Manufacturer, https://pharmaceuticalmanufacturer.media/pharmaceutical-industry-insights/latest-pharmaceutical-manufacturing-industry-insights/oil-and-gas-technology-for-continuous-bio-processing-in-phar/
9. Dr Marc Piepenbrock, Ehrfield Mikrotechnik, “ Mesostructured Flow Reactors – Principles, Scale-Up Concepts and Applications”, 11th International Conference Flow Chemistry 2024
10. https://en.wikipedia.org/wiki/Mixing_%28process_engineering%29