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In the Lab

Multiphase Continuous Flow Reactors for the Synthesis of Molecules and Materials

***Johnson Matthey Technology Review* features new laboratory research**

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About the Researcher

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About the Research

Multiphase reactions, which involve reactants in more than one fluid phase (often accompanied by a homogeneous or heterogeneous catalyst), are ubiquitous in the petrochemical, fine chemical and pharmaceutical industries. Reactions such as hydrogenation and oxidation are mainstays in the manufacture of valuable molecules or intermediates. There is also an increasing interest in multiphase reactions promoted by visible light photocatalysis. These reactions typically involve a strong interplay between physical transport processes, such as the transfer of molecules across fluid phases or heat dissipation and intrinsic chemical rate processes. As a result, the rates of industrial processes are often limited by heat and mass transport, especially in batch reactors used in the fine chemical and pharmaceutical industries. Aggressive process conditions (such as high temperatures and pressures) are typically required to achieve viable productivity.

Milli- or mesoscale multiphase flow reactors, in which the characteristic transverse dimension of the reactor is in the 1–5 mm range (with lengths ranging from 0.1 m to >10 m), offer an exciting alternative to these challenges, especially for industries that produce low-volume and high-value materials. Such reactors offer the benefits of

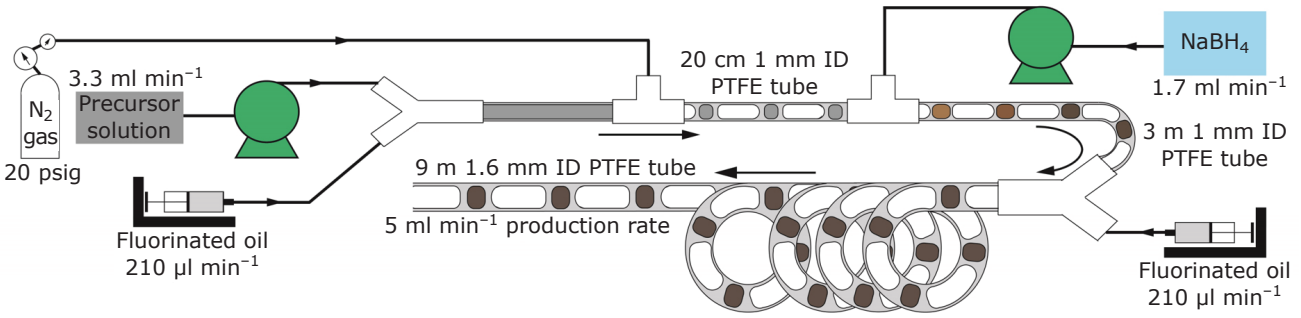

Fig. 1. Schematic of a triphasic segmented flow reactor for the continuous synthesis of catalytically active palladium nanoparticles at the ~10 l day^{-1} scale – Adapted from (3) by permission of The Royal Society of Chemistry

highly controlled multiphase flow patterns and tremendously intensified transport processes, while also allowing production of valuable molecules and materials at the kilograms per day scale with a desktop footprint.

Researchers at Khan Lab are actively engaged in the design and prototyping of multiphase continuous flow reactors and processes for the synthesis of molecules and materials ranging from catalytic nanoparticles to molecular drug crystals. For example, triphasic segmented flow reactors have been developed for highly intensified hydrogenations under ambient conditions with the use of a colloidal metal catalyst (1). A proof of concept eight-fold parallelised system with complete catalyst recovery and recycle has also been demonstrated (2). This reactor concept has been recently deployed for the robust, non-fouling synthesis of catalytically active palladium nanoparticles at the 10 l day^{-1} scale, in a collaborative project with Johnson Matthey (see **Figure 1**) (3). This reaction is particularly challenging to control in a conventional flow reactor, given the aggressive reagent (sodium borohydride) used to reduce the aqueous palladium precursor solution; uncontrolled evolution of hydrogen gas typically leads to severe reactor fouling. The highly intensified mass transport in the triphasic flow reactor allows the rapid mixing of reagents and removal of evolved hydrogen gas into co-flowing nitrogen 'sink' bubbles, thereby preventing outgassing and fouling.

In addition to flow chemistry, methods for the controlled continuous production of microscale solid particles, such as drug products or intermediates, are also a strong focus of research interest at Khan Lab; recent demonstrations in this area include a continuous emulsions to particles process for the production of spherical crystalline drug materials or composites, in collaboration with GSK (4, 5).

Other ongoing projects at Khan Lab include: (a) the development of small-scale reactor systems that allow effective deconvolution of physical and chemical rate processes, thereby enabling the measurement of kinetic data for intrinsically fast multiphase reactions; (b) the design of novel photocatalytic flow reactors that intensify photon flux in light-limited scenarios; and (c) the combination of high throughput microfluidic materials synthesis and machine learning methods to map and learn patterns in complex, non-equilibrium materials synthesis spaces.

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