Mass Production Of Micromixers: A Comprehensive Review

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Abstract. Micromixers are vital components of microreactors, which are utilized across diverse fields such as medicine, biochemistry, analytical chemistryand drug delivery systems. They aid in the thorough mixing of reactants in micro-fluid applications. The emergence of microreactor technologies has opened new avenues for innovation, promising unprecedented levels of precision and control in chemical processes. This literature review paper offers an extensive overview of microreactor technology and micromixers, encompassing design, manufacturing techniques, challenges with respect to mass production.

Keywords: Microfluids, Micromixers, Lithography, 3D Printing, Micro machining.

1 Introduction

In the recent years, the field of chemical process engineering has experienced significant advancements, such as the emergence of microreactors (<1 mm) and microreactor-based applications [1]. A microreactor is a device designed to facilitate chemical reactions within narrow capillary channels. They offer a versatile platform to perform intricate chemical processes. These downscaled chemical reactors primarily offer controlled and high-throughput methods for chemical synthesis, delivering outstanding yield, selectivity, stability, and energy efficiency.

Most researches have concentrated on the utilization, design and fabrication of individual microreactors, which makes it difficult to figure out how best to take advantage of their unique qualities in large scale applications. These attributes encompass crucial aspects such as the manufacturing processes necessary to achieve the desired size and precision, determining the appropriate time frame for widespread commercial adoption, and identifying potential areas where these microreactors can be applied [2]. This comprehensive literature study investigates micromixers, which are significant components of microreactors, with an emphasis on design and manufacturing methods with respect to large scale production.

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2 Overview of Microreactors

Microreactors are essential instruments in analytical chemistry for synthesizing and analyzing molecules, hence helping to the creation of new materials and chemicals. Furthermore, microreactors have had a considerable influence on the area of medication delivery, since they allow for the regulated and targeted release of medicines, hence improving therapy efficacy and patient outcomes.The potential of microreactors in the industrial landscape is transformational. Microfluidic reactors present several benefits over traditional batch reactors [3]. These advantages include enhanced controllability and uniformity in the characteristics of nanomaterials These devices hold the promise of optimizing production processes, reducing waste generation, and increasing the overall sustainability of chemical manufacturing. Due to their small footprint, elevated surface-to-volume ratio, and improved heat and mass transfer characteristics, microreactors are well-suited for the creation of efficient and eco-friendly industrial reactors. Moreover, the exceptional heat transfer capabilities of microfabricated devices help mitigate the potential for significant industrial accidents arising from thermal runaway [4]. Microfluidic microreactors face challenges related to low throughput, hindering their industrial adoption. One strategy to enhance throughput involves multiplication and parallelization of the microreactors. Commonly cited drawbacks of microreactors include high fabrication costs, limited throughput, incompatibility with solids, and the failure to realize cost reductions through scale-up effects. These factors collectively contribute to the continued limited industrial acceptance of microreactor technology [5].

Microreactors find extensive application across diverse scientific and industrial sectors. They facilitate rapid and controlled biochemical reactions, enabling researchers to conduct analyses and tests with unparalleled precision. In tritium recovery processes, microreactors are utilized for converting various tritiated streams into water. Additionally, from an oxidation standpoint, microreactors are demonstrated to be safer compared to conventional oxidation reactors. Another significant advantage is the ability to design microreactors to achieve high recombination efficiency, surpassing 99.9% if necessary. This paper aims to address issues related to the design, computation, and production of a highly efficient microreactor suitable for converting tritiated streams into water [6]. Micromixers have the potential to serve as sensors in point of care testing (POCT) and in environmental monitoring applications, such as the detection of ammonia in water-based solutions. Hinsmann et al.'s micromixer was used to analyze fast chemical processes in solution with stopped-flow TR-FTIR. (TR-FTIR stands for Fourier transform infrared spectroscopy) [7].

3 Design for Micromixers

The efficiency of mixing in microreactors is measured using various performance metrics such as mixing index, pressure drop, Péclet number and Reynolds number. Micromixers are generally categorized into two types – Active and Passive. The classification of these mixers depends on the presence of mechanical agitation and external forces. Active micromixers commonly incorporate phenomena resulting from electrokinetic, dielectrophoretic, acoustic/ultrasound, and magneto-hydrodynamic (MHD) forces while passive micro mixers depend on their special geometries to disturb the fluid flow thus resulting in the mixing of reactants [8]. In the laminar flow conditions of passive micromixers, mixing mostly occurs via molecular diffusion and chaotic advection. Passive micro mixers are relatively easier to fabricate than active mixers as they rely on their geometry and have fewer moving parts. T and Y are the most basic type of passive micro mixers. The mixing length within the channel typically relies on factors such as the diffusion coefficient, channel dimensions (width and height), fluid inlet velocities, fluid viscosity, and the geometric arrangement of the micro-mixer. [9].

Mills et al. (2007) review microreactor technology developments in catalytic systems, focusing on pilot plants and scale-up methods. It highlights advancements in microreactor scale-out, construction materials, and performance effects. Critical factors influencing the adoption of MRT include safety, performance improvement, environmental considerations, decentralized manufacturing, and the utilization of computer-aided design tools. The discussion also encompasses MRT's involvement in portable power systems [10]. Amador et al. (2004) in this paper studies flow distribution for consecutive and bifurcation manifold structures, ensuring consistent residence time in all micro channels for heat/mass transfer and reactions. The validity of the analytical model is confirmed through comparison with finite element simulations and can be utilized for both circular and rectangular channel geometries. It offers guidance on suitability across various operational scenarios, fabrication limitations, and design goals [11]. Fu et al. (2007) in this study examine the evolution of two-phase flow patterns and pressure drop in silicon based micro channels with a hydraulic diameter of 128 μm and CO2 bubbles generated by chemical reactions of sulfuric acid and sodium bicarbonate. It investigates three concentrations of reactants and 10 flow rates. Flow visualization is accomplished through the utilization of a high-speed digital camera. The findings indicate that a low void fraction at the inlet encourages CO2 generation, irrespective of whether the channel is converging or diverging [12]. Kim, K. et al. (2019) conducted a study investigating the utilization of fractal structures to enhance the efficiency of micromixers. The authors introduce three distinct designs named YSUSAR, YTUSAR, and YSTUSAR, which are analyzed, characterized, and experimentally tested for their mixing capabilities. The findings suggest that YSUSAR is the most promising design for enhancing mixing performance in micromixers [13]. Most researches have concentrated on mathematical modeling and optimization, thus employed CFD simulations to determine the mixing efficiency of the design but only fewer researches have validated their results with physical experiments such as flow visualization tests. The configuration of micro channels plays a significant role in achieving optimal performance. While many micro channels are currently designed through trial and error, there is a growing need for the development of a systematic approach to design and validate micromixers. Establishing such a method would enable more efficient and effective design processes, ultimately leading to improved performance outcomes.

4 Fabrication Techniques

Fabrication of microreactors, particularly in the context of micromixers, necessitates a meticulous approach, given the small scales and intricate designs involved. There are several manufacturing processes available, each catering to different requirements and complications inherent in microreactor construction. To fabricate these micro scale devices, various methods such as micromachining, wet etching, injection moulding, laser ablation, micro-forming, soft lithography, photolithography, hot embossing, nano imprinting, electroforming, and micro-electro-discharge machining are employed.

Compact and efficient microreactors are more than mere laboratory novelties. The requirement for efficient procedures and process chains to create micromixers on a commercial scale is critical in this setting. When choosing an acceptable manufacturing process, several criteria must be addressed, including cost-effectiveness, repeatability, scalability, and the capacity to build complicated and accurate micro fluidic structures.

4.1 Micro-machining

According to Jain et al. (2014), there is a great deal of promise for accurate micromachining of non-conductive materials like quartz with Electrochemical Spark Machining (ECSM), a novel hybrid machining technique that combines concepts from Electric Discharge Machining (EDM) and Electrochemical Machining (ECM). The goal of the research is to determine the ideal machining settings. Specifically, it looks at how voltage and workpiece feed rate affect a number of machining characteristics, including the rate of material removal, micro-channel diameters, and the heat-affected zone. Due to the lack of a feedback system, one major obstacle identified in the study was the difficulty in establishing consistent microchannel depths along the machining process. To solve this issue, the researchers proposed developing a feedback or servo system specialized to non-conductive workpieces in order to maintain uniform microchannel depths, hence improving productivity. [14].

Chung et al. (2009) addressed the issues connected with the manufacturing of microfluidic devices, particularly micromixers, in their study, emphasizing the necessity for a quick and cost-effective procedure. For creating master moulds, previous approaches employing SU-8 photolithography were found to be time consuming and costly. They used a more efficient fabrication procedure to circumvent these constraints. A CO2 laser was used to generate a PMMA master mould in their planned micromixer fabrication procedure. This method made it simple to create microchannels with high aspect ratios [15].

Vafaie R.H. et al. (2013) state that the surface microchannel technology for producing miniaturized electro-osmotically-driven micromixers offer a viable method for the integration of diverse microfluidic components with better material compatibility, such as micro-pumps and micro-separators. In this manufacturing process, a silicon nitride layer is first deposited onto a silicon wafer, after which semi-circle shaped electrodes are patterned at the bottom of the microchannel. Unlike previous techniques that used electrodes on the channel sidewalls, this design avoids the requirement for bridging to make contact with the electrodes [16]. Shiu et al. (2009) in their paper describe a novel approach for producing metallic micro-moulds with high aspect ratios. Laser micromachining is employed to carve two-dimensional profiles and fluidic network designs into a 100 m thick brass sheet, while electro-discharge micromachining (micro-EDM) is utilized to fabricate the positive relief pattern. This substrate is then moulded for elastomer casting or thermoplastic hot embossing. The technique is proven experimentally using a T-channel micromixer and illustrated with a Y-channel micromixer with a 4-aspect ratio. When compared to typical electroplating processes, the technology enables substrate material diversity, potentially reducing manufacturing downtime and costs for reproducing polymeric microfluidic devices [17].

Chen et al. (2016) in their research paper describe a novel method for converting a two-layer microfluidic chip into a more advanced four-layer 3D microfluidic chip fully built of polymethylmethacrylate (PMMA). CO2 laser cutting of PMMA sheets is used to build precise microfluidic channels, with an orthogonal experimental method optimizing process parameters for stability. This approach offered a cost-effective, efficient, and reliable means of fabricating multilayer PMMA-based microfluidic devices, enhancing their potential for various applications [18]. Valentincic et al. (2018) provided the process chain that includes waterjet (WJ) and abrasive waterjet (AWJ) machining, die-sinking electrical discharge machining (EDM), and polydimethylsiloxane (PDMS) casting. WJ machining has the greatest influence on dimensional accuracy, whereas AWJ performs better but has broader kerf widths. Die-sinking EDM is effective, particularly for rough and delicate machining. Casting is appropriate for serial manufacturing but less so for mass production due to parameter control issues [19]. Ahmmed et al. (2014) stated that due to ease of use and scalability, femtosecond laser micromachining has quickly acquired recognition as a versatile approach for micro/nanostructure production. Although femtosecond laser micromachining enables the creation of diverse surface patterns on metals and alloys, further research is required to understand the intricacies of their formation [20]. Zhou et al. (2014) investigated the use of laser micro-milling techniques in fabricating microchannels for hydrogen production. The findings indicate that both scanning speed and laser output power have a considerable impact on the surface morphology and geometric dimensions of the microchannels. The microchannels served as catalyst support for methanol steam reforming reactions, demonstrating the suitability of the laser micro-milling process for commercial applications [21].

4.2 Lithography

Mondal et al. (2020) offered an efficient and successful method for creating micromixers out of poly-di-methyl-siloxane (PDMS), a critical component in microfluidic systems, in this work. The emphasis here is on the development of two distinct wavy micromixers, the raccoon and serpentine designs, via a well-structured two-step approach comprising mould preparation and device fabrication. In the initial phase, the micromixers are fabricated by employing CO2-assisted laser machining on poly-methyl-meth-acrylate (PMMA), ensuring precise mould dimensions. Subsequently, the micromixers are replicated using the soft lithography technique and PDMS material. The study emphasizes the significance of machine parameters in laser machining, notably in preserving channel depth and surface smoothness, as well as the importance of thorough mould preparation to achieve accurate micromixer dimensions [22].

Sarwar et al. (2014) describe an innovative and cost-effective manufacturing technique for creating three-dimensional micro patterns in carbon nano tube (CNT) forests. This is accomplished through the utilization of an advanced UV-LIGA process in conjunction with an innovative photo resist system and electroplating to generate a high-density array of copper electrodes for dry micro-electro-discharge machining (EDM) [23]. Yang et al. (2017) state that the LIGA technique fabricates high aspect ratio micro components with sub micrometric accuracy and nanometre surface finish. However, this complex and expensive process requires deep X-ray lithography and synchrotron radiation. Micro electrical discharge machining (Micro EDM) and focused ion beam (FIB) machining offer cost-effective alternatives, although micro EDM micro mould inserts may require additional machining with FIB to achieve higher accuracy and surface finish [24]. Takahata et al. (1999) investigates a novel micromachining technique employing micro electro discharge machining to fabricate ultrafine patterned high-aspect-ratio micro components from materials not suitable for silicon or LIGA processes. This approach effectively fabricated structures from stainless steel and tungsten carbide super hard alloy within short machining durations. Copper electrodes, electroplated using the LIGA process, demonstrated favourable wear resistance in the fine discharge energy range. The production of multiple structures in parallel utilizing an electrode array showcased the potential of this method for manufacturing high-aspect-ratio micro components [25].

Nakahara, T. et al. (2011) present a novel approach to microfluidic device fabrication and showcase its application in the development of a highly efficient micromixer. The use of inclined UV lithography to create a three-dimensional multi-layered flow generator is a significant innovation in microfluidics and holds promise for various applications within the field. The development of a rapid and versatile fabrication process, along with its successful application in micro mixing, highlights the potential for numerous microfluidic device applications. The inclusion of experimental and numerical validation enhances the reliability of the results [26].

4.3 Injection Moulding

Kim et al. (2006) presents a micro fluidic biochip incorporating flow-splitting micro channels, chaotic micromixers, response micro chambers, and detection micro filters designed for effective blood typing. Notably, the emphasis here is on the fabrication process, with an emphasis on cost-effectiveness and speed. The biochip is fabricated within approximately 20 minutes through microinjection moulding of cyclic olefin copolymer (COC) followed by thermal bonding. Metallic nickel mould inserts, created with SU-8 photolithography and nickel electroplating, increase the possibilities for mass production. The biochip effectively determined ABO blood types in 3 minutes, demonstrating its promise for cost-effective, quick, and reliable blood typing with clinical diagnostic applications [27]. Yang et al. (2012) describes the manufacturing method for a polymer micromixer, which is specifically intended to take advantage of the capabilities of ultraprecision micromachining and microinjection moulding. The major material for micromixer fabrication was polymethyl methacrylate, an amorphous polymer. The research aimed to investigate the impact of processing parameters on the quality of micromixer replication, focusing on four key aspects in microinjection moulding: melt temperature, injection velocity, packing pressure, and packing time [28].

Li. L et al. (2010) describe the creation of a low-cost split-and-recombine polymer static micromixer. When compared to cleanroom procedures, the micromixer's design utilizes ultra precision micromachining and microinjection moulding, providing advantages such as reduced machining time, increased productivity, and flexibility. The experimental and numerical results emphasize the critical roles of packing pressure and packing duration in replication, with melt temperature also having a major impact. However, injection velocity had little effect [29]. Rizkin et al. (2019) state that micro fabrication technologies, particularly LIGA (lithography, electroplating, and moulding), were developed in Germany and have revolutionized microstructure production. This versatile method can be applied to a range of materials, such as metals, polymers, and plastics. LIGA uses electronic X-ray radiation to accurately shape and mould materials, as the name implies. This process involves three fundamental stages: initially transferring patterns onto a photosensitive material, typically a resin; followed by electroplating to incrementally build up the material's surface by selectively removing specific layers; and finally, conducting photo irradiation removal, facilitated by the photo resistor or photo sensor [30]. LIGA technology has considerably aided the growth of micro fabrication, allowing the manufacture of detailed microstructures across a wide range of materials and industries, ultimately driving innovation in microtechnology and miniaturization.

4.4 3D Printing

Tachibana, D. et al. (2019) explores the utilization of micromixers in micro total analysis systems and lab-on-a-chip applications, particularly emphasizing their role in point-of-care testing within medical and industrial environments. It highlights that while micromixers have great potential, their fabrication and setup have become more complex over time. To address this issue, he suggested that rapid prototyping using 3D printing technology with micro-scale resolutions can simplify the design and production of micromixers [31].

Enders, A. et al. (2018) comprehensive exploration of the application of 3D printing technology in redesigning and fabricating passive micromixers for microfluidic systems used in biological and chemical applications. Mixing different fluids rapidly is a fundamental operation in microfluidics, and this study addresses the challenges associated with achieving efficient mixing in laminar flow profiles, where molecular diffusion is the primary mixing mechanism. They redesign and produce five different passive micromixers using high-definition MultiJet 3D printing, systematically assessing their mixing performance through both experimental and numerical analyses. The use of sodium hydroxide and phenolphthalein solutions as test fluids allows for a clear demonstration of the micromixers' capabilities [32]. Zhang, H. et al. (2019) introduces an approach to microfluidic mixing by introducing a 3D metal-printed showerhead mixer designed to efficiently blend two reagent streams within a limited mixing volume. The novel design, supported by experimental evidence and CFD simulations, showcases the potential of 3D metal printing in creating efficient microfluidic devices. The paper's contribution to the field of microfluidics and its practical applications, particularly in low Reynolds number scenarios [33].

Bhargava, K. et al. (2017) presents an innovative approach to microfluidic mixing using 3D-printed modular components. These components are designed to split and recombine fluid streams in order to reduce interstream diffusion length, ultimately achieving efficient mixing. The study also compares these modular mixers to helical mixers that rely on chaotic advection principles, leveraging the capabilities of 3D printing technology. The systematic evaluation of mixing efficiency and the trade-off analysis between different parameters provide valuable insights for researchers in the field of microfluidics [34].

On comparison, Techniques like Lithography offer high-resolution patterning of microstructures with precise control over feature sizes and shapes. Once the lithographic mask is established, it can be replicated, facilitating the large volume production of micromixers but it is an expensive and time-consuming technique. Micro machining processes such as micro-milling have good efficiency and can create features with decently high aspect ratios. Micro-milling is considered a good alternative to LIGA process. Energy-assisted machining processes like EDM have good geometric accuracy in machining conductive materials but demand meticulous optimization of process parameters to achieve desired production rates while minimizing tool wear and upholding quality. Additive manufacturing methods such as 3D printing are increasingly being adopted by researchers in the recent times as they offer a one step process to fabricate the mixer as well show potential for on-demand manufacturing capabilities conducive to mass production. An inherent benefit of SLA fabrication lies in its ability to achieve high precision in surface resolution. SLA systems excel at producing products with exceptional resolution while maintaining cost-effectiveness, primarily due to their efficient utilization of liquid medium. 3D printing technique do encounter constraints concerning material selection, surface finish, and production speed in comparison to traditional machining processes. Additional post-processing steps may be necessary to attain the desired surface quality and functionality.

In most cases the micro mixer fabrication requires a sequence of different processes to attain desired features and quality. In context of mass production, it might be efficient to create the molds using above mentioned techniques and produce large volumes of micro mixers with the molds using techniques such as Injection molding.

5 Polymer Materials

Micromixers produced by injection molding processes are typically made from various engineering thermoplastics, suitable for microfluidic applications. These materials are chosen for their compatibility with the specific chemical and thermal conditions of the mixing process, as well as their ability to be effectively molded at a small scale. It is important that the material being worked on supports a wide range of industrial chemical reactions. While silicon or glass are commonly used for fabricating microfluidic devices, polymers offer a broader spectrum of chemical and physical properties, as well as surface modification capabilities, compared to inorganic materials. Polymers may have limitations in terms of mechanical strength, chemical resistance, and thermal stability, necessitating careful material selection to meet the performance requirements of the micro mixer. The most common material is Polymethyl Methacrylate (PMMA). PMMA, also known as acrylic, is transparent and has good chemical resistance, making it suitable for micro fluidic applications where visualization is essential. Other potential materials under consideration include Polycarbonate and polydimethylsiloxane (PDMS). The affordability of PDMS materials facilitates the widespread development of various microfluidic-based technologies. This holds significant advantages for industries by enabling cost-effective mass production, thereby enhancing production capacities and bringing researchers' innovative ideas and projects to fruition, as stated in Azouz et al’s work on microfluidic cell development through cyclic olefin copolymerization methods [35]. Polypropylene (PP) and polyethylene (PE) are among the potential options, along with cyclic olefin copolymer (COC) and cyclic olefin polymer (COP).

6 Challenges and Discussion

The transition from laboratory-scale prototypes to large-scale industrial applications presents a unique set of challenges. Traditional manufacturing methods are not very suitable for scaling down to such smaller dimensions. Hence, there is a research opportunity to design efficient micro tools customized for mass production techniques like injection moulding, hot embossing. The successful implementation of these mass production processes necessitates a comprehensive approach encompassing material selection, mould design, and process optimization. Achieving high levels of precision, reliability and reproducibility is essential to meet the stringent demands of industrial and medical applications.

While studies have separately investigated micro feature accuracy, insert fatigue life, and fabrication costs, there remains a lack of comprehensive research that addresses all three challenges simultaneously to achieve a beneficial trade-off.

To enhance the precision and fidelity of microreactor inserts, there is an need to explore advanced manufacturing techniques and materials.

For microreactors to transition from laboratory settings to full-fledged commercial manufacturing, integration with various sensors and actuators is imperative. This integration enables real-time monitoring and control of microreactor performance, facilitating optimization and customization for specific applications.

By holistically addressing these three aspects, an integrated solution can be developed that bridges the existing research gap and advances the field of microreactor technology. Such a solution will yield cost-effective, dependable, and highly accessible microreactor inserts, paving the way for widespread adoption and utilization in a multitude of engineering applications.

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