Micro Reactors
Advantages & Selections

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Microreactor systems involve micro and milli structured reactor systems that achieve the advantages of process intensification, providing an easy route to scale-up. The article introduces the concept of microreactors, discusses its advantages and limitations, presents the Ehrfeld microreactor system and discloses examples of its application, in particular for scale-up of energy efficient chemical processes such as lithiation. Distributed modular plant concepts are also discussed.

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There is a distinct initiative in the chemical industry especially the specialty chemical industry to move towards continuous flow processing. One of the strongest tools to enable the move from conventional batch processes to continuous processing plants is microreactors. Though microstructured devices were around for quite some time, the first application of microstructured devices for applications like mixing and heat exchange started in the mid 1990s. Microreactors are defined as devices/ equipment with micro structured internals i.e. internals with characteristic dimensions ranging from 10 -2000 μm.

Advantages of microreactors

What differentiates microreactors from other reactors is the surface to volume ratio which greatly enhances the mass transfer and makes the reactors highly efficient. To get a better idea of the surface /volume ratios refer Table 1 below.

With this enhanced surface to volume ratio, major advantages are seen in mass transfer(higher diffusion) and heat transfer. This is evident from the actual experimental data collected on the diffusion times and heat exchange times varying with the characteristic dimensions of the reactors. With lower characteristic dimensions, the times are drastically reduced.

With high surface to volume ratios, the resultant benefits in terms of actual application are:

a. There is very low hold up in the reactor. This leads to increased safety especially while handling highly explosive, flammable or toxic chemicals.
b. Heat generated during reactions can be efficiently and rapidly removed with very good control on the operating temperature and no generation of hot spots.
c. Due to drastic improvement in mass transfer, some reactions can move from a solvent based approach to a water based approach leading to cleaner processes.
d. Due to uniform mixing and no dead legs, formation of undesired byproducts can be avoided. This results in uniformity in purity of products, lower downstream separation requirements and higher possibility of recycling.

Table 1

Sr. No.	Reactor type	Surface/Volume ratio (m^2/m^3)
1.	Continuous stirred tank reactor	4-40
2.	Multitubular reactor	100-400
3.	Monolithic reactor	1500-4000
4.	Microreactor	4000-20000

What differentiates microreactors from other reactors is the surface to volume ratio which greatly enhances the mass transfer and makes the reactors highly efficient.

e. Microreactors assist in converting batch processes to continuous flow processes. This has obvious benefits for plants with small footprints and better control on process parameters.

Typical applications/ Reactions for Microreactors

With respect to usage, microreactors can be used in three areas of process applications:

a. **Generation of data during research**

During process development, a lot of data needs to be generated in laboratory for a proper design of the scaled up plant. Microreactors can be used as a very effective tool for such data generation as it is very easy and fast to changeover between experiments and parameter monitoring is also easy. This enables huge amount of data can be generated over a short period of time.

b. **Process Development**

During new process development, it is imperative to try out various process routes. Another challenge is that the chemistry and behavior is unknown so the safety risks are unknown. Microreactors addresses both these concerns and can speed up the process development and also enable implementation of processes which would be difficult to execute in conventional glassware or autoclaves.

c. **Production of chemicals**

The biggest commercial application for microreactors is the actual production of chemicals. Microreactors can be used in kilogram to multi ton production scales using proper devices during process development and utilizing appropriate scale up methodology. They are already being used widely in applications in pharmaceutical and speciality chemical industry and there are also some applications in the polymer industry.

In terms of applications, the major focus areas for using microreactors are:

a. Highly exothermic reactions
b. Reactions with high reaction rates but mass transfer limited
c. Emulsification/ dispersion application requiring a high degree of mixing

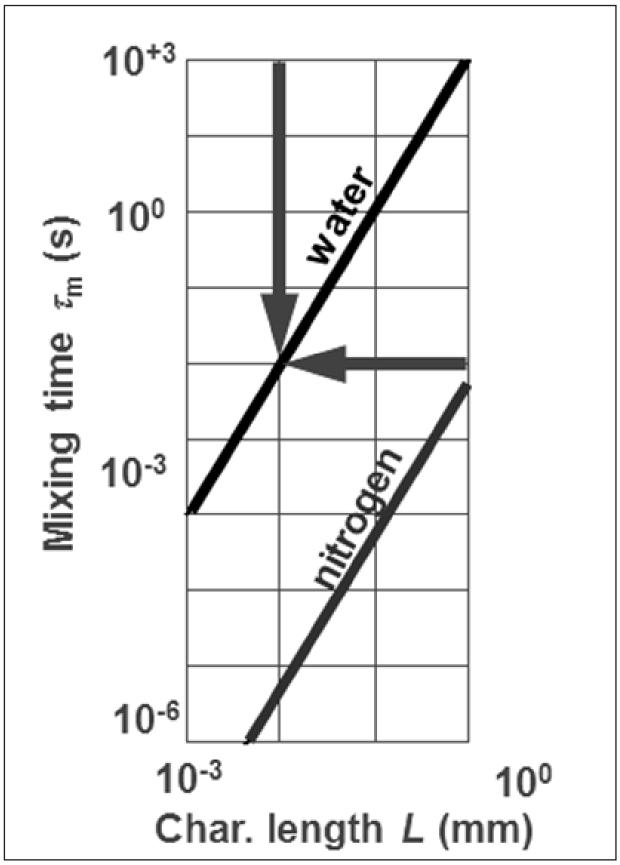

Figure 1 : Variation of diffusion time with characteristic dimensions

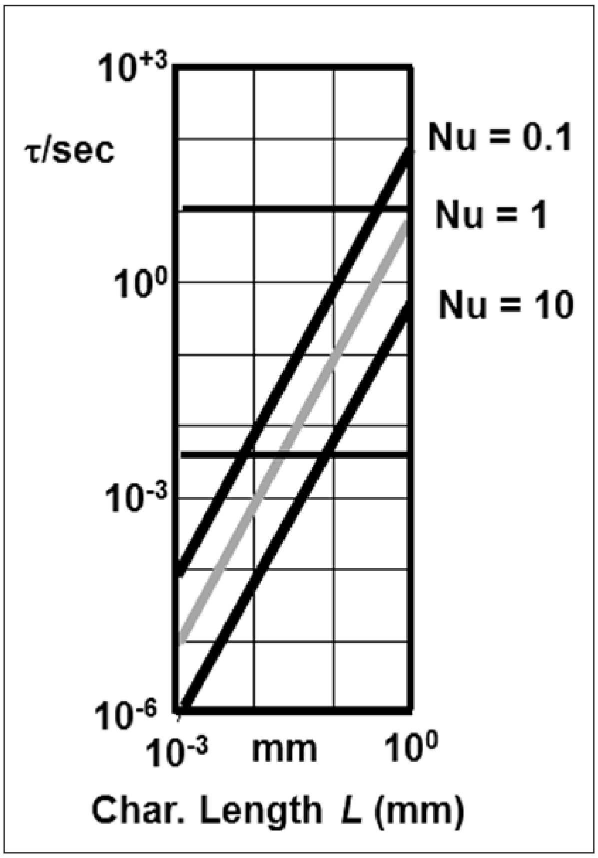

Figure 2 : Variation of heat exchange time with characteristic dimensions

d. Separation processes limited by mass transfer
e. Reaction systems requirement precise input of energy like photosynthetic and photocatalytic reactions

Selection criteria for microreactors

The most important question for any company starting off with the microreactors is whether and how they should go about using microreactors for their application.

a. The first step is to identify which stage (out of the three mentioned above) the microreactor is to be used. It could be that all three stages are applicable especially if it is a new process development.
b. If the intention is to replace an existing batch process that has to be converted into a continuous flow process, one needs to identify what are the clear benefits in terms of product quality, safety, operation costs are being targeted in the conversion.
c. Microreactors especially during development stage are used for a wide range of pressure, temperature and pH ranges. Knowing the limits of these key process parameters is very critical to ensure that appropriate microreactors are chosen.
d. Presence of solids is another important factor in the selection of microreactors. There are certain models of microreactors which can handle solids, but for correct usage, the concentration and particle size distribution of the solids is essential. Also it has to be known whether the solids are present at the start of reaction or generated during the reaction. With this information, appropriate system for the handling of the solids can be devised to ensure that the reactors are not choked during operation.
e. The final production scale needs to be known in terms of whether it will be in terms of kilogram or multiton level. With this knowledge appropriate microreactor module can be chosen which can be scaled up later easily to the desired production capacity.

During the application of microreactors it is very important to realize that the process development is effective only if there is a good co-operation between the end user and the microreactor supplier. The end user has the complete knowledge of the chemistry of the process where as the microreactor supplier has the knowledge of the behavior of the reactor. Only if these two are effectively combined there can be a good and robust process development which can be a success at production scale.

It is very important that the critical process parameters which need to be controlled are identified and appropriate online monitoring instruments are incorporated in the lab microreactor setup so that firstly good data is collected for the development and also the control scheme for the production level can be easily developed later on.

Scale up methodology

One of the most important factors in usage of microreactors is the scale up. With the final intention of using microreactors at production level, it is crucial to choose microreactors at lab level which can be scaled up to the appropriate capacity.

There are two scale up strategies which are been used in the scale up of microreactors.

a. Numbering up

This involves just using multiple microreactors of same capacity used at lab level for actual production. Though this is the easiest scale up strategy but has considerable limitations. This scale up can be effectively used for kilogram level production. The scale up factors are limited to lower single digits. Any higher scale up has the issue of effectively distributing the reactants uniformly to all the reactors in parallel and also in case of sensitive products effectively collecting the products and carrying out downstream separation processes.

b. Dimensional scaleup

The alternate scale up method is to have the bigger reactor with the same characteristic dimensions as the lab level reactor. This scale up is more complex in terms of equipment design but is the most effective if the appropriate microreactor module is chosen at lab level. With this scale up method, very high scale factors can be applied and the lab level process can be scaled up reliably to production levels even in multiton capacities.

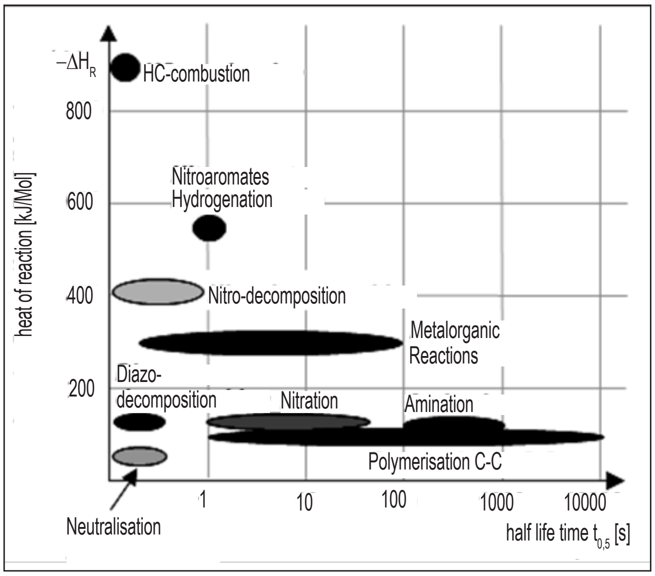

Figure 3 : Examples of reactions with fast reaction time and high heat of reaction (Suitable candidates for microreactors)

Solutions available

There are many options available commercially in microreactors. Microreactors are available in a wide range of materials like stainless steel,alloys, hastelloy, titanium, tantalum, glass which would handle pretty much all corrosive substances and ranges of pH.

The operating range for temperature are typically between -100°C to 200°C. There are specialized microreactors available for higher temperature conditions especially for catalytic reactions.

In terms of operating pressure, the range available is 0-100 bar g. Higher pressure reactors can be manufactured but need to be customized.

Most of the microreactors on the market address mixing and heat transfer. However there are microreactor solutions available for specific applications like precipitation, photocatalysis, filtration and some separation processes.

One of the major application for microreactors is the production of pharmaceutical ingredients. Considering the regulatory GMP requirements for pharmaceutical production, microreactors which are GMP compliant are also available on the commercial scale.

Figure 4 : Example of Scale up of Microreactor

These reactors are checked and certified for cleanability and surface finishes as per GMP and can be easily integrated in an internationally GMP compliant process.

Integration into continuous flow processes

It has to be taken into consideration that though it is a very effective tool for conversion of batch processes to continuous processes, microreactor is just one of the options in such a process intensification exercise. There are other available reactors like standard plug flow reactor for continuous processing and the suitability of the type of reactor needs to carefully evaluated considering the reaction, process conditions and critical process parameters.

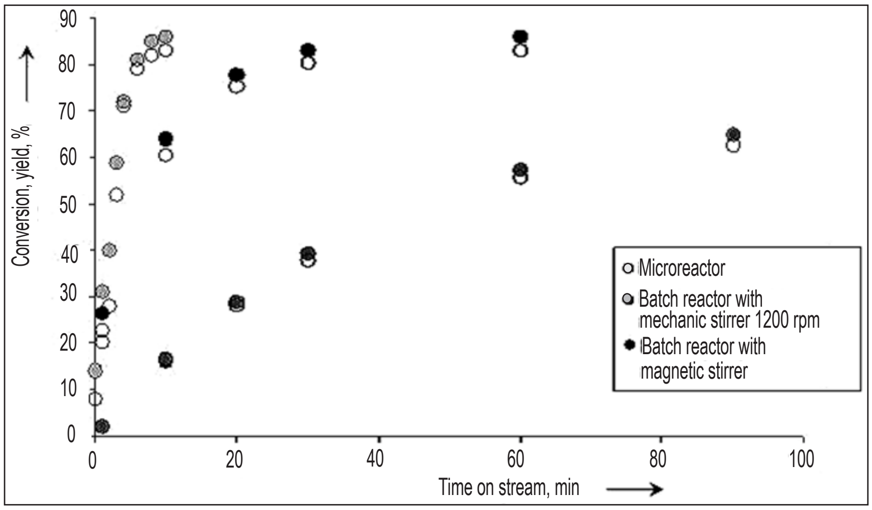

Fig 5. Case Study: Performance of microreactors compared with batch reactors (Rate of completion)

Microreactors are only one component of the process plant. While shifting to continuous processing it is critical that upstream components like pumps and downstream separation equipment also need to be assessed to have a complete continuous stable process.

Also critical are the analytics and process monitoring devices. It is very important that the critical process parameters which need to be controlled are identified and appropriate online monitoring instruments are incorporated in the lab microreactor setup so that firstly good data is collected for the development and also the control scheme for the production level can be easily developed later on.

Case Study: Alkylation of phenylacetonitrile by phase transfer catalysis

The research was carried by St. Petersburg State university of Technology and Institute of Industrial Chemistry, Dresden. The reaction considered for the study was alkylation of phenyl acetonitrile by phase transfer catalysis. The reaction product was an important pharma intermediate. Reaction is conventionally carried out with metal hydrides with use of solvents like benzene. In the study the performance with batch reactor and microreactor was compared and parameters optmised for the use of microreactor in the reaction.

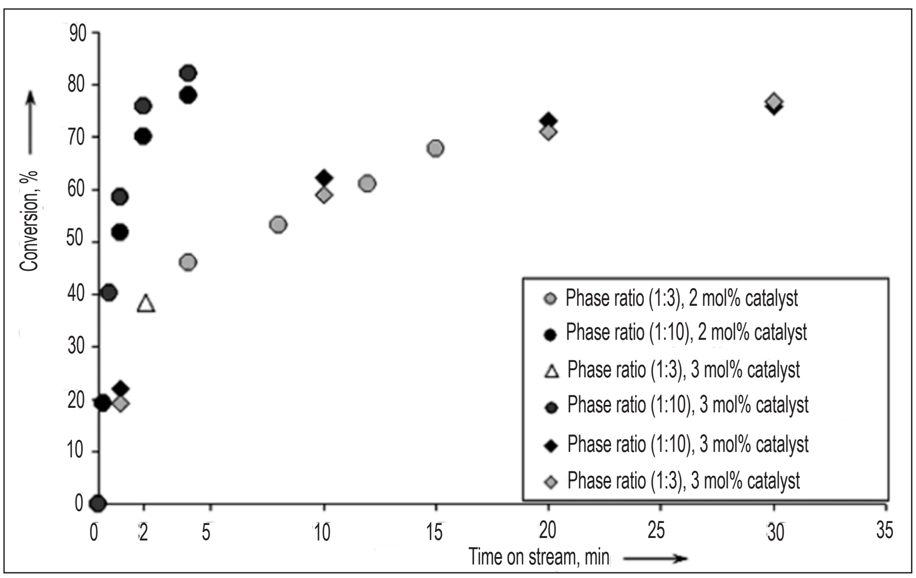

Fig 6. Case Study: Reduction of solvent phase in microreactors

Reaction setup

Batch Reactor

- Reaction in round bottom flask with mechanical/magnetic stirrer with reflux cooler
- Ethyl bromide added dropwise to reaction mixture
- Reaction product is extracted by ethyl acetate and analyzed by GC

Microreactor setup

- Microreactor was chosen with 70 μm channels. Reynolds number varied in the range 10-100
- Reactants were preheated using thermostat and pumped
- Product collected in flask containing ethyl acetate and analyzed by GC.

The results of the study which are summarized in the attached graphs can be summarized as below:

- Reaction was appreciably faster in microreactor compared to batch reactor
- Lower organic ratio leading to lower recovery cost
- Lower catalyst loading leading to lower operating cost
- Multiple options evaluated within a short time

Constraints in applications

1. Microreactors have very limited application when the reaction rate is controlled and slow. They would not give appreciable improvement in performance over other reactor types.

2. Batch processes cannot be translated as a replica to continuous flow processes. The transport phenomenon needs to be understood and even the reaction mechanism varies in both cases. It might be required to explore and change the operating conditions like pressure, temperature, pH, concentrations to get an optimized output. However it has to be noted that with the inherent nature of microreactor systems, a wide range of operating conditions can be tried out in a very short period of time giving advantage in the development process.

3. Solids are a major factor which impede the development in case of microreactors. This constraint can be effectively handled in some case if the nature of solids is known. For example, in solid catalysis reaction, the solid catalysis can be pumped in a fine dispersion with one of the reactants. Also devices like valve assisted mixer can be used to prevent the precipitated solids in a reaction from settling down in the reactor.

4. Scale up strategy or rather the lack of one can be one of the major constraints in use of microreactors. If the scale up strategy is not fixed at the start of the development phase it can lead to a scenario that the entire development is done at the lab level with a type of microreactor which cannot be scaled up to the desired levels. This could be either due to the limitations of the equipment itself or the problem of distributing reactants to multiple reactors uniformly.

Summary

Microreactors are a very effective tool for continuous flow processes. They can help transform the chemical industry by creating highly compact plants with a low ecological and environment footprint. Judicious use of microreactors in chemical processes is the future with increasing focus of the chemical industry on sustainable processes. It is time that the Indian chemical industry realizes potential of microreactors and takes the initiative of applying microreactors in processes. ❄