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Perspective

# Recent Advancements in Microfluidic Enzymatic Reactors

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## DESCRIPTION

A micro-reactor is a small device consisting of micron-wide capillaries or channels. Such devices are designed to perform a wide variety of biological and chemical reactions with inherent advantages of reduced reagent consumption, flexible and well-controlled operation, and easy integration with other units. Designed to a common feature of micro-reactors is their high specific surface area, which enables fast reaction rates.

The use of enzymes in reactors has increased over the last decades, especially in Immobilized Enzyme Reactor (IMER) applications where enzymes are confined to solid supports. These reactors can be assembled from conventional laboratory equipment such as tubes, valves, or reactor chambers, but these reactors can also be miniaturized and in microchip format. Enzyme immobilization offers the potential for reusability, easy handling, and easy separation of the product from the enzyme, as well as increased stability of the enzyme against changes in operating conditions.

The development and application of IMER has received great attention due to its advantages over traditional large-scale analytical systems. These advantages include improved heat and mass transfer, high surface area-to-volume ratio, improved catalytic efficiency, reduced diffusion distance, and high operational reliability. The operating costs of IMER are typically very low, as immobilization can significantly reduce enzyme consumption. These microfluidic devices are often inexpensive and disposable, thus avoiding maintenance and regeneration. The high enzyme-to-substrate ratio achievable with IMER improves digestion efficiency of low-level proteins. Since the enzymatic reaction takes place under liquid flow, reagents and products are continuously removed from the reactor surface and do not interfere with the catalytic process. Another advantage of using IMER over living whole cells is the need for simpler purification procedures. Following the original initiative of the lab-on-a-chip concept, several sequential steps can be integrated into the chip. This can be a reactor with various immobilized enzymes or the IMER can be integrated into other microfluidic devices (for separation, enrichment, derivatization and detection).

The advantages of IMER in terms of short reaction/analysis times and high efficiency of catalytic reactions have been widely discussed in many articles and reviews. Perhaps the biggest drawback of microfluidic reactors is the limited amount of components that can be produced in the device. This can be mitigated by parallelizing the channel/reactor system. On the other hand, some fields of cheminformatics, identification and analysis still allow sub-microgram amounts of ingredients.

Microfluidic chips fulfill the most important requirement for high IMER efficiency, namely the large specific surface area of the solid support. Support materials can be uniformly introduced into microfluidic systems and monolithic IMERs, and enzymes are immobilized in micro pores and channels provided by the mesoporous and microporous networks of monolithic materials. There are several other solid supports used in IMER that use slightly different approaches *via* membrane, paper, or gel-based supports. Although the simplest method of immobilizing the enzyme on the interior/walls of the channel itself can be achieved, the most commonly used conventional methods to improve the S/V of the support are micro packs or membranes. Such a wide variety of micro reactor designs also means variability in performance.

Capillary and chip based devices are the main types of microfluidic reactors. Capillary reactors can be easily scaled up with longer capillaries and easily connected to other microfluidic devices and standard separation and detection techniques. Chip reactors offer complexity and flexibility in channel pattern design, and dead volumes between components of the fluidic system are not expected.

A common problem when working with microfluidic devices is clogging of channels or fine patterns. This can be resolved by a channel design that includes bypass routes when part of the channel is blocked. If the cost is low and disposable is possible, simply discard the device and apply high flushing pressure.

Materials for IMER should be compatible with enzyme immobilization methods and efficient working conditions for enzyme function. Most capillary based IMERS use commercially available fused silica capillaries to house the enzyme. Greater

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flexibility regarding reactor layout and chip architecture is enabled by (often) home-made micro fabricated components.

## CONCLUSION

Initially, hard materials such as silicon, quartz, and glass were used to fabricate the chips, and etching techniques were used to build the channel system. Glass microchips are still used, but softer polymer-based materials are used polydimethylsiloxane has received considerable attention, one of the most commonly used polymers due to its low cost, biocompatibility, optical transparency and flexibility. However, its application is limited to academic research culture, probably due to its low mechanical strength. In addition, they are highly hydrophobic and lack surface functional units. Therefore, surface treatment is required to prevent non-specific adsorption of molecules.

In addition to optical transparency and low cost, the chips offer improved solvent resistance and the ability to tailor surface chemistry by adjusting monomer stoichiometry.

The fabrication of such TE-based chips is a simple process based on the principle of replica molding. Microchips are made by replicating a master mold containing the desired channel structure.