Accessing multidimensional mixing via 3D printing and showerhead micromixer design

Zhang Haomiao (Orcid ID: 0000-0001-7933-3155)
Jensen Klavs (Orcid ID: 0000-0001-7192-580X)

Accessing multidimensional mixing via 3D printing and showerhead micromixer design

Haomiao Zhang[a,b], Thomas Kopfmüller[b], Ramona Achermann[b], Jisong Zhang[b], Andrew Teixeira[b,c], Yi Shen[b], Klavs F. Jensen[b,*]

a. State Key Laboratory of Chemical Engineering, College of Chemical and Biological Engineering, Zhejiang University, Hangzhou 310027, PR China
b. Department of Chemical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA
c. Department of Chemical Engineering, Worcester Polytechnic Institute, 100 Institute Road, Worcester, MA 01609, USA

* Corresponding author. E-mail address: kfjensen@mit.edu

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/aic.16873

Abstract

We present a 3D metal printing showerhead mixer to blend effectively two reagent streams into a confined mixing volume. Each stream is pre-distributed to multiple channels to increase the contact area in the mixing zone, which enables high mixing performance with smaller pressure drop. The showerhead mixer shows excellent mixing performance owing to its ability to intersperse rapidly the two streams as characterized by the diazo coupling reactions and CFD simulations. Experimental results demonstrate superior performance of the showerhead mixer compared to two common commercial micro T-mixers, especially in low Reynolds number regime. CFD results are employed to i) help understand the mixing mechanism, ii) reproduce the experimental observations, and iii) inform the design specifications for optimal performance. Good agreement between experiments and simulations is achieved. The final design includes multiple side-fed inlets for improved mixing performance of the showerhead mixer, as suggested by the validated CFD models.

Keywords

Microreactor, Static Mixer, Diazo Coupling Reaction, CFD

Introduction

Additive manufacturing (3D Printing) technologies have emerged as an important tool to quickly create 3D products from computer aided design (CAD) systems. [1-3] Different from conventional “subtractive manufacturing” processes (i.e. CNC machining) that remove material from a monolithic system, 3D printing adds material in a layer-by-layer method to create the final prototype, which potentially reduces components of product during manufacturing. Moreover, 3D printing can open new design freedom and thus create complex structures that are difficult or even impossible to make using subtractive manufacturing processes. In addition, quicker prototyping of parts becomes possible as computer developed models can be iterated upon to create new prototypes in a short time.

Recently, 3D printing has enabled applications in numerous areas of scientific research, whereby plastic material printing is most commonly employed in reactors for organic synthesis [4,5], microfluidics topics [6-8], biological applications [3,9,10], and advanced materials design and development [11-13]; but all of those applications are generally limited by the system-allowed pressure and temperature as well as the chemical compatibility and stability of material for safe operation [14]. Therefore, we decide to explore 3D metal printing technologies for continuous flow mixer/reactor design. These technologies have the potential to handle highly exothermic reactions, highly pressurized fluid system, catalysts coating for heterogeneous catalytic reactions, and corrosive environments. Furthermore,

we aim to start by fabricating mixers/reactors in lab scale (microscale/milliscale), by anticipating the design limitations for 3D metal printing, and more importantly, taking full advantage of the advanced properties of this novel technology by leveraging the unique geometries that can be accessed.

When evaluating microscale/milliscale reactors, their mixing performance has been the primary area of interest to engineers in chemical industry. [15-17] In particular, static mixers are largely used to enhance mixing in continuous flow reactors and have a critical impact on reaction processes. [18-20] Beyond commercialized T/Y-mixers, helical mixers, splitting/recombining type mixers, and packed beds, we propose a new type mixer/reactor with similar mixing mechanism, by introducing a bundle of micro T-mixers and combining them into a laminated “showerhead” structure. It is impossible to machine this prototype from a single metal part using conventional subtractive manufacturing methods; 3D printing techniques, however, enable quick fabrication of this structure to precise specifications. Based on desired chemical and temperature stability, we focus on two commercial 3D metal printing services to fabricate the mixer: The binder jetting process (commercially available in ExOne, PA, USA) requires the smallest features to be 0.762 mm for 3D printing a matrix metal material composed of 60% stainless steel and 40% bronze infiltrant. This technique is notably low-cost whereas the direct metal laser sintering (DMLS, commercially available in Proto Labs, MN, USA) technique, is more expensive than binder jetting. The latter method has similar feature resolution but is

capable of 3D printing purely with 316L stainless steel, which has better chemical compatibility than metal matrix including bronze. Herein, we test both methods for fabricating the showerhead mixer and engineer the smallest feature inside the structure to be 0.889 mm in order to achieve optimal print quality.

An effective continuous flow reactor requires good mixing to ensure precise reaction control. Regarding mixing characterization experiments, the Villermaux-Dushman reaction in a competitive parallel reaction system has been widely employed by the microfluidics community for mixing evaluation with the advantages of being cheap and easy to handle. [21,22] The reaction is very fast and thus useful for evaluating micromixers that have very short mixing time scales. [23,24] However, for intermediate time scales mixers, such as the showerhead mixer in this study, the Dushman reaction is no longer suitable for quantifying the mixing performance. [25] Instead, Bourne reactions [26], such as the diazo coupling reaction in a competitive consecutive reaction system (Figure 1), offer a better solution in determining the mixing effects in this regime. Moreover, the rate constants of diazo coupling reaction are known, enabling simulations with CFD solvers. In addition, the mixing performance as well as internal flow pattern and pressure drop is investigated with CFD simulations, which enable better understanding and further improvements on the mixer structure.

Materials and method

Materials

3D printing materials – The mixers employed in this study were 3D printed through commercial 3D printing services into both 60% 316 stainless steel and 40% bronze using binder jetting (ExOne, $27 in 2017) and 316L stainless steel using direct metal laser sintering (DMLS, Proto Labs, $650). The bronze did not influence the diazo coupling mixing experiments.

Diazo coupling materials – 1-naphthol (≥ 99 %), sulphanilic acid (99.3%), sodium nitrite (≥ 99.0%), sulphamic acid (99.3%), sodium carbonate (≥ 99.5%), sodium bicarbonate (≥ 99.7%), hydrochloric acid (c_{HCl} = 1 mol/L), and potassium iodide starch papers were purchased from Sigma Aldrich.

3D printed showerhead mixer

We designed a showerhead mixer to effectively blend two reagent streams into a confined reaction volume, which is 3D printed using metal powder into an integrated structure. Figure 2 depicts the 3D mixing structure and the 3D printed prototypes using binder jetting (Figure 2b) and DMLS (Figure 2c). The mixer has 2 stream inlets (shown in red and blue color in Figure 2a, respectively) where fluids come in and 1 stream outlet for subsequent in-line mixing/reaction analysis. The red stream, flowing through the bottom inlet, is divided into 37 inner channels, each of which has a diameter of 0.889 mm, then flows into

a confined hexagonal reaction zone (1.524 mm height, ~ 500 μL volume, on top of the green color zone in Figure 2a). The blue stream, flowing through the side inlet, circulates within the shell of the mixer but outside the inner micro channels (blue color in Figure 2a), then flows into the mixing/reaction volume through 27 holes, each of which has a diameter of 1.041 mm. By design, the cross-section area ratio for both fluids is unity ($\frac{n_I \cdot A_I}{n_{II} \cdot A_{II}} = \frac{37 \times 0.889^2}{27 \times 1.041^2} \cong 1$). Prior to the mixing volume, both streams are isolated. During operations, the outlet is placed upward and gravity influence can be ignored as for the calculated Bond number in the narrowest region is smaller than 0.1. To help remove metal powder from the interior space during 3D printing, 0.762 mm fillets were employed. The thickness of all reactor walls is kept to 0.762 mm. The printed mixer is hooked up into the continuous flow system using PEEK fittings (IDEX) after 1/4-28 threads were tapped in the inlet/outlet ports.

Diazo coupling reaction experiment

The principle behind the diazo coupling reaction procedures is based upon the rate competition of a quasi-instantaneous reaction between 1-naphthol (**A**) and diazotized sulphanilic acid (**B**) and a very fast reaction between diazotized sulphanilic acid (**B**) and the two primary coupling products (**p-R** and **o-R**, respectively). In perfect mixing conditions, **A** instantaneously consumes all of **B** so that no secondary coupling reactions

would occur. However, if the mixing time scale is comparable to or even longer than the reaction time scale, local unreacted **B** would react with **p-R** and/or **o-R** to form the secondary coupling product **S**. Therefore, the yield of the secondary coupling product bisazo dye (Y_S) can be employed as an indicator for mixing performance.

To prepare the starting solutions, 1-naphthol (**A**) was dissolved into a $Na_2CO_3/NaHCO_3$ buffer solution, in which temperature was 298 K, *pH* was 9.9, and ionic strength was 444.4 mol/m^3, aided by 2 hours sonication in order to obtain a homogeneous solution, where $c_{A0} = 3.6\ mol/m^3$. Diazotized sulphanilic acid (**B**) solution ($c_{B0} = 3\ mol/m^3$) was prepared by diazotization of a mixture containing sulphanilic acid, sodium nitrite, and hydrochloric acid. Excess nitrite ions in the solution were eliminated by dropwise adding sulphamic acid. The presence of nitrite ions in the solution was monitored by potassium iodide starch papers. It requires that no nitrite ions are present in the solution and freshly prepared solutions are used in the experiments due to the poor shelf life of both the reagent solutions.

With the reagent solutions ready, they were fed into the respective micromixer at identical flowrates via syringe pumps (Harvard Apparatus PHD 2000) for precise flowrate control. During experiments, total flowrates from 2 mL/min to as high as 200 mL/min were investigated. It is worth mentioning that the sealing between the 3D printed mixer and PEEK fittings worked well even when the flow apparatus was tested at 300 mL/min. In order to evaluate pressure drop, digital pressure transducers (SSI Technologies Inc.)

were hooked up in the system. We used an in-flow UV-vis (Ocean Optics) to monitor products, but collected samples for more accurate stationary UV-vis measurements when stable readings were observed in the flow UV-vis. Typically, samples were taken at the mixer outlet after 5 mean residence times to make sure that the system reached hydrodynamic steady state. The collected samples were immediately diluted with the above $Na_2CO_3/NaHCO_3$ buffer solution to quench the reaction and subsequently employed for UV-vis analysis (Shimadzu UV-3101 PC UV-VIS-NIR Scanning Spectrophotometer) at a wavelength range of 400 – 700 nm.

We created an in-house MATLAB multilinear regression algorithm to determine the concentrations of products, based upon the literature reported molar extinction coefficients of **o-R**, **p-R**, and **S**. [26] The absorption peaks in the monoazo isomers (**p-R** and **o-R**) fully overlap, making it impossible to separate those monoazo isomers using this method, however, we were able to determine their concentrations in sum ($c_{p-R} + c_{o-R}$). Since diazotized sulphanilic acid (**B**) is the limiting reagent in the system and participates in all reactions, the analysis of reaction (i.e. mass balance, product yield) is referenced to the initial concentration of **B** (c_{B0}). In the above reaction system, the mass balance is reported in Eq. 1 and the yield of bisazo dye **S** (Y_S) is calculated using Eq. 2 ($V_A = V_B$ is employed in experiments):

$$V_B c_{B0} = (V_A + V_B)\left(c_{p-R} + c_{o-R} + 2c_S\right) \quad (1)$$

$$Y_S = \frac{4c_S}{c_{B0}} = \frac{2c_S}{c_{o-R} + c_{p-R} + 2c_S} \quad (2)$$

where V_A is the flowrate of reagent solution of **A**, V_B is the flowrate of reagent solution of **B**, c_{B0} is the initial concentration of **B**, c_{p-R} is the concentration of **p-R**, c_{o-R} is the concentration of **o-R**, and c_S is the concentration of **S**. For low Y_S, the mass balance closes very well (fitting error is smaller than 2%), while in conditions of $Y_S > 25\%$, the fitting error increases due to the formation of unknown byproducts [27,28], but the qualitative conclusions of the mixing performance are still valid in this regime.

CFD simulations

We conducted three dimensional computational fluid dynamics (CFD) simulations via COMSOL Multiphysics 5.3a to further understand the working mechanism of the showerhead mixer and reveal more detailed information absence from experimental results. Due to the symmetric property of the mixing structure, half of the whole 3D geometry was solved to reduce computational cost without losing physical information. The Navier-Stokes equation (Eq. 3) in conjunction with the continuity equation (assuming incompressible flow, Eq. 4) was solved in steady state (assuming laminar flow), with boundary conditions applied corresponding to (i) inlet flowrates, (ii) outlet atmospheric pressure, (iii) no-slip wall, and (iv) symmetry plane.

$$\rho(\boldsymbol{u}\cdot\nabla)\boldsymbol{u} = -\nabla p + \mu\nabla^2\boldsymbol{u} \quad (3)$$

$$\nabla\cdot\boldsymbol{u} = 0 \quad (4)$$

where ρ is the density of the mixture solution (estimated by 1,000 kg/m^3), $\boldsymbol{u}$ is the velocity vector, p is the local pressure, and μ is the dynamic viscosity of the mixture solution (estimated by 0.001 $\mathrm{Pa}\cdot\mathrm{s}$). Notably, it is reasonable to assume that the diazo coupling reactions occur isothermally at 298 K for that the solution is dilute and the thermal diffusivity is about two orders of magnitude greater than the mass diffusivity.[29,30] The solution for the velocity field was used as input to solve for the species concentration profiles in the next step.

The second simulation aims to describe the mixing of the two streams in the absence of any reaction. The corresponding convective-diffusive mass transport equation of both reagents (described by Eq. 5) is solved using stationary solvers given the velocity field solution from the previous simulation ($\boldsymbol{u}$). This one-direction coupling between fluid flow and mass transfer is a reasonable assumption since variations in physical properties of the solution (density and viscosity) caused by concentration changes are negligible.

$$\boldsymbol{u}\cdot\nabla c_i = \nabla\cdot(D_i\nabla c_i) \quad (5)$$

Here c_i is the concentration of reagent i, and D_i is the diffusion coefficient of reagent i in water. The corresponding boundary conditions used are (i) inlet species concentration, (ii) outflow, (iii) no-flux wall, and (iv) symmetry plane. In general, the stationary

concentration map provides enough information for mixing evaluation, for example, using the concept of "mixing intensity (I_M)". [24] Alternatively, mixing could be evaluated by adding a homogeneous reaction term to Eq. 5 and simulating the yield of **S** by including the diazo coupling reaction; however, the steady state solver converges poorly at these operating conditions due to the large source term in the system (reaction rate constant as high as 12,238 $m^3/(mol \cdot s)$).

This computational capability for obtaining Y_S using simulation facilitates investigation of the relationship between mixing and reaction, thus enabling rapid iteration of new mixer designs. Therefore, time dependent simulations were further conducted to obtain the dynamic analysis of reactions. While a main drawback for such transient calculation over 3D structure is the large computational cost, this was mitigated by only simulating the mean residence time (total volume / total flowrate). The corresponding species transport equation of each species with reaction (reagents: **A**, **B**; formed products: **p-R**, **o-R**, **S**) is described by Eq. 6:

$$\frac{\partial c_i}{\partial t} + \boldsymbol{u} \cdot \nabla c_i = \nabla \cdot (D_i \nabla c_i) + R_i \qquad (6)$$

where the velocity vector $\boldsymbol{u}$ is the result of step 1, R_i is the reaction rate of reagent/product i. Boundary conditions for Eq. 5 and Eq. 6 are listed in Table 1, where $\boldsymbol{u}$ is the velocity vector, U_0 is the initial velocity magnitude, p is the local pressure, p_0 is the

atmosphere pressure, $\boldsymbol{n}$ is a unit normal vector, c_i is the concentration of reagent i, $c_{0,i}$ is the initial concentration of reagent i, and D_i is the diffusion coefficient of reagent i in water.

As a standard procedure of simulation, mesh independence was checked and confirmed prior to each step (Supporting Information Figure S1). To reduce computational cost, we built coarser grids in the regions where both inlet fluids are isolated while much finer grids in the space where reactions would occur (See Figure S2). All simulations were performed on a ThinkPad P50 Workstation with Intel Core i7-6820HQ CPU @ 2.70 GHz and 64 GB RAM.

Results and discussion

Diazo coupling reaction experiment

We conducted experiments using the showerhead mixers made of both (i) 316L stainless steel, and (ii) the matrix material of 60% 316 stainless steel and 40% bronze, respectively, and obtained very similar results, indicating that both methods (binder jetting and DMLS) provided good resolution when the characteristic length was > 0.762 mm. All the reported experimental results in the following sections were based upon the mixer in the matrix material, for which the corrosion problems were mitigated by short mean residence times (0.54 – 54 s) and a 15 min DI water flushing after each use.

As reported in Figure 3, we compared the variations of Y_S of the showerhead mixer with the results of the commercial micro T-mixers with inner diameter of 0.5 and 1.25 mm ($T_{0.5}$-mixer, and $T_{1.25}$-mixer, respectively) obtained using the same experimental conditions, as reported by Schwolow et al. [28]. For both T-mixers, mixing performance is poor in the low Re regime ($Y_S > 40\%$ at Re < 200), while becomes better when Re reaches 300 for $T_{1.25}$-mixer, and 700 for $T_{0.5}$-mixer, respectively. However, the showerhead mixer performs better in mixing than both micro T-mixers when operated in small Re regime (Re < 200). In addition, its mixing performance significantly increases with increasing Re at Re < 50, and slowly increases and then finally approaches to perfect mixing conditions when Re reaches 200, indicated by $Y_S|_{Re=200} < 0.5\%$. In comparison, both T-mixers end up with a Y_S of 0 – 0.5% when Re is sufficiently large (Re ~ 1000), confirming that, at any Re, the showerhead mixer provides the best mixing. Moreover, the pressure drop in the showerhead mixer is measured to be one order of magnitude smaller than that in the micro T-mixers, suggesting less energy intensive operation at larger Re. This is due to the parallelization of smaller T-mixers effectively dropping the flowrate in each contacting zone of the showerhead, and thus, decreasing the overall pressure drop while maintaining efficient mixing. The showerhead mixer works as a bundle of combined T-mixers, which increases the contact area between the fluids in the confined mixing volume, significantly enhancing mixing performance. The good mixing performance of the showerhead mixer even at low flowrates is desirable for flow chemistry studies with long residence times.

CFD simulations

CFD simulations were conducted to gain further insights of the mixing principle by solving the momentum and mass equations in the mixing system. Figure 4a illustrates the velocity streamlines in the showerhead mixer at hydrodynamic steady state when $V_A = V_B = 40\ ml/min$, confirming that materials are uniformly distributed through all interior channels. Furthermore, the velocity profiles indicate that the highest velocity magnitude is observed in the entrance region of the central channel, where the highest pressure exists (Figure 4b), due to the shrinking channel size there (0.889 mm). The hydrodynamic solver converges well in the test range ($total\ flowrate = 2 - 200\ ml/min$) at steady state and the velocity streamlines remain unchanged, indicating that laminar flow condition is maintained in any localized region of the mixer and the flow is in similar hydrodynamic regime in the test range.

Steady state concentration profiles are subsequently calculated for variations of inlet flowrate in the test range ($2 - 200\ ml/min$). A typical result obtained at $V_A = V_B = 40\ ml/min,\ c_{A0} = 3.6\ mol/m^3, c_{B0} = 3.0\ mol/m^3$ is shown in Figure 5a, indicating that materials coming through both inlets are well blended in the mixing zone when flowing out at steady state conditions. In the map of c_A (**A** flows through the side inlet), there is a concentration rich zone on its left (close to inlet of **A**) and a large volume around the edge

where c_A is almost zero, while the map of c_B looks opposite to that of c_A. This effect reflects that, at hydrodynamic steady state, the pressure induced from the incoming **B** stream on the far side of the **A** inlet is too large to overcome, thus making the paths of less resistance (those nearer to the inlet of **A**). Despite of this "dead volume", the overall mixing performance of the showerhead remains strong, since the concentrations of both **A** and **B** on the outlet surface are very well blended.

Transient simulations of concentration profiles show that after the mean residence time **A** is preferentially filled into the left half (Figure 5b) while **B** is uniformly distributed. This uneven distribution of **A** implies that it would take longer time for **A** to transport to the right region, which is not ideal for an effective mixer. As a consequence, we modified the structure as discussed in the next section.

The reaction yield obtained using simulation (5.4%) is higher than the experimental one (2.2%), which we attribute to simulations only including the mixer structure whereas there are additional downstream connectors and tubing in the experiments. These additional downstream sections allow for additional secondary reactions prior to the quench. The higher simulated reaction yield could also be a result of fabrication tolerances. Simulations performed at different flowrates ($V_A = V_B = 20\,ml/min\,, and\, V_A = V_B = 10\,ml/min$) correlate well with the experimental data (Table 2) indicating that the CFD models are useful for predicting of mixing behavior.

Improvements on design

Inspired by the above results, we investigated several strategies to mitigate the dead volume. The current showerhead structure can be easily modified by adding extra inlets on the side, both in CAD software and 3D printing process. In the hexagon shape, the two side inlets structure could have the second inlet towards the original inlet, as illustrated in Figure 6a; the three side inlets structure could have the second and third inlets 120^{o} and 240^{o} from the original inlet, as illustrated in Figure 6b. Figure 6 shows the structures of these 2 modified mixers, and simulations are achieved by applying symmetry constraints in the validated CFD approach to substantially reduce the memory requirements and solution time.

In order to quickly check the mixing performance over different structures, the mixing intensity (I_M) concept is employed. [24] If I_M is closer to 1, mixing is almost complete, and if I_M is small, mixing is incomplete. Figure 7a-c compare the mixing intensities on the mixer outlet surface obtained using the original showerhead mixer, and the modified mixers with double and triple side inlets. The results show that in the original structure (Figure 7a), there still are poor mixing areas where dark blue color (denoting the local I_M to be 0) exists. The blue regions (Figure 7a) on the left and in the center, respectively, make a clear argument that the inlet of **A** needs further optimizing. By introducing one

extra side inlet, the poor mixing region corresponding to the side inlet is largely mitigated (Figure 7b), whereas the central blue region appears unchanged. However, using the structural configuration as shown in Figure 6b, both the edge and central poor mixing regions are reduced (Figure 7c) and its surface averaged I_M is the largest among the three ($I_{M,c} > I_{M,b} > I_{M,a}$). Therefore, the 3 side inlets configuration facilitates mixing the most by reducing pressure gradients across the inlet manifold.

We further employ time-dependent simulation including the diazo coupling kinetics in the mass transport study to reveal more information for this evaluation. Both the original mixer and the two modified mixers are simulated for one mean residence time (total flowrate 80 ml/min). Figure 8a-c illustrate the 2D maps of Y_S on the mixer outlet surface and the corresponding surface averaged Y_S of the 3 mixers are 5.4%, 3.3%, and 0.7%, respectively, indicating that with 3 side inlets the modified mixer exhibits the best mixing profile. Interestingly, the edge region in Figure 8a and the central region in Figure 8b both have lighter blue color, indicating a larger local Y_S, both of which coincide with the interpretations of Figure 7 for poor mixing regions. The results show that using multiple side inlets facilitates reducing the time for the side inlet reagent **A** to fill in the whole space with minimal, uniform resistance.

Conclusion

We designed an in-line 3D showerhead mixer and fabricated it using two commercial 3D metal printing services (binder jetting and DMLS). The unique structure of this mixer provided intensified mixing between the feed streams, while inducing minimal pressure drop. The mixing performance of the showerhead mixer was systematically investigated using diazo coupling reaction experiments and CFD simulations. Results indicated that the showerhead mixer performs better than the 2 common commercial micro T-mixers, especially in the low Re regime, and the experimental results were reproduced using CFD. The validated CFD models further suggested that flow distribution of the feeds is an important design consideration for improved mixing performance of showerhead mixers.

Acknowledgments

We thank MIT Energy Initiative fund (ExxonMobil) for financial support. HZ thanks the Fundamental Research Funds for the Central Universities of China (2019QNA4045) and the fund from State Key Laboratory of Chemical Engineering of China (SKL-ChE-19T05) for partial support of his work.

Literature Cited

1. Mueller B. *Additive Manufacturing Technologies – Rapid Prototyping to Direct Digital Manufacturing.* Springer, Boston, MA, 2012.

2. Hod Lipson MK. *Fabricated: The New World of 3D Printing,* Wiley, 2013.

3. Gross BC, Erkal JL, Lockwood SY, Chen C, Spence DM. Evaluation of 3D Printing and Its Potential Impact on Biotechnology and the Chemical Sciences. *Analytical Chemistry.* 2014;86(7):3240-3253.

4. Kitson PJ, Marie G, Francoia JP, et al. Digitization of multistep organic synthesis in reactionware for on-demand pharmaceuticals. *Science.* 2018;359(6373):314-319.

5. Symes MD, Kitson PJ, Yan J, et al. Integrated 3D-printed reactionware for chemical synthesis and analysis. *Nature Chemistry.* 2012;4:349-354.

6. Bhattacharjee N, Urrios A, Kang S, Folch A. The upcoming 3D-printing revolution in microfluidics. *Lab on a Chip.* 2016;16(10):1720-1742.

7. Au AK, Huynh W, Horowitz LF, Folch A. 3D-Printed Microfluidics. *Angew Chem Int Ed Engl.* 2016;55(12):3862-3881.

8. Comina G, Suska A, Filippini D. PDMS lab-on-a-chip fabrication using 3D printed templates. *Lab Chip.* 2014;14(2):424-430.

9. Guvendiren M, Molde J, Soares RMD, Kohn J. Designing Biomaterials for 3D Printing. *ACS Biomaterials Science & Engineering.* 2016;2(10):1679-1693.

10. Murphy SV, Atala A. 3D bioprinting of tissues and organs. *Nature Biotechnology.* 2014;32:773-785.

11. Lee J-Y, An J, Chua CK. Fundamentals and applications of 3D printing for novel materials. *Applied Materials Today.* 2017;7:120-133.

12. Zhang Y, Zhang F, Yan Z, et al. Printing, folding and assembly methods for forming 3D mesostructures in advanced materials. *Nature Reviews Materials.* 2017;2:17019.

13. Truby RL, Lewis JA. Printing soft matter in three dimensions. *Nature.* 2016;540:371-378.

14. Capel AJ, Edmondson S, Christie SDR, Goodridge RD, Bibb RJ, Thurstans M. Design and additive manufacture for flow chemistry. *Lab on a Chip.* 2013;13(23):4583-4590.

15. Jensen KF. Microreaction engineering — is small better. *Chemical Engineering Science.* 2001;56:293-303.

16. Stroock AD, Dertinger SK, Ajdari A, Mezic I, Stone HA, Whitesides GM. Chaotic mixer for microchannels. *Science.* 2002;295(5555):647-651.

17. Jensen KF. Flow chemistry-Microreaction technology comes of age. *AIChE Journal.* 2017;63(3):858-869.

18. Nguyen N-T, Wu Z. Micromixers—a review. *Journal of Micromechanics and Microengineering.* 2005;15(2):R1-R16.

19. Stankiewicz A. The Static Mixer as a Chemical Reactor. *Chemical Engineering Science.* 2001;56:359-364.

20. Thakur RK, Vial C, Nigam KDP, Nauman EB, Djelveh G. Static Mixers in the Process Industries—A Review. *Chemical Engineering Research and Design.* 2003;81(7):787-826.

21. Pierrette Guichardon LF. Characterisation of micromixing efficiency by the iodide–iodate reaction system. Part I - experimental procedure. *Chemical Engineering Science.* 2000;55:4233-4243.

22. Pierrette Guichardon LF, Jacques Villermaux. Characterisation of micromixing efficiency by the iodide–iodate reaction system. Part II - kinetic study. *Chemical Engineering Science.* 2000;55:4245-4253.

23. Zhang J, Wang K, Teixeira AR, Jensen KF, Luo G. Design and Scaling Up of Microchemical Systems: A Review. *Annu Rev Chem Biomol Eng.* 2017;8:285-305.

24. Wang K, Zhang H, Shen Y, Adamo A, Jensen KF. Thermoformed fluoropolymer tubing for in-line mixing. *Reaction Chemistry & Engineering.* 2018;3(5):707-713.

25. Bourne JR. Comments on the iodide/iodate method for characterising micromixing. *Chemical Engineering Journal.* 2008;140(1-3):638-641.

26. John R. Bourne OMK, Joachim Lenzner, Horst Maire. Kinetics of the Diazo Coupling between l-Naphthol and Diazotized Sulfanilic Acid. *Ind. Eng. Chem. Res.* 1990;29:1761-1765.

27. Baldyga J, Bourne JR. *Turbulent mixing and chemical reactions*: Wiley, 1999.

28. Schwolow S, Hollmann J, Schenkel B, Röder T. Application-Oriented Analysis of Mixing Performance in Microreactors. *Organic Process Research & Development.* 2012;16(9):1513-1522.

29. Bourne JR, Kozicki F, Rys P. Mixing and fast chemical reaction—I: Test reactions to determine segregation. *Chemical Engineering Science.* 1981;36(10):1643-1648.

30. Belevi H, Bourne JR, Rys P. Mixing and fast chemical reaction—II: Diffusion-reaction model for the CSTR. *Chemical Engineering Science.* 1981;36(10):1649-1654.

Figure & Table captions:

Figure 1. Diazo Coupling reactions between 1-naphthol (**A**) and diazotized sulphanilic acid (**B**) form primary coupling products 4-[(4'-sulphophenyl)azo]-1-naphthol (**p-R**) and 2-[(4'-sulphophenyl)azo]-1-naphthol (**o-R**) and secondary coupling product 2,4-bis[(4'-sulphophenyl)azo]-1-naphthol (**S**). The rate constants ($m^3/(mol \cdot s)$) are reported for a temperature of 298 K, *pH* of 9.9, and an ionic strength of 444.4 mol/m^3 as follows: k_{1p} = 12,238 ± 446, k_{1o} = 921 ± 31, k_{2p} = 22.25 ± 0.25, and k_{2o} = 1.835 ± 0.018. [26]

Figure 2. 3D printing showerhead mixer. (a) The CAD file. Blue color denotes pathway of fluid I coming from side inlet; red color denotes pathway of fluid II coming from bottom inlet; green color denotes mixing zone on top; (b) 3D printed mixer using binder jetting in a matrix material of 60% 316 stainless steel and 40% bronze; (c) 3D printed mixer using DMLS in 316L stainless steel.

Figure 3. Results of the diazo coupling reaction experiments are exhibited, in which the showerhead mixer shows superior mixing and less pressure drop. (a) Variations in Y_S with Re in the showerhead mixer and the 2 standard commercial micro T-mixers (data extracted from Schwolow's work [28]). (b) Pressure drop versus Re in all three mixers.

Figure 4. Stationary CFD hydrodynamic simulations of the showerhead mixer. (a) Velocity streamlines through the mixer and slices showing 3D velocity profiles. (b)

Pressure contours filled inside the mixer. The flowrate used in (a) and (b) is $V_A = V_B = 40\ ml/min$ $(Re = 100)$.

Figure 5. Concentration profiles of the showerhead mixer at (a) steady state condition, and (b) transient condition, respectively. Flowrates: $V_A = V_B = 40\ ml/min$ $(Re = 100)$, corresponding to a mean residence time of 2.7 s. (a) Maps of c_A and c_B of the mixing zone and the mixer outlet surface, all at steady state; (b) Maps of c_A, c_B, and c_S in the mixer, and c_S at the mixer outlet surface, all at t = 2.7 s.

Figure 6. Showerhead mixer with (a) double and (b) triple side inlets. Top views show the symmetry elements. Blue color denotes the pathway of fluid I, red color denotes the pathway of fluid II, green color denotes the mixing zone, and yellow color denotes symmetry planes. The angle between the symmetry planes is (a) 90º and (b) 60º.

Figure 7. 2D maps of the mixing intensity (I_M) on the mixer outlet obtained using stationary simulation in (a) the original showerhead mixer ($V_A = V_B = 40\ ml/min$), and the modified mixers with (b) double ($2V_{A1} = 2V_{A2} = V_B = 40\ ml/min$) and (c) triple ($3V_{A1} = 3V_{A2} = 3V_{A3} = V_B = 40\ ml/min$) side inlets.

Figure 8. Transient simulation results of the yield of **S** (Y_S) at one mean residence time (2.7 s) in (a) the original showerhead mixer ($V_A = V_B = 40\ ml/min$), and the modified mixers with (b) double ($2V_{A1} = 2V_{A2} = V_B = 40\ ml/min$) and (c) triple ($3V_{A1} = 3V_{A2} =$

$3V_{A3} = V_B = 40\ ml/min$) side inlets. 2D maps of Y_S are shown on the mixer outlet surface and the corresponding surface averaged Y_S are (a) 5.4%, (b) 3.3%, and (c) 0.7%.

Table 1. Boundary conditions for fluid flow (5) and mass transfer (6) simulations.

Table 2. Comparisons of experimental and simulated Y_S values at the mixer outlet.