Microreactor Production by PolyJet Matrix 3D-Printing Technology: Hydrodynamic Characterization

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SUMMARY

In this work, the methodology of producing a 3D-printed microreactor from acrylic resin was investigated by PolyJet Matrix process. The PolyJet Matrix technology employs different materials or combinations to generate 3D-printed structures with different material properties and to achieve small structures as well as complex geometries. The geometry and production of the microreactor and its hydrodynamic characterization were evaluated by experimental and numerical methods. The operational limits of the single-phase flow in the microchannels, further improvements and possible applications of the microreactor were assessed based on the hydrodynamic characterisation.

Key words: 3D-printing, PolyJet Matrix process, microreactor, hydrodynamic characterisation

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INTRODUCTION

Advanced processing methods have been used recently in producing microreactors and their microfluidic components. Such devices have been created with a goal of accommodating and controlling mass-flows through microchannels with very small cross sections of only 10-500 µm. Additive manufacturing (e.g. 3D-printing) has significant scope in terms of microreactor design and manufacturing (1,2). Additive manufacturing processes are established techniques for the rapid prototyping of complex structures. Using the layer-by-layer principle to build structures, additive manufacturing processes enable the production of very complex geometries based only on a Computer-aided design (CAD) model of the future product.

Permanent development and improvement of new materials, as well as new printing processes and equipment, results in the constantly increasing application of additive manufacturing technologies (3,4). To design and produce microfluidics from polymer materials, five additive manufacturing technologies have been implemented (stereolithography, fused deposition modeling, multi-jet modeling, selective laser sintering and selective laser melting). Components of microfluidics system (housing structure and microchannels plate) have been also produced with direct metal laser sintering technology (DMLS) which uses a metal powder. DMLS allows production of microreactor components with aluminum alloys. Generally, this technology can be also used for the production of other metal materials such as cobalt-chrome, nickel, stainless-steel and titanium alloys. (5). Each of the mentioned techniques is not useful without its own engineering and material issues which needs to be fully considered before 3D printing. The main disadvantage is unavailability of different types of the materials (6). Microchannels are usually fabricated from silicon or quartz materials by stereolithographic methods. The microfabrication techniques are also extended to soft lithography techniques with the goal to improve the created microfluidic structures (7).

Microreactors offer many advantages. Faster reaction kinetics is achieved in automated microreactor systems and this significantly reduces the time needed for the kinetic parameter determination and process development. Also, microreactors are a great tool for rapid testing of different systems, which results in reducing time and money needed for experimentation (8). Moreover, the precise control of reaction conditions and reproducibility represents the most important aspects of microreactors. In addition, the flow characterisation is important when overall reaction is limited by heat and mass transfer. In other cases, important advantages of microreactors can be found in fields of reduction of hazardous waste, safe synthesis of hazardous compounds, and isolation of sensitive compounds. Advantages
of microreactors are reviewed in a recent literature (8, 9,10). However, miniaturization and reproducibility are not the only important factors in microreactor applications. Especially in research environments, an easy adaption of microreactors to the processes in development is important. Modular systems can be adapted to different needs, e.g. adjusting aging time and flow-rate, but optimization is limited by the available components (11). One strategy is therefore to produce customized microreactors based on cheap materials with affordable machinery directly by the researcher. Such rapid prototypes for process development do not need exceptional material stability because they are mostly employed for a limited number of experiments (12).

There has been a prominent focus on a single-phase flow of a fluid in uniform microreactors microchannels with the goal to characterize transport phenomena and hydrodynamics. This flow is usually directed, symmetric and mostly laminar. A potential challenge of using microreactors for accurate kinetic and reaction scale up investigations is the residence time distribution (13). It can be noticed that laminar flow operation in a microreactor creates a parabolic velocity profile-material moving along the center of the reactor channel flows faster than the material near the walls. This variation in velocity corresponds to variation in the amount of time that the reaction material spends in the reactor. Accordingly, the residence time distribution can be measured using tracer injection methods or approximated by using well known flow models. Distributions can be used afterwards in the prediction of the appropriate operating conditions of larger reactors for successful scale up (14).

However, the literature references bring information on uniform cross-sectional area that are produced in different shapes (for example being rectangular, circular, triangular, or trapezoidal). In stereolithography, plasma etching can be tailored to provide rounded corners to silicon negative masters that yield elastomeric microchannels with semi-circular profiles after spin coating (15). Rounded edges of semicircular profiles help to promote cell seeding and proliferation in microfluidic devices developed for tissue engineering. Current studies in biomedicine biotechnology are focused on the following: (i) the analysis of shear stress effects on endothelial cells in curved microvessels, (ii) the evaluation of micro machined flow cytometers with integrated optics, (iii) the creation of a magneto hydrodynamic micro pump, (iv) the application of microfluidic devices for capillary electrophoresis, and (v) biohybrid artificial lung modules with semicircular endothelialized blood microchannels subjacent to rectangular gas microchannels. Semi-circular microchannels that are fabricated using hard or soft micromachining are characterized as partial semi-circular microchannels, in which the radius of the curved-side is thinner than the radius along the flat-side (16, 17).
In any continuous processes the fluid flow hydrodynamic characteristics in the reactors has significant importance. One of the major steps in the process development and the characterisation of the reactor performance is the determination of the flow pattern. Two ideal flow patterns are presented as plug-flow and ideal mixing. Plug flow is an ideal case describing flow through pipe or tube, with the fluid moving as a plug at a defined velocity (18). A reactor with such flow characteristics is called “plug flow” reactor (other extreme is ideal mixing reactor with the homogeneous distribution across reactor volume). Plug-flow has overall advantages in the continuous process development and can be used for the control of the resident time and the fine tuning of reaction conditions (each fluid elements in the reactor has the same residence and reaction time; 19). Consequently, the reaction mixture is processed under identical conditions in the axial axis. If the deviations from plug-flow occur in the reactor, conversion rate decreases and the selectivity of the processes is reduced. However, in the slow flowing system ideal plug-flow pattern is rarely achieved because of the viscosity and development of the gradients and dispersion across the axial reactor cross-section (20). One of the solutions to overcome the influence of the viscosity on the ideal plug flow pattern is utilisation of the tubular reactor with the small channels diameters. In this system influence of the molecular diffusion overcomes the effect of the viscosity and reduces the axial dispersion of the fluid (21). The resident time distribution curves become narrower than expected from the profile associate with slow and laminar flow. The residence time distribution curves can provide necessary information for better understanding of the flow pattern and the hydrodynamic characteristics of reactors (22). Therefore, the measurement of resident time distribution in microchannel for the different microchannel geometry and processes was measured in numerous investigations and experimental data were confirmed by a simulation using the axial dispersion model and the Levenspiel model (23-25).

The purpose of this research work is to apply the classical theory of residence time in order to characterize a microreactor produced by 3D-printing technology. Instead of the traditional machining approach to generate parts of microreactor, we have chosen additive 3D-printing by the PolyJet Matrix technology to produce a microreactor in two parts for quick assembly. Two polymeric components were used to generate an integrated seal at the interface of the two halves in a single printing process and prevent leaking from microchannels. Hydrodynamic properties of 3D-printed semi-circular microchannels with uniform main microchannel area were determined experimentally and numerically. Experimentally measured residence time distribution was compared with theoretical predictions and numerical solutions. Using a dispersion model for microchannels, hydrodynamic characterisation, and
Experimental results the plug-flow conditions for small axial dispersion were determined. The obtained results can be used to enhance microreactor performance and to select appropriate microreactor applications.

MATERIALS AND METHODS

Microreactor fabrication

The CAD design of the microreactor was transformed into a physical model using a 3D-printing process PolyJet Matrix. The PolyJet Matrix belongs to the liquid-based processes where a material jetting principle is used for the generating each layer of the printed product. This means that the build (as well as the support) materials are jetted in liquid state onto the building platform (and afterwards on the previous layer) by a printing head with nozzles and cured by a UV lamp. In the first step, the photosensitive polymer resin was jetted on the building platform and immediately cured by UV light. After curing the first layer, the building platform was lowered for new layer thickness (in this case for 16 µm) and the process was repeated until the microreactor was finished (Fig. 1; 26). The supplementary material was used to support the build material during the short time between jetting and curing and to support structures that would otherwise be printed "on the air" (e.g. structures that are not supported by a previous layer of a build material). For the hydrodynamic characterisation a microreactor with rather small dimensions (geometric area 60 x 60 mm) with microchannels integrated into one-half of the microreactor has been developed. The diameter of microchannels was 0.66 mm with a half-circle cross-section. The total length of the microchannels was 600 mm (Fig. 1b (left)). As the channels were designed on the contact surface of two microreactor’s halves, the area around the microchannel had to be appropriately sealed by a second polymer (rubber-like acrylic resin TangoBlackPlus). The microscopy image of microchannels (Fig. 1b (right)) was photographed using Stereo Microscope Leica MZ6 with enlargement of 7.88x.

Surface roughness was tested by a contact method using the Perthometer S8P measuring instrument with Gauss filter $\lambda_c = 0.8$ mm, reference length $l_n = 4$ mm and radius of spike $r = 5 \mu$m. The value of roughness is usually measured regarding the mean reference line of the profile of uneven areas $m$, which divides the profile so that within the measurement length $l_n$ the value of all the squares of profile deviation from that line is minimal. The surface roughness is determined perpendicularly to the direction of production. Measurement was performed at the four roughness profiles. In the area of each profile two measurements were performed. From the obtained values of the parameters of surface roughness, the arithmetic mean $\bar{x}$, standard deviation $S$ and range $R$ ($R = \text{Max} – \text{Min}$) were determined.
Experimental setup

A schematic diagram of the experimental setup is shown in Fig. 1c. It consists of the Y-shaped front section with two converging microchannels with a semi-circular cross-sectional area and a similarly shaped main channel, a syringe pump (World Precision Instrument (WPI) AL-4000 and Harvard Apparatus (HA) PHD 4400) and a control and data acquisition system (Syrris, Asia Process Optimization Systems). The syringe pump uses two syringe tubes to drive the deionised water and tracer into different inlet chambers. The two liquid streams meet at the intersection of the two front channels and the main channel. The mixtures output from the main channel are drained to a flow-through cuvette placed in a spectrophotometer, which allowed the determination of the residence time distribution as the function of flow rate. To measure the pressure drop, a gauge pressure transducer Huba 692 was fixed at the channel inlet with the T-junctions. Measured pressure was then monitored and recorded with a computerized data acquisition system. The flow was considered to have reached the steady-state, when the readings of the pressure drop did not change with time. The present study employs deionized water as the working fluid. The single-phase flow of deionized water in the 3D printed microreactor was studied, and the volumetric flow rate of water ($F$) was controlled in a range from 0.2 – 2.0 mL/min. Linear velocity $u$ was determined as the quotient of the flow rate and the channels cross section area.

Determination of hydraulic diameter, Reynolds number and pressure drop in the microchannels

The hydraulic diameter ($d_h$) of microchannel was calculated in the order to determine Reynolds number using equations below (27):

$$d_h = \frac{4A}{P} = \frac{4 \text{area}}{\text{wetted perimeter}}$$

/1/

$$Re = \frac{\rho u d_h}{\mu}$$

/2/

According to relatively small microchannels size, the mean Reynolds number ($Re$) ranges from 7-136 in the 3D printed microchannels. The flow in a microchannels is assumed to be laminar, and the frictional pressure drop can be approximately evaluated using the following equation according to Hagen-Poiseuille relation in a laminar regimen:
\[
\Delta p = \frac{96}{Re} \cdot \rho \frac{u^2}{2} \cdot \frac{L}{2e} /3/
\]

where \( L \) is the length of the channel, \( \rho \) is the density of the liquid or mixture, \( u \) is the linear velocity of fluid and \( e \) is depth of the channel.

The pressure drop and flowrate relationship for partial semi-circular (PSC) cross-sections microchannels was characterized by introducing a correction factor, \( K \), to the Hagen-Poiseuille relation Eq.4, in which \( K \) represents the proportion by which the flow resistance is increased in a PSC microchannel compared to a circular profile of the same diameter (28).

\[
\Delta p = K \frac{32uL\mu}{d^2} /4/
\]

A correction factor \( (K) \) to the Hagen-Poiseuille relation was determined and was well-fitted by the power-law relationship using Eq.5 (28).

\[
K = 5.299 / k^{2.56} /5/
\]

The overall pressure drop is comprised of the pressure loss due to the flow in the connecting tubes \( (P_c) \), the inlet and exit losses \( (P_{in} \) and \( P_{ex} \)), the developing region loss \( (P_D) \), the pressure drop in the fully developed region \( (P_{FD}) \), and the pressure drop due to 180° bends \( (P_b) \).

\[
P_{measured} = P_c + P_{in} + P_D + P_{FD} + P_{ex} + 30P_b /6/
\]

Since the fully developed pressure drop is at the focus of this study, the right hand side losses except \( P_{FD} \) must be subtracted from the measured pressure drop. The connecting tube \( (P_c) \) pressure drop includes the losses due to all fittings and the capillary tube from the transducer to the microchannel inlet. We measured this loss directly at each flow rate when there was no microchannel at the end of the tubing. The measurements were carefully conducted with the conditions identical to the case when a microchannel was added to the end of the connecting tube to avoid the effects of hydrostatic pressure. Since the viscous boundary layer inherently grows faster in microchannels than at macroscales, the developing region
pressure drop \(P_D\) in most cases is negligible \((29)\). Other pressure losses associated with the measured pressure drop are inlet \(P_{in}\), exit \(P_{ex}\), and bend losses \(P_b\). These losses are negligible compared to the measured pressure drop.

**Pulse response experiments and residence time distribution**

Fig. 1c depicts the schematic representation of the experimental setup for the residence time distribution (RTD) measurements. Experiments were performed at different flow rates \(0.2 - 2.0\) mL/min which were adjusted by a syringe pump (Harvard Apparatus (HA)PHD 4400). The residence time distribution was determined by pulse response experiments. After pulse application (time \(t_0\)), the output concentration was monitored and recorded using a spectrophotometer (PerkinElmer, LAMBDA 650) until the pulse response returned to the baseline (time \(t_f\)). 0.1 mM of the tracer dye Direct blue 78 was injected at a very short time interval into the microreactor. The residence time distribution \((E_z)\) was calculated from the inlet tracer substance concentration changes:

\[
E_z = \frac{\Delta(c - c_0)}{\sum \Delta(c - c_0)} \quad /7/
\]

where \(E_z\) is normalized residence time, \(c\) concentration of tracer substance at the time \(t\) and \(c_0\) concentration of tracer substance at the time \(t_0\). Obtained experimental response was further evaluated by fitting (using a nonlinear least squares solver in Wolfram Mathematica) to RTD models, the Levenspiel model with ideal mixing compartments and the axial dispersion model.

The number of ideal mixing compartments \((N)\) was calculated using the Levenspiel equations \((30)\):

\[
\bar{t} = \frac{\sum t_i c_i}{\sum c_i} \quad /8/
\]

\[
\sigma^2 = \frac{\sum t_i^2 c_i}{\sum c_i} - \bar{t}^2 = \frac{\sum t_i^2 c_i}{\sum c_i} - \left(\frac{\sum t_i c_i}{\sum c_i}\right)^2 \quad /9/
\]

\[
\sigma^2 = \frac{\sum t_i^2 c_i}{\sum c_i} - \bar{t}^2 \quad /10/
\]
The Levenspiel model with ideal mixing compartments is presented by Eq.12 (30):

\[ E_Z(F,N) = \frac{N(N\cdot F)^{N-1}}{(N-1)!} e^{-N\cdot F} \]

The error \((E_n)\) between experiment and simulation was performed by calculating the global minimum of variance between experimental and simulated variables (Eq.13):

\[ E_n = \frac{1}{n_u} \sum_{i=1}^{n_u} \left( \frac{E_{Z,exp}^i - E_{Z,sim}^i}{E_{Z,exp}^i} \right)^2 \]

Numerical simulations were performed using the Wolfram Mathematica software.

**Axial Dispersion model**

The mass flow due to dispersion can be described by Fick’s law:

\[ J = -D_{ax} \frac{dC}{dz} \]

In this model (30), the main microreactor parameters are the axial diffusion constant \(D_{ax}\) and Bodenstein number \((Bo)\).

\[ Bo = \frac{u}{D_{ax}} \cdot L \]

The Bodenstein number characterizes the ratio between the convection and the axial diffusion in a tube of length \(L\) where a fluid flows at an axial velocity \(u\). The axial diffusion is calculated using the following expression (31):

\[ \frac{D_{ax}}{u} = \frac{D_m}{u} + \frac{u \cdot d_D^2}{\chi D_m} \]
In Eq. 16, $\chi$ is a coefficient equal to 192 and $D_m$ is the molecular diffusion constant equal to $1 \times 10^{-8}$ m$^2$/s.

$Bo$ thus varies with the velocity and its optimum can be calculated:

$$\left(\frac{u}{D_{ax}}\right)_{\text{max}} \text{ for } \quad u = \sqrt{\frac{D_m}{d_h}}$$

RESULTS AND DISCUSSION

Benefits of the 3D-printed microreactor

In order to assure visible control of the occurrences inside the microreactor the transparent acrylic resin *VeroClear* with a transparency similar to Polymethylmethacrylate (PMMA or acrylic glass) was used to build the microreactor (Table 1; 32). The PolyJet Matrix process enables, by a combination of two different building materials, the generation of up to 14 different so-called *Digital Materials*. As the microreactor has to be sealed on the contact surface of both microreactor halves, for the second material, the rubber-like acrylic resin *TangoBlackPlus* was used (Table 1; 32). The hardness of this material is in the range of 26 to 28 Shore A, which offers a good sealing behaviour at the contact surface with other microreactor half. The seal was printed as a coating along the whole outside surface of the second microreactor half that didn't contain microchannels, thus enabling good sealing across the whole contact surface and avoiding the risk of separation of the seal. All surfaces of the flow system in the microreactor were printed with *VeroClear*, which has better mechanical properties and higher chemical resistance than the *TangoBlackPlus* material, which results in a thermal stability of up to 50 $^\circ$C, which was considered to be appropriate for this application.

The whole process of 3D printing was finished within 3 h, which is significantly shorter compared to the traditional approach with metal machining. In a traditional production process, such small channels could be produced only by an electro-erosion process, which is time-consuming and costly. Moreover, in the case of metal machining the microreactor would not be transparent. With PolyJet technology it is possible to create even smaller channels (down to 0.25 mm in diameter), or to create channels that are not straight but proceed in a zig-zag manner, which additionally enlarges the channel length and increases the mixing of fluids. These possibilities promote the 3D-printing technology as an excellent solution to develop and produce microreactors.
Main parameters for determination of surface roughness was mean arithmetic deviation of profile $R_a$ and mean height of unevenness $R_z$ (Table 2). According to previous research for Polyjet products, roughness is about $1 \mu$m (33), but in this case, due to contact with the other half of the microreactor, the contact surface was made with the finishing parameters „glossy“ on the PolyJet machine, thus reducing the roughness to $R_a = 0.566 \mu$m.

Optimal flow pattern for 3D printed microreactor

This research was focused on the characterisation and the optimisation of the flow patterns in the microchannels. This was done by procedures developed for one-phase systems. Therefore, the Reynolds number for one-phase system was calculated, and it was in the range of $7 – 136$ with the corresponding flow rates of $0.2 – 2.0 \text{ mL/min}$. According to the literature (27,28) the flow in tubular channels is laminar for Reynolds numbers below $2100$ and turbulent above this value. But some recent publications doubt the application of this theory in the case of microchannels. The relatively high roughness of microchannels might reduce the critical Reynolds number for the transition from laminar to turbulent flow. Peng et al. (34) detected transitions to turbulence flow at Reynolds numbers between $200$ and $700$, with the transition value depending on the hydraulic diameter. This was, however, contradicted by Pfund et al. (35). Transitions to turbulence were observed with flow visualization and the flow was laminar for $Re < 1700$ in the $263 \text{ mm deep channel}$. Further $Re$ number increase was related to the turbulent flow. In any case, the Reynolds numbers achieved in our microchannel are much lower than the critical Reynolds number. Therefore, a laminar flow can be assumed in the entire application range of our microsystem. As a consequence, mixing occurs only by diffusion and not by convection as in the case of turbulent flow.

In the range of the used flow rates ($0.2 – 2.0 \text{ mL/min}$) the pressure drop varies between $1530$ and $8530 \text{ Pa}$. This corresponds to a $\Delta p/L_{tot}$ ranging between $25.50$ and $142.16 \text{ kPa/m}$. Soft and hard micromachining techniques used to develop microfluidic devices can yield microchannels of many different cross-sectional profiles. For semi-circular microchannels, these techniques often produce only partial semicircular cross-sections. Fig. 2 shows the calculated pressure drop using Eqs.3 and 4 from the corresponding combination of linear velocity and microchannel length. The variance between experimental results and the model were $E_K=18.52 \cdot 10^{-3}$ (for Hagen-Poiseuille relation; Eq.3) and $E_K=0.87 \cdot 10^{-3}$ (for Hagen-Poiseuille relation with a correction factor; Eq.4. Eq.4 presents a better agreement between experimental results and simulated mode compared to Eq.3. Using regression analyses, a correction factor $K$ was determined for 3D-printed microreactor. The correction factor $K$
represents the proportion by which the flow resistance \( \Delta P/Q \) is increased in a partial semicircular (PSC) cross-sections microchannel compared to a circular duct of diameter, \( D \). The correction factor computed from simulations was 7.45. The flow correction factor increased by decreased \( k \) value \((k=1 \text{ for a semi-circular micro-channel})\) (28).

The knowledge of the pressure drop is crucial for the pump (compressor) selection and the cost estimation. An increase in the pressure drop can promote leaking and damaging of the seals in the microreactor system. When comparing the pressure drop of this microreactor to a packed-bed reactor of similar efficiency, it becomes obvious that a 3D-printed microreactor with a similar surface-to-volume ratio has a far lower pressure drop. From the discussion above, it is obvious that a 3D-printed microreactor needs less energy for pumping and bears and consequently it has greater potential for energy savings than a packed-bed reactor.

**Residence time distribution and dispersion model**

Characteristics of liquid flow in horizontal tubular microreactors are possible to describe by one-parameter (dispersion and cascade model) and multi-parameters mathematical models (36). One-parameter axial dispersion model is the most often used model for mixing (or flow) characterization in horizontal tubular bioreactors and it is based on the mass balance of medium component in the liquid phase of the bioreactor. The equation is also very often expressed in dimensionless form using the Bodenstein (\( Bo \)) number. This equation cannot be solved analytically when the change of liquid flow behaviour (ideal mixing flow into plug flow or reverse) occurs in the point of pulse introduction and in the measuring point. In axial dispersion model radial flow of liquid phase in bioreactor is neglected. When designing a plug-flow reactor, two important parameters must be observed: axial diffusion and the Bodenstein number \( Bo \). \( Bo \) characterizes the ratio between convection and axial diffusion in a tube of length \( L \) where a fluid flows at an axial velocity \( u \). \( Bo \) is infinite for an ideal plug-flow reactor and zero if back mixing is dominant. In the latter case, the reactor behaves more like a continuous stirred tank reactor. The profile in the channel is considered as being a plug-flow when \( Bo \) exceeds 400. The axial diffusion calculated by Eq. 16 varies with the linear velocity and thus with the space time in the channel when the same design is used (31).

Characteristics of liquid flow was determined by using axial dispersion model and Bodenstein number. Variations of the axial diffusion and Bodenstein number with the mean linear velocity of the medium are shown in **Fig. 3**. For linear velocity exceeding 0.05 m/s, the \( Bo \) is higher than 400 and the microreactor behaves like a plug-flow microreactor. In the range of linear velocity currently used (from 0.033 to 0.333 m/s), back mixing is thus negligible in the
range of 0.05 to 0.10 m/s. The corresponding range of flow-rates is between 0.30 and 0.60 mL/min in the microchannels i.e. between 0.15 and 0.30 mL/min for each inlet. Plug flow was maximised for mean linear velocity 0.075 m/s and flow-rate 0.45 mL/min. This calculation is in the agreement with the residence time distribution measured for the given channels geometry. A high dispersion leads to axial concentration gradients in the microchannel and reduces system performances. Therefore, in this work a liquid flow-rate of 0.45 mL/min for the further experiment in order to minimise dispersion and ensure plug-flow conditions was chosen. Additionally, the level of plug flow achieved was quantified by the cascade (tank in series) model and compared to the difference in the RTD profiles.

The cascade (tank in series) model was used for mixing (or flow) characterization in horizontal tubular bioreactors. The liquid flow in bioreactor is simulated by the series of ideally mixed cascades \( M \) and the number of cascades is the variable parameter of this model. The model is defined by the Eq. 12. The plug flow conditions are present in horizontal tubular bioreactors when \( N \geq 5 \), while ideal mixed flow behaviour is realized when \( N = 1 \) (18). Plug-flow conditions are related to the creation of concentration and/or temperature gradients along the bioreactor (37). A stable plug-flow can be achieved by employing various types of mixers: X-, T- or Y-mixers. Y-mixers might be the best choice, as the risk of back-flow and consequent fouling is greatly reduced due to the geometry. The flow conditions were investigated by performing residence time distribution experiments and pulse response methodology. Fig. 4 presents the residence time distribution as the function of the flow-rate and the bioreactor length represented by the number of ideal mixing compartments (\( N \)) (30). The residence time distribution (RTD) is narrower than the Gaussian with the same inflow rates and low number (\( N = 1 – 10 \)) of ideal mixing compartments (\( N \)) it is significantly distorted in comparison to the normal distribution, while for (\( N >15 \)) it is nearly symmetric but followed by a long tail, which is almost invisible in the graph. The tail is formed by the liquid ejected from the near boundary layer, i.e., a small amount of the solute persists in the channel much longer than is predicted by the Gaussian RTD. A longer microchannel and a higher flow-rate contribute to the fluid flow approach plug flow conditions. Additionally, differences in RTD profile indicate that the flow-rate affect the quality of plug flow. The profile becomes symmetrical as the flow conditions tend towards plug flow. Fig. 4 clearly shows this symmetry. The profile peaks become more symmetrical as the quality of plug flow increases. These results are good indicator of plug flow in the ink-jet 3D-printed microchannel of microreactor. The RTD experiments were performed at a flow-rate of 0.45 mL/min (black curves in the Fig.4). The number of ideal mixing compartments was calculated using Eqs. 7-12, which resulted in 25 plates. These results
confirm plug-flow conditions in the constructed microreactor, which is a result of the long and smooth microchannels. Theoretical considerations for the one-phase regime in microreactors estimate that approximately 15 plates should be suitable for the plug-flow characterization (30). The variance between experimental results and model were from $E_N(\text{min})=0.7 \cdot 10^{-3}$ ($u=0.02$ m/s) to $E_N(\text{max})=1.52 \cdot 10^{-3}$ ($u=0.07$ m/s) and represents a good agreement between experimental results and simulated model. However, for the deeper insights in the flow characteristics methods such: micro particle image velocimetry (m-PIV), molecular tagging velocimetry (MTV), nuclear magnetic resonance (NMR) velocity imaging have to be utilized (38).

CONCLUSIONS

The production of microreactors by the PolyJet Matrix technology comes with some benefits compared to traditional machining. A microreactor can be easily constructed by CAD and transferred to the 3D-printer, which reduces the development time of a microreactor prototype. The 3D-printing process for this reactor was 3 h, which is relatively fast when compared to other production techniques. Also the low costs for the construction material is important when considering multiple design variations for different prototypes. The microreactor with a semi-circular microchannel (0.66 mm diameter, length 600 mm) was produced from a PMMA-like, clear acrylic resin with good resistance towards pressure, temperature and chemicals. A coating with rubber-like acrylic resin accomplished high quality sealing between two halves of the microreactor.

Moreover, in this work the characterisation of the hydrodynamic conditions in 3D-printed microreactor channels was performed. The 3D-printed microreactor exhibited a high surface-to-volume ratio and a relatively low pressure drop. These characteristics are beneficial for chemical and biochemical reactions, and the hydrodynamic characterisation defined ranges for plug-flow operation ($Bo>400$ for the linear velocities between 0.05-0.10 m/s). Higher conversion rates were a consequence of plug-flow conditions in the microreactors and selectivity of the processes was improved. Related to the formation of concentration gradients along the bioreactor length, the inhibition and/or repression bioprocess kinetics can be avoided. Achieving plug-flow is important to perform accurate kinetic measurements, in diagnostic applications, cell culture, drug discovery, organs-on-chip, or even forensic analysis. Therefore it can be concluded that the PolyJet Matrix technology can be easily used for the production of microreactors and the obtained hydrodynamic characteristics are competitive, which advances the production and application of 3D-printed microreactors.
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Fig. 1. Graphic presentation of: a) PolyJet Matrix process principles, b) microreactor half - CAD model (left); microscopy image of microchannels (right) and c) schematic representation of the experimental setup for the measurements of pressure drop and residence time distribution.
Fig. 2. Pressure drop in the microchannel with the corresponding combination of linear velocity and microchannel length (Hager-Poison equation simulation-brown plate; simulation with correction factor-blue plate; measured data black curve)

Fig. 3. Variation of the axial diffusion and Bodenstein number with the mean linear velocity of the medium
Fig. 4. Resident time distribution as the function of flow rate and bioreactor length (the black curve indicate experimental results for the 600 mm microchannel)
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Table 1. General mechanical and thermal properties of VeroClear and TangoBlackPlus materials (32)

| VeroClear RGD810                  | Unit | METRIC       | Unit | IMPERIAL       |
|-----------------------------------|------|--------------|------|----------------|
| Tensile strength                  | MPa  | 50-65        | psi  | 7250-9450      |
| Elongation at break               | %    | 10-25        | %    | 10-25          |
| Modulus of elasticity             | MPa  | 2000-3000    | psi  | 290 000-435 000|
| Flexural strength                 | MPa  | 75-110       | psi  | 11 000-16 000  |
| Flexural modulus                  | MPa  | 2200-3200    | psi  | 320 000-465 000|
| HDT, °C @ 0.45 MPa                | °C   | 45-50        | °F   | 113-122        |
| HDT, °C @ 1.82 MPa                | °C   | 45-50        | °F   | 113-122        |
| Izod Notched Impact               | J/m  | 20-30        | ftlb/inch | 0.375-0.562  |
| Water Absorption                  | %    | 1.1-1.5      | %    | 1.1-1.5        |
| T<sub>g</sub>                     | °C   | 52-54        | °F   | 126-129        |
| Shore Hardness (D)                | Scale D | 83-86       | Scale D | 83-86       |
| Rockwell Hardness                 | Scale M | 73-76        | Scale M | 73-76       |
| Polymerized density               | g/cm³ | 1.18-1.19   | -    | -             |
| Ash content                       | %    | 0.02-0.06    | %    | 0.02-0.06      |

| TangoBlackPlus FLX980             | Units | METRIC       | Units | IMPERIAL       |
|-----------------------------------|-------|--------------|-------|----------------|
| Tensile strength                  | MPa   | 0.8-1.5      | psi   | 115-220        |
| Elongation at break               | %     | 170-220      | %     | 170-220        |
| Compressive set                   | %     | 4-5          | %     | 4-5            |
| Shore Hardness (A)                | Scale A | 26-28       | Scale A | 26-28       |
| Tensile tear resistance           | kg/cm | 2-4          | Lb/in | 18-22          |
| Polymerized density               | g/cm³ | 1.12-1.13    | -     | -              |
Table 2. Surface roughness

| Measurement profiles | No. | $R_a/\mu m$ | $R_z/\mu m$ |
|----------------------|-----|-------------|-------------|
| a                    | 1.  | 0.495       | 2.172       |
|                      | 2.  | 0.565       | 2.843       |
| b                    | 3.  | 0.471       | 2.222       |
|                      | 4.  | 0.394       | 2.296       |
| c                    | 5.  | 0.652       | 2.168       |
|                      | 6.  | 0.649       | 2.209       |
| d                    | 7.  | 0.632       | 2.370       |
|                      | 8.  | 0.673       | 2.600       |
| $\bar{x}$            |     | 0.566       | 2.360       |
| $S$                  |     | 0.103       | 0.242       |
| $R$                  |     | 0.279       | 0.675       |