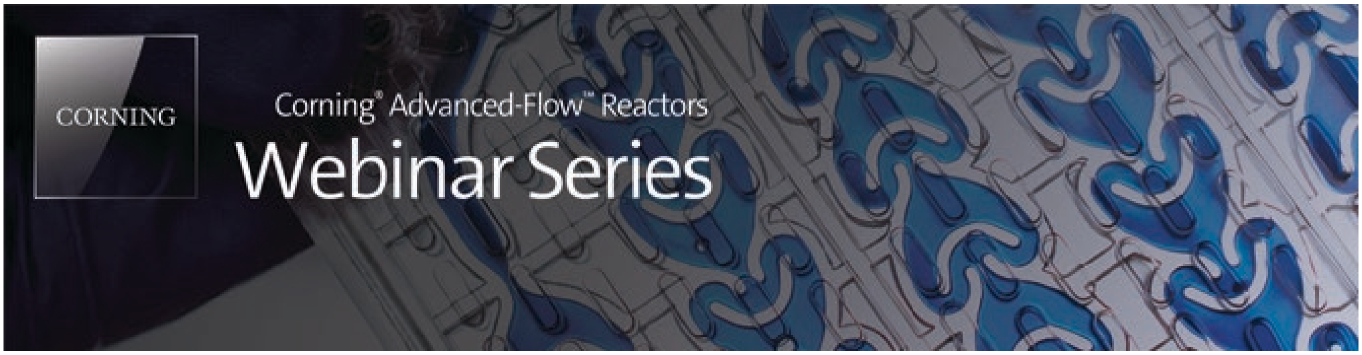
Corning® Advanced-Flow™ Reactor Webinar Series
Webinar 3: “Stepping into Corning® Advanced-Flow™ Reactor Technology: Making the Switch to Flow Chemistry: How to decide if implementing flow chemistry is feasible for your process”
Tuesday, Jan. 12 – 11am Central European Time | Thursday, Jan. 14 – 10am Eastern Standard Time



Questions & Answers

Q1: - How can your experience help us to start a project using AFR?

Over the last 20 years, we have installed more than 60 industrial units and more than 300 pilot units all over the world. Our team has experience with hundreds of different chemical reactions. All this experience has been acquired by our multidisciplinary and multicultural team including chemists, chemical, mechanical, automation and material engineers, quality experts and many others. We have been always focused on our customers’ satisfaction and as a technology provider, innovation is at the heart of our work.

Q2: How do you ensure the same mixing and heat transfer on scale up? What parameters are kept equal in order to keep the same heat and mass transfer?

Corning reactors have been designed to keep both heat exchange, mass transfer coefficients and residence time distribution (RTD) consistent across all reactors, ensuring a fast-pace scale-up process. In the scale-up phase, some parameters can be slightly tuned, but typically they do not involve a new optimization, hence a swift scale-up. The general rule to follow when scaling up using our technology is to keep the same residence time per plate, ensuring the mixing and heat exchange capacity will remain the same whatever scale is used.

Many examples exist of multiphasic systems (liq/liq, liq/gas and even liq/gas/sol) which greatly benefit from flow technology. To give you a sense of how our mixer performed, you can check related articles available on our website (https://www.corning.com/worldwide/en/innovation/corning-emerging-innovations/advanced-flow-reactors.html). Similarly, the heat exchange and RTD of our reactors has been optimized and validated both through modeling and characterization in laboratory experiments.

Q3: Is glass suitable material of construction (MOC) at commercial scale considering its brittle and fragile nature?

Glass materials can be sensitive to mechanical shock. In view of this, our reactors and the materials used in our reactors have been engineered to minimize mechanical constraints on glass and unintended shocks. Due to these attributes, it is a MoC which is already widely used and very well known in the chemical and pharmaceutical industry as many large-scale equipment are installed and successfully run for years. Corning's glass is manufactured with care, is designed to be tough and resistant. A lot of experience is available on how to safely use and operate glass equipment.

Q4: What is the final ratio (%) in all the chemistry where flow reactors are suitable? I didn't understand that on slide 15.

In the specific paper from D. Roberge on reactions performed at Lonza, about 50% of the chemistries showed to be transferable to flow based on kinetical considerations but this fraction is reduced to about 20% because of the solids involved in some of the reactions. A good understanding of the kinetics and the presence of solids is key to assess the suitability for flow of a specific reaction. In addition, finding ways to avoid solids (e.g., by change of solvents, higher temperatures, different reagents, …) could make many reactions suitable.

Q5: How do flow reactors have better mixing than batch reactors with stirrers?

An efficient mass transfer requires a high interface together with an improved mass transfer coefficient. Corning reactors have been designed to ensure a very high mixing capability. Corning's "Heat Exchange and Advanced Reaction Technology" (HEART) fluidic module has been thoroughly characterized and demonstrated it can facilitate 100x better mass transfer than batch processors. The mixing of miscible liquids was characterized using the Villermaux reaction, the non-miscible liquids by liquid-liquid extraction while the liquid-gas mixture by a gas liquid reaction and visualization.

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Q6: What is the usual concentration at which a flow process is run?

There is no typical concentration and this will be directly linked to your process. But in general, a flow process is typically run as concentrated as possible, and, when possible, avoiding the use of a solvent.

Q7: Can you please share the maximum allowable temperature?

Advanced-Flow Reactors can work from -60°C up to 200°C. For our reactors the upper temperature limit is link to the plastic connectors we use to maintain a fully metal free system.

Q8: Can we do the same process for solid materials?

Flow processes exist for solids, but it is a different technology and will require different considerations. Extrusion is typically a solid flow process for polymers.

Q9: How low can the temperature go for your flow reactor, like -78°C?

AFR Technology could work from -60°C up to 200°C. Very few flow process need very low temperature, as the heat management is better than comparable batch processes. For example, most Li exchange reactions can be performed around 0°C in flow instead of -78°C in batch.

Q10: Any thoughts on pumping slurries into reactors if the slurry is bound to froth out?

It would be necessary to have more details and a good understanding of the parameters impacting the behavior of the fluid. The design of the complete line needs to be adapted, from the choice and potential agitation needed in the storage vessel, to the sizing of the lines to keep a high speed, to the choice and design of the pump head, usually a membrane pump.

Q11: Any test results or technical papers that give details for heat and mass transfer being kept constant at different scales?

You can find references on our website here.

You can also watch our first webinar: Webinar #1 Stepping into Corning® Advanced-Flow™ Reactor Technology: An Industrial Overview. In this webinar we speak about real industrial cases shared by our customers.

Q12: Can we perform hydrogenation with 1-2 % catalyst? If yes, what will be recommended particle size in G1?

Solid handling is always a tricky question and should be addressed on a case by case basis. Dealing with solids depends on many parameters, including the size of the solid. This is reaction-dependent although the main trend is that these types of reactions may not be the best for flow reactors if solids tend to be big, concentrated or eager to aggregate. In general, solids amount of 1-2% is considered within the normal range of operation. Regarding particle size, 70 µm is a typical maximum, but this number could vary depending on the solid behavior in solution and its interaction with the fluidic module surface.

Q13: How are you expecting to perform Hydrogenation using Pd/C catalyst? If it is a slurry flow of Pd/C catalyst, then how can you make sure that the slurry of catalyst is homogeneously flowing throughout the reactor?

When considering slurry solution, the critical point will be the pumping system. This part of the unit will control how homogenous your solution will be for your reaction in the flow reactor. Obviously, your particle should not stick to the reactor wall, which is generally not the case with Pd/C. Inside of the reactor the high velocity inside of the channels and the intense continuous agitation keeps the particle suspended and prevents any settling.

Q14: Do Corning reactors come in other MOC i.e. PFA or SiC?

A: We provide reactors in glass and SiC.

Q15: Is there any possibility to scale the same process at plant?

To scale up a process in flow, the optimized, and already intensified process conditions (temperature, concentrations, ratios, reaction time, heat exchange capacity, mixing quality, residence time distribution, etc.) need to be maintained constant while increasing the throughput. This can be achieved by increasing the volume of the reactor by the same factor as the throughput (a 100 times higher throughput requires a 100 times larger reactor to maintain the same residence time). To achieve continuous production capacities of kilograms per week a throughput of only around 10 ml/min is needed (10 ml/min times 1440 min per day = 14,4L per day). With 10 L/min running 7000h per year you can achieve capacities of up to 4200 T/y.

For additional information on our seamless scale-up approach to maintain critical processing parameters constant whatever the scale, please consider attending our Webinar dedicated to this topic in March. Visit our website at www.corning.com/AFRwebinars to learn more and register.

Also, examples of scale-up have been shared during our Webinar #1 Stepping into Corning® Advanced-Flow™ Reactor Technology: An Industrial Overview.

Q16: What is the highest particle size for the lab scale Corning glass reactor?

Dealing with solids with our lab scale equipment (Low-Flow and Lab Reactor) can be tricky as the channels are very small. We usually don't recommend using any solid of micrometer scale, although nanoparticles have been shown to behave well in these small reactors.

Q17: Are the tube reactors or CSTRs better than such modular reactors? How?

Tube reactors and CSTR are good for different tasks. They are a good way to economically provide long residence time, and in case of the CSTR, to handle solids, but their mixing and heat exchange capacities are far below meso flow reactors. The different types of technologies can easily be combined according to the need of a process, using an efficient Advanced-Flow Reactor for the demanding first part of a reaction and finishing the reaction in a tube or CSTR to achieve the last percent of conversion.

We also have customers cases, such as the G5 example (https://www.corning.com/worldwide/en/about-us/news-events/corning-advances-flow-reactor-technology-for-industrial-chemical-production.html) which use our technology for the initial mixing and then switch to a tubular reactor to provide enough residence time with lower pressure drop. Hybrid solutions should be considered when needed.

Q18: If you mix a pure liquid as reagent with a solution of the other reagent, you will have much different molarities; how can you ensure dosing precision?

It is easier to mix solution at similar flow rate, meaning both pumping systems will run more or less the same. Accurate dosing line is then a must if you consider very different flow rate for your solutions. In some cases, considering a dilution of the pure reagent, or even better the concentration of the second one should be considered.

Q19: Why the pressure limitation at 18 bar? Isn't it just the ptfe/pfa connectors and the glass should be able to handle much higher pressures?

Our reactors follow the European "Pressure Equipment Directive" which applies to the design, manufacture and conformity assessment of stationary pressure equipment. So we apply the safety factors recommended to ensure a high level of safety. Performance limitation is mainly linked to the plastic connectors and the O-rings system. Our glass and SiC fluidic modules are manufactured and tested to handle over 90 bars of pressure.

Q20: Can we use Corning's system for highly corrosive reactions?

Corning's reactors can handle corrosive reactions, with proper temperature and concentration parameters. For example, nitration, a very common chemical reaction, can be run in our reactors, along with other corrosive chemicals. Corrosive reactions involving fluorine work very well but require the use of our SiC reactors.

Q21: What is the impact of reaction viscosity on the design of your flow reactors?

A high viscosity can quickly become a limitation for the throughput when using flow reactors due to the combination of viscosity, duration of the reaction and throughput. As a rule of thumb, we consider that applications with viscosities of 50 to 100 cPo can only be run if the reaction time does not exceed a few 10th of seconds.

Q22: What is the actual alternative to glass on the large scale?

We use glass up to the G3 reactor size. For larger scale reactors (e.g., G4 and G5), we use SiC.

Q23: Is a heterogeneous system applicable?

Heterogeneous reactions can either mean gas/liquid or liquid/solid reaction. The first case benefits from Corning's high mixing capability. On the other hand, dealing with solids depends on many parameters, including the size of the solid. This is reaction-dependent although the main trend is that these types of reactions may not be the best for flow reactors if solids tends to be big, concentrated or eager to aggregate.

The ability to work under pressure and with a high heat exchange can allow reactions to perform more smoothly. The turbulence is increased by adding static mixers in the system. Corning uses its patented HEART-shape fluidic module design in its systems to enable a state-of-the-art mixing capability and help the system make the most of the reactivity.

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Q24: What were the safety precautions that need to be taken to perform fluorination in G1AFR SiC with 10% fluorine gas and Alloy 400 auxiliaries?

On top of using gas flowmeters, we recommend using special care and adequate procedures (e.g., procedures related to starting, stopping, emergency stop and cleaning) to prevent potential leaks. Examples of special care can include using a second gas line dedicated to test other concentrations by dilutions and also flushing the system. We also recommend using check valves, working within a fume hood, and cleaning capacity to dispose of leftover fluorine. Another potential recommendation is using a dry system without humidity traces.

Q25: Is it 200°C batch or in the jacket side of plates please?

As heat transfer is efficient within our reactor, the temperature of the heat exchange fluid will be the same as the reactive fluid most of the time. In some instances. heat exchange is higher than standard jacket batch by about 1000 times.

Q26: Can you recommend a method (or any specific tools) for estimating potential cost savings of continuous process flow processes (vs. batch processes) - including capital, labor, utilities, etc?

As you mentioned, many parameters need to be integrated into the assessment to capture the full potential savings of a flow process compared to a batch but there is not "one" method or tool that covers all scenarios. Typically, the costs linked to the different downstream processes, separation and purification steps need to be included as they will be strongly impacted by the, usually, better quality of the product stream in a flow process. Other important costs factors to consider are all costs linked to safety equipment and procedures, to the footprint of the full process, to the energy consumption, reduced waste handling and to the higher level of automation. On existing processes, it might be even possible to get and include data on the "none-quality" costs of out of spec batches. We know of several consultants and service companies that offer this type comparison.

Q27: What would be a technical solution if I have a gas evolution? BPR? or other?

If a gas is produced in the course of a reaction, it can flush the liquid in the system and therefore decrease the actual residence time while making the process less reliable.

However, there are ways around it. One suggestion is using a back pressure regulator to put pressure up to 18 bars in the system. Therefore, the gas produced will take up a much more limited space in the reactor and keep the process reliable.

On the downstream side, a system can be implemented to safely deal with the gas.

Q28: I am specifically interested in photo flow chemistry. Might you have some introductory / general comments? How do you choose what wavelength to use, source and its power, etc.?

The first thing to choose is the wavelength by checking the full available spectrum and selecting the wavelength with the highest absorption or, if applicable, the most appropriate photosensitizer (wavelength, cost, stability, …). The reliability of the light source should be evaluated in view of the duration of photochemical reactions . The power should be tuned as well (using the optimal concentration).

Corning offers photochemistry options on all systems from the Lab Photo Reactor up to the G3 and including the G1 photo reactor. An upcoming webinar will introduce flow photochemistry in more details – visit our website at www.corning.com/AFRwebinars to learn more and register.

Q29: Is it possible to scale-up photochlorination of long chain waxes using flow reactors? Current challenges are highly viscous material at end - g-l-s mixture.

The presence of solids and of a viscous material will be a challenge as they will quickly generate higher pressure drops, limiting the throughput of the reactor. One suggestion is to reduce the viscosity as much as possible to optimize the productivity of the photoreactor, either by modifying the temperature or adding a solvent.

Q30: How to "quantify" the benefits of flow chemistry in terms of safety (to compare to batch and to have argument to convince to make investment). How to transform the safety benefits of flow chemistry" into "cost benefits"?

Safety savings is very difficult to estimate as this is mostly linked to a specific process and local regulations. Typical benefit will be linked to the low hold-up of reactive species and the high level of automation possible.

Our team is available to discuss your project more specifically.

Q31: Does it support multiple feeds to take care of in-situ reactions?

Yes, for sure, you can have multiple inlet available.

Q32: If any gas generated during a reaction has a tendency to react with product, can it be converted to continuous flow?

In general, our reactors can manage reactions where gas is generated but an outlet may be required to allow the gas to be removed. Gas release can be more challenging than injecting a gas, as the gas released will occupy space inside the reactor and lower the global residence time. The main challenge may be due to the kinetics of the reaction. If it is too low, it will be difficult to simultaneously maintain a high mixing and a long residence time.

The specific case where the produced gas can react with the product is more challenging. As mixing in our reactors is high, it might improve the reactivity of your gas with your product. You should control the parameters that influence the most this side reaction, in order to minimize it.

Q33: If the reaction is very fast (< 1 min) then how do you evaluate process parameters perturbation and their effects on product quality? Can you share any references?

Very fast reactions are sensitive to the mixing quality, to the ratio of the feed streams and, in some cases to the residence time control. The accuracy and reliability of the feeding systems can control the quality of such reactions. To evaluate the perturbations and define an acceptable operating window for the production process and set of specific experiments, often called parametric study or process robustness, is necessary. The use of modelling and simulation tools can help to minimize the number of tests to perform and lead to a quality by design approach.

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