









CONTACT INFORMATION

FlowJEM Inc. PO Box 21422 Toronto, ON, Canada M5T 0A1

> Phone: +1-647-478-8938 Fax: +1-647-849-1174

www.flowjem.com info@flowjem.com FlowJEM Microfluidics on Twitter: @FlowJEM

TABLE OF CONTENTS

1. DROPLET GENERATORS	
1.1 - SINGLE DROPLET GENERATORS1	
1.2 - DOUBLE DROPLET GENERATORS	
1.3 - DROPLET MODULES	
2. DROPSEQ DEVICES	
3. MICROFLUIDIC REACTORS	
3.1 - DROPLET MICROREACTORS	
3.2 - CONTINUOUS MICROREACTORS	
3.3 - PASSIVE MICROMIXERS	
5. ANALYTICAL MICROFLUIDIC DEVICES	
6. CUSTOMIZED DESIGN	
7. QUALITY CONTROL	
8. MATERIALS	1
9. INTERFACE ACCESSORIES	,
10. PRESSURE ADAPTER	
REFERENCES	.)



1. DROPLET GENERATORS

FlowJEM offers standard microfluidic droplet and bubble generators for a variety of applications in chemistry, materials science, biology, diagnostics and pharmaceutical science (see Applications). Microfluidic droplet generators can be fabricated in PDMS or thermoplastic materials (see Materials).

FlowJEM also offers droplet generators with custom-based designs in PDMS and thermoplastic materials with different types of surface modification.



Image is acquired from Angew. Chem. Int. Ed. 48, 5300-5304 (2009).

1.1 – SINGLE DROPLET GENERATORS Typical standard designs of single droplet



SDG-1001



SDG-1003



SDG-1002



SDG-1004

Typical standard designs of single droplet generators designs are reported the literature¹⁻⁴ for extremely monodispersed water-in-oil (W/O) and oil-in-water (O/W) droplets, and bubbles. Product numbers are SDG-1001 to SDG-1004 (left)

Any design aspect can be customized. These include changes to the in flow focusing area (inset sub figures left) such as approach angle between dispersed and continuous phases (eg., SDG-1001 vs. SDG-1002), and thickness or length of neck. Channel modifications can include length/width, of downstream channels, inclusion of upstream pressure-drop channels, etc.





STC-1001

Other designs are available such as three-way T-junctions, or 4-way junctions. The design on the left shows a standard twoin-one design featuring one of each junction along with peripheral inlets for FlowJEM world-to-chip interface accessory (see section 7)

1.2 – DOUBLE DROPLET GENERATORS

Typical designs of double droplet generators are reported in the following publications⁵⁻⁸ and are used for the generation of double emulsions, e.g., water-in-oil-in-water (W/O/W), oil-in-oil-in-water (O/O/W), water-in-water-in-oil (W/W/O), and oil-in-water-in-oil (O/W/O)). These emulsions (also known as 'emulsions of emulsions') are extensively used in formulations in food, cosmetic and pharmaceutical industries. Customizations discussed in the previous section are also applicable.

Two design examples include DDR-001 and DDR-002 (below).



DDR-001

DDR-002

1.3 – DROPLET MODULES

The inclusion of an alighted manifold layer paralyzes each process (MMG-001 and MMG 002). Connecting multiple modules in parallel can significantly increase throughput.^{9,10}







2. DROPSEQ DEVICES

DropSeq devices are used for the analysis of RNA expression. DropSeq technology is developed to enable biologists to analyze RNA expression genome-wide in thousands of individual cells at once. It is reported by McCarroll et al. in Cell 2015, 161,1202-1214.

FlowJEM is an endorsed supplier of DropSeq devices fabricated in PDMS.

Standard DropSeq design: 26 droplet generators per device.

Standard bonding: oxygen plasma bonding to glass slide.

Customization includes the change in the dimensions and number of droplet generators per chip, the size of inlet/outlet holes, and different types of surface modification.



1000s of DNA-barcoded single-cell transcriptomes



"FlowJEM caught our attention based on positive customer feedback on their fabrication process and competitive pricing for PDMS chips. Based on our experience, the ease of use and high quality of FlowJEM's DropSeq devices allow one to perform and reliable and reproducible experiments for DropSeq applications with next-generation sequencing (NGS) protocols"

-Adam Meziane, Product Manager for Droplet Based Solutions, Fluigent



3. MICROFLUIDIC REACTORS

FlowJEM offers droplet and continuous microfluidic reactors for inorganic, organic, and bioorganic syntheses and for the generation of polymer microbeads and microgels.

Microfluidic droplet reactors can be fabricated in PDMS and thermoplastic materials.

FlowJEM also provides prototyping of microfluidic droplet reactors and various types of their surface modification.



Images of polymer particles are reported in Angew. Chem. Int. Ed. 44, 724-728 (2005), Langmuir 21, 4773-4775 (2005), J. Am. Chem. Soc. 128, 9408-9412 (2006), and J. Am. Chem. Soc. 127, 8058-8063 (2005).

3.1 – DROPLET MICROREACTORS

Standard designs of droplet microfluidic microreactors are reported in the following publications¹¹⁻¹⁷ and used for

(i) generation of polymer particles with exquisite control of dimensions, compositions, shapes, and morphologies;

(ii) organic and inorganic chemical reactions conducted in droplets (solution chemistry);

(iii) DNA analysis and polymerase chain reaction (PCR).



DMR-001



DMR-002



3.2 – CONTINUOUS MICROREACTORS

Typical designs of continuous microreactors are reported in the following publications¹⁸⁻²⁰ and are used for the synthesis of organic and inorganic compounds, polymers, biomaterials, nanoparticles, and drugs, all with excellent control of mass and heat transfer.







CMR-002-01 (H:0.1 mm)

CMR-002-02 (H: 0.2 mm)

CMR-001-01 (H:0.1 mm) CMR-001-02 (H: 0.2 mm)

CMR-003

3.3 – PASSIVE MICROMIXERS

FlowJEM offers micromixers for rapid mixing of multiple components in microfluidic channels. Typical designs of passive micromixers, e.g., 3D serpentine, twisted, or zigzag structures are reported in the following publications21-24 and are used to increase the surface area of microfluidic channels, in which laminar flow is dominant

Micromixers can be fabricated in PDMS or thermoplastic materials.

FlowJEM also offers customized surface modification of microreactors.













PMR-002

PMR-003



PMR-004



PMR-005



PMR-006



PMR-007



PMR-008



PMR-009



PMR-010



PMR-011



PMR-012



4. CUSTOMIZED DESIGN

Customers can take advantage of FlowJEM prototyping services. These services include fabrication of microfluidic devices with new designs. Alternatively, customers can send their own drawings, following the requirements listed below.

- Minimum feature/gap size: $\geq 2 \ \mu m$
- Tolerance in feature height: ±15% of the channel height (or ±8% with our premium service)
- For silicon wafers, all features should be placed in a 3.5" circle (for 4" wafer), or 4.5"-6.0" circle (for 6" wafer).



Accepted file formats:

Preferred file format: .dxf and .dwg. Other AutoCAD-compatible file formats (e.g., .sldprt and .gds) are acceptable.

Note that a different CAD format may not be compatible with FlowJEM graphical systems. The rules listed below will enable FlowJEM to complete your order in the timely and costeffective manner. If design changes are needed to meet FlowJEM's requirements, an additional fee may apply and the turnaround time may increase.

Regardless of the type of CAD software, zerowidth closed polylines should be used for boundaries. Hint: use a "Close" command to ensure that the area is completely closed.

- Do not use hatching to identify filled surfaces on the mask.
- Use a grid and turn on snap function.
- Ensure that "User Coordinate System" is set to "World".
- Do not allow boundaries to overlap or self-intersect. Touching, or "re-entrant" boundaries are acceptable.
- Purge all unused layers, objects and text before creating a .dxf file
- Units should be either millimeters, or micrometers.

"We switched to FlowJEM from another company in 2018 and have been really happy with their products ever since. We find that FlowJEM products are consistently high quality and they are very receptive when it comes to manufacturing custom devices. Overall, we've had a wonderful experience."

-Deepti Pant, Beth Israel Deaconess Medical Centre, Harvard Medical School



5. ANALYTICAL MICROFLUIDIC DEVICES

Unlock the Secrets Inside Your Microchannels with Chemical Characterization by FTIR Spectroscopy



We are excited to introduce our groundbreaking microfluidic product line, FlowSPEC. Our newest capabilities provide you with device equipped with an embedded ATR (Attenuated Total Reflectance) element, revolutionizing the way you analyze and understand on-chip chemical compositions. FTIR (Fourier Transform Infrared) spectroscopy is the ultimate tool in the arsenal of analytical chemistry, and here's why.

FTIR spectroscopy works like a molecular fingerprint scanner. By measuring how molecules interact with infrared light, FTIR reveals a wealth of information about chemical composition, functional groups, molecular structures and biological substances. With FlowSPEC, you can now introduce this capability with virtually any microchannel design. With FTIR spectroscopy, you can:

• Identify Compounds: Quickly and accurately identify unknown substances in your samples. FTIR can distinguish between different compounds, even in complex mixtures.

• Monitor Reactions in Real-Time: Watch chemical reactions unfold in real-time, allowing you to optimize processes, ensure product quality, and save time and resources.

• Quantify Components: Determine the concentration of specific components within your samples, crucial for quality control and research.

• Investigate Molecular Structures: Understand the structure of organic and inorganic compounds, helping you to design better materials and products.

• Non-Destructive Analysis: FTIR spectroscopy is non-destructive, meaning you can analyze samples without altering or damaging them.

• Units should be either millimeters, or micrometers.

Incorporating FTIR spectroscopy into our microfluidic device opens up a world of possibilities for scientists, researchers, and industries across the spectrum. Whether you're in pharmaceuticals, environmental science, materials science, or any field that requires precise chemical characterization, our product will empower you to achieve more.

Consider your microfluidic design with embedded ATR-FTIR spectroscopy and uncover the hidden stories within your samples!

As an example, we present four FlowSPEC devices that have been recently featured in the literature: https://pubs.rsc.org/en/content/articlelanding/2023/lc/d3lc00388d/unauth AND https://pubs.rsc.org/en/content/articlelanding/2023/ay/d3ay00842h/unauth



AMD-001



AMD-002



AMD-003



AMD-004

6. QUALITY CONTROL

FlowJEM adheres to strict quality control to ensure all jobs fit within the required design tolerances. Every mould part produced by FlowJEM is rigorously analysed to eliminate defects and to quantify the 3D channel environment. A technical report accompanies each report. These data are guaranteed to be accurate and can be used with 100% confidence by customers in their technical reports and journal submissions.

Custom reports, including 3D imaging of channel dimensions and higher measurement densities can easily be accommodated.

Reports include:

- A list of specific quality control measures that were used to ensure quality.
- A table of z-profile measurements from optical profilometry and reference image indicating measurement locations.
- (optional) 3D channel imaging

Rest St. George Street U4-627 Torotto, Orthoanto State Polymer Microfiluidic Technology	RO 94. George Street LM-627 Tourise, Or Dario Moss Street Polymer Microfiluidic Technology According by measuring channel heights at 4 points in the device.
Technical Report Feb., 5, 2020 1. Inventory Table 1-Order inventory: Table 1-Order inventory: Microfluidic device(s) Microfluidic device(s) Microfluidic device(s) Oplycarbonate (PC) Oplycarbonate (PC)	Aragea feature height was determine in Figure 1. Table 2 shows the argue height measurements at the indicated audition in the customer supplied table 3 shows the argue height measurements were taken from 4 feature locations and the average also and statistical analyses are listed. Table 2 shows the suprements (unit: micrometer) for 4 feature locations (white cult) and table 2 shows the argue resolution designation. Table 2 shows the suprements (unit: micrometer) for 4 feature locations (white cult) and table 2 shows the suprements (unit: micrometer) for 4 feature locations (white cult) and table 2 shows the suprements (unit: micrometer) for 4 feature locations (white cult) and table 2 shows the suprements (unit: micrometer) for 4 feature locations (white cult) and table 2 shows the suprements (unit: micrometer) for 4 feature locations (white cult) and table 2 shows the suprements (unit: micrometer) for 4 feature locations (white cult) and table 2 shows the suprements (unit: micrometer) for 4 feature locations (unit: micrometer) f
2. Quality Control Measurements The following quality control measures are undertaken by Flow/EM: • Visual inspection using optical microscope • Hard basked for better mechanical property • Mould silarization for easy de mouiding of DMS As a courtesy, we have undertaken the following additional control measurements: <u>Feature height</u> Characterization of feature heights.	1 Figure 1. Schematics of Design. Letters 1, 2, 3, 4 and corresponding squares mark the locations of optical profiler measurements (values reported in Table 2). 1 Figure 1. Schematics of Design. Letters 1, 2, 3, 4 and corresponding squares mark the locations of profiler measurements (values reported in Table 2). 1 Figure 1. Schematics of Design. Letters 1, 2, 3, 4 and corresponding squares mark the locations of profiler measurements (values reported in Table 2). 1 Figure 2.



7. MATERIALS

FlowJEM fabricates microfluidic devices in different materials. These materials have different characteristics, e.g. chemical resistance, gas permeability, surface properties, or softening temperature.

The choice of material depends on the application of microfluidic device (see e.g. Thermoplastic microfluidic devices for targeted chemical and biological applications. RSC Adv., 2017, 7, 2884).

Polydimethylsiloxane (PDMS) is an organosilicon polymer. It is optically clear, non-toxic, and gas-permeable. It is not stable in aromatic and hydrocarbon organic solvents and is typically used as a material of microfluidic devices working in aqueous systems.

FlowJEM offers different kinds of PDMS modification to fabricate microfluidic devices with hydrophobic, hydrophilic, or fluorophilic surfaces.

PDMS can be bonded to glass, silicon, or thermoplastic polymers.

Thermoplastic polymers. Microfluidic devices fabricated in thermoplastic polymers are stable in nonpolar, polar aprotic, and polar protic solvents, stable up to 100-120 °C, have low gas permeability, are optically clear, and are biocompatible. FlowJEM offers microfluidic devices fabricated in:

- Polystyrene
- Polypropylene
- Polycarbonate
- Cyclic olefin copolymer (COC)
- Poly(methyl methacrylate)
- Poly (vinyl chloride)

R

8. INTERFACE ACCESSORIES

FlowJEM's offers accessory packages to enhance functionality of microfluidic reactors.

Connection package includes:

- Ferrules
- Threaded connectors
- Inlet/outlet tubing (1/16") with inlet syringe adaptor

Optional interface systems can accommodate up to 8 fluidic connections and provides:

- Interfacing of fluidic connections with a microfluidic reactor.
- Interfacing of miniaturized probes with a microfluidic channel.
- Reinforcement of the sealed microfluidic reactor with O-rings to operate at high pressures and flow rates with no leaks.



Optional interface systems can accommodate up to 8 fluidic connections and provides:

- Interfacing of fluidic connections with a microfluidic reactor
- Interfacing of miniaturized probes with a microfluidic channel
- Reinforcement of the sealed microfluidic reactor with O-rings to operate at high pressures and flow rates with no leaks.



9. PRESSURE ADAPTER

FlowJEM offers a 3D printed multilevel pressure adapter which can be integrated with a multiplexed (multichannel) microfluidic device to operate it using a <u>single</u> pressuredriven source. This adapter is used to supply different liquids to multiple microchannels for e.g., optimization of chemical formulations.

An exemplary pressure adapter shown below has 3 inlets that can be connected to 4, 8, or 16 reservoirs to supply distinct liquids to 4, 8, or 16



channels, respectively, of the microfluidic device.

Customized adapters with a single inlet and 4, 8, or 16 outlets are available.

FlowJEM offers a 3D printed multilevel pressure adapter which can be integrated with a multiplexed (multichannel) microfluidic device to operate it using a <u>single</u> pressuredriven source. This adapter is used to supply different liquids to multiple microchannels for e.g., optimization of chemical formulations.

An exemplary pressure adapter shown below has 3 inlets that can be connected to 4, 8, or 16 reservoirs to supply distinct liquids to 4, 8, or 16 channels, respectively, of the microfluidic device.

Customized adapters with a single inlet and 4, 8, or 16 outlets are available.



REFERENCES

1. Thorsen, T.; Roberts, R. W.; Arnold, F. H.; Quake, S. R., Dynamic pattern formation in a vesicle-generating microfluidic device. Phys. Rev. Lett. 2001, 86, 4163-4166.

2. Anna, S. L.; Bontoux, N.; Stone, H. A., Formation of dispersions using "flow focusing" in microchannels. Appl. Phys. Lett. 2003, 82, 364-366.

3. Garstecki, P.; Gitlin, I.; DiLuzio, W.; Whitesides, G. M.; Kumacheva, E.; Stone, H. A., Formation of monodisperse bubbles in a microfluidic flow-focusing device. Appl. Phys. Lett. 2004, 85, 2649-2651.

4. Squires, T. M.; Quake, S. R., Microfluidics: Fluid physics at the nanoliter scale. Rev. Mod. Phys. 2005, 77, 977-1026.

5. Okushima, S.; Nisisako, T.; Torii, T.; Higuchi, T., Controlled production of monodisperse double emulsions by two-step droplet breakup in microfluidic devices. Langmuir 2004, 20, 9905-9908.

6. Nie, Z. H.; Xu, S. Q.; Seo, M.; Lewis, P. C.; Kumacheva, E., Polymer particles with various shapes and morphologies produced in continuous microfluidic reactors. J. Am. Chem. Soc. 2005, 127, 8058-8063.

7. Utada, A. S.; Lorenceau, E.; Link, D. R.; Kaplan, P. D.; Stone, H. A.; Weitz, D. A., Monodisperse double emulsions generated from a microcapillary device. Science 2005, 308, 537-541.

8. Seo, M.; Paquet, C.; Nie, Z. H.; Xu, S. Q.; Kumacheva, E., Microfluidic consecutive flowfocusing droplet generators. Soft Matter 2007, 3, 986-992.

9. Li, W., Young, E. W. K., Seo, M., Nie, Z., Garstecki, P., Simmons, C. A. and Kumacheva, E.,

Simultaneous generation of droplets with different dimensions in parallel integrated microfluidic droplet generators. Soft Matter 2008, 4, 258-262.

10. Li, W., Greener, J., Voicu, D. and Kumacheva, E., Multiple modular microfluidic (M-3) reactors for the synthesis of polymer particles. Lab Chip 2009, 9, 2715-2721.

11. Xu, S. Q.; Nie, Z. H.; Seo, M.; Lewis, P.; Kumacheva, E.; Stone, H. A.; Garstecki, P.; Weibel, D. B.; Gitlin, I.; Whitesides, G. M., Generation of monodisperse particles by using microfluidics: Control over size, shape, and composition. Angew. Chem. Int. Edit. 2005, 44, 724-728.

12. Seo, M.; Nie, Z. H.; Xu, S. Q.; Mok, M.; Lewis, P. C.; Graham, R.; Kumacheva, E.

Continuous microfluidic reactors for polymer particles. Langmuir 2005, 21, 11614-11622.

13. Song, H.; Chen, D. L.; Ismagilov, R. F., Reactions in droplets in microflulidic channels. Angew. Chem. Int. Edit. 2006, 45, 7336-7356.

14. Nie, Z. H.; Li, W.; Seo, M.; Xu, S. Q.; Kumacheva, E., Janus and ternary particles generated by microfluidic synthesis: Design, synthesis, and self-assembly. J. Am. Chem. Soc. 2006, 128, 9408-9412.

15. DeMello, A. J., Control and detection of chemical reactions in microfluidic systems. Nature 2006, 442, 394-402.

16. Chu, L. Y.; Utada, A. S.; Shah, R. K.; Kim, J. W.; Weitz, D. A., Controllable monodisperse multiple emulsions. Angew. Chem. Int. Edit. 2007, 46, 8970-8974.

17. Teh, S. Y.; Lin, R.; Hung, L. H.; Lee, A. P., Droplet microfluidics. Lab Chip 2008, 8, 198-220.



18. Hartman, R. L. and Jensen, K. F., Microchemical systems for continuous-flow synthesis. Lab Chip 2009, 9, 2495-2507.

19. Marre, S. and Jensen, K. F., Synthesis of micro and nanostructures in microfluidic systems. Chem. Soc. Rev. 2010, 39, 1183-1202.

20. Voicu, D., Scholl, C., Li, W., Jagadeesan, D., Nasimova, I., Greener, J. and Kumacheva, E., Kinetics of Multicomponent Polymerization Reaction Studied in a Microfluidic Format. Macromolecules 2012, 45, 4469-4475.

21. Beebe, D. J.; Mensing, G. A.; Walker, G. M., Physics and applications of microfluidics in biology. Annu. Rev. Biomed. Eng. 2002, 4, 261-286.

22. Stroock, A. D.; Dertinger, S. K. W.; Ajdari, A.; Mezic, I.; Stone, H. A.; Whitesides, G. M., Chaotic Mixer for Microchannels. Science 2002, 295, 647-651.

23. Therriault, D.; White, S. R.; Lewis, J. A., Chaotic mixing in three-dimensional microvascular

networks fabricated by direct-write assembly. Nat.ure Mater. 2003, 2, 265-271.

24. Nguyen, N. T.; Wu, Z. G., Micromixers - a review. J. Micromech. Microeng. 2005, 15, R1-R16.