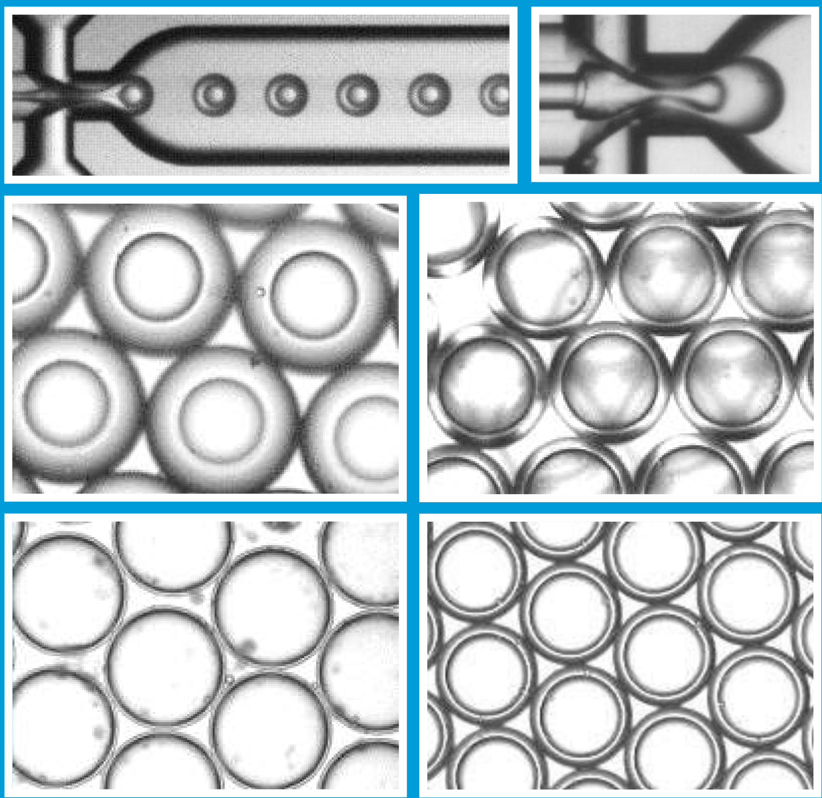
Water in Mineral Oil in Water (W-O-W) Double Emulsion Production using SDS, PGPR and Tween® 80 as Emulsifiers

Dolomite's Double Emulsion System



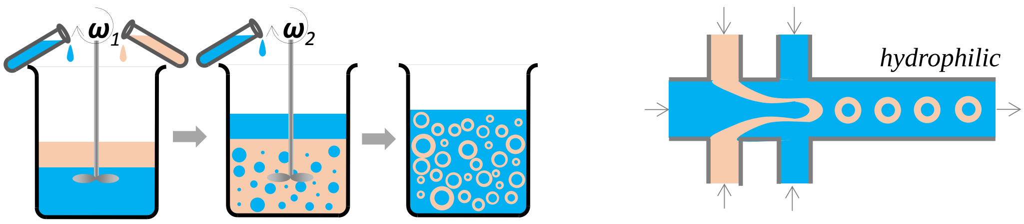
dolomite

Application Note	Page
Summary of Double Emulsion Production	2
Introduction to Dolomite's Double Emulsion System	3
Test Setup & Materials	4
Results & Analysis	6
Conclusion	15
Appendices - Component List, Note on Surfactants, & FAQ's)	16
IP License	20

Summary of Double Emulsion Production

This application note reports on the production of monodisperse double emulsion droplets produced in a single step using a microfluidic approach. Double emulsions are engineered fluids consisting of one or more micrometer sized liquid emulsion droplets containing still smaller liquid droplets encapsulated within. At least two immiscible fluids are used in order for a liquid-liquid interface to develop. Here, the inner phase is water with SDS, the middle phase is mineral oil with PGPR, and the outer phase is water with Tween-80.

Fluidic structure of a W/O/W double emulsion. Left: 1 droplet of water in 1 droplet of oil, which is in turn in surrounded by water. Right: Multiple droplets of water in 1 droplet of oil, which is in turn in surrounded by water.



Left: 2 step batch method. $\omega_2 << \omega_1$ .In addition to the physical mechanism, surfactant chemistry is essential for stability. Right: A single step continuous flow method in a microfluidic device enables much greater control and reproducibility.

Key Applications

- Drug delivery and enzyme immobilization
- Taste masking food products
- Key ingredient delivery vehicle for cosmetics
- In-vitro encapsulation and flow cytometry
- Micro shells as delivery vehicles

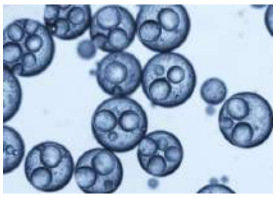
Dolomite's Double Emulsion System using standard products is based on continuous flow method using a precision microfabricated glass device. The system has a high yield with highly consistent and monodisperse droplets produced. Furthermore, the ability to control droplet sizes, analyse the droplets using automated software and tune volume ratios between inner and outer droplets makes this system particularly unique. The use of Dolomite's standard products for pumping, valving, imaging and analysis make this a flexible and reliable method.

The system is shown to make double emulsions of different sizes and inner/outer droplet volume ratios. Overall, the system is shown to be quick to set up and easy to start producing a high quality product.

Introduction to Dolomite's Double Emulsion System

Multiple emulsions in the past have usually been produced in a two-step emulsification process using conventional rotor-stator or high pressure valve homogenizers. The primary W/O or O/W emulsion is prepared under high-shear conditions (ω_1) to obtain small inner droplets, while the secondary emulsification step is carried out with less shear ($\omega_2 << \omega_1$) to avoid rupture of the liquid membrane between the innermost and outermost phase. The second step often results in highly polydisperse outer drops (if homogenizing conditions are too mild) or in small encapsulation efficiency (if homogenization is too intensive).

Microfluidic methods in contrast are attractive as the higher surface to volume ratio means that surface coatings control the order of the outer fluid layers. More recently, multiple emulsions have been produced by forcing a primary emulsion through a flow focussing geometry into a continuous phase liquid. This results in much less shear than in conventional emulsification processes so that the droplets are intact. Use of a flow-focussing method, ultra-thin shells can now be generated.



Left: Double emulsions made up of an aqueous core (w), an organic shell (o), and an aqueous continuous fluid (w). Right: Oil droplets with multiple water droplets within. Typical droplet sizes range between 50µm and 150µm.

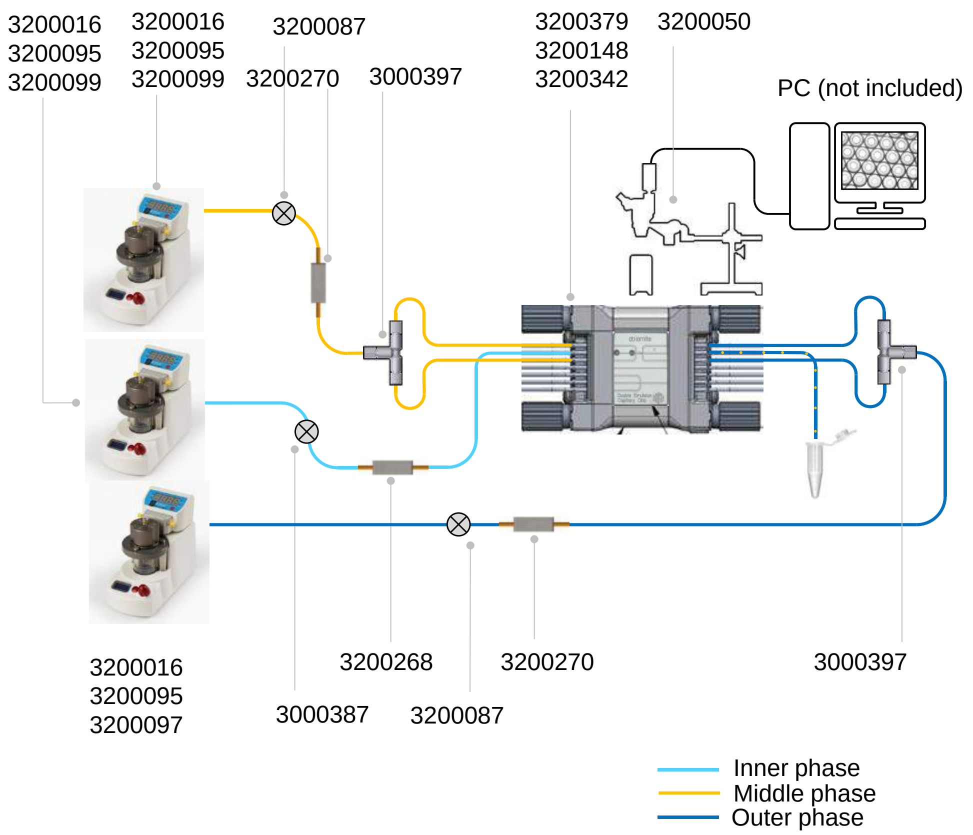
In addition to the physical mechanism, the surfactant chemistry has an important role in stabilizing the emulsion. At least two different emulsifiers are necessary for their stabilization: one with a low hydrophilic-lipophilic balance (HLB) for the W/O interface and a second one with a high HLB for the O/W interface. Emulsifiers investigated in this article are commonly used in cosmetics as well as permitted in pharmaceutical applications in their respective purity grades.

The two key elements of the system are the Mitos P-Pump (pressure pump) which delivers precise flow to ensure droplet monodispersity, and the precision fabricated Double Emulsion Capillary Chip offering excellent dimensional tolerance. The droplet size can be tuned by controlling the fluid flows using the P-Pump.

The test results conclude that with a given chemistry, the Double Emulsion System is capable of making high quality double emulsions. Further, it is well suited to continuous production, thereby allowing very large quantities to be produced, relevant to industry scale production capacities.

Here we report the application of monodisperse double emulsion droplets, produced in a single step within a microfluidic device with a surface functionalized engineered surface. This application note describes the operation of Dolomite's Double Emulsion System for the production of double emulsions where the inner phase is water with sodium dodecyl sulphate (SDS), the middle phase is mineral oil with polyglycerol polyricinoleate (PGPR), and the outer phase is water with polysorbate 80 (Tween-80).

Test Setup and Materials



FEP tubing of OD 0.8mm and ID 0.25mm is used for connections. Lengths are indicated by numbers in brackets. Schematic not to scale.

	Inner phase	Middle phase	Outer phase
P-pump to Flow sensor	0.25, 1.6, 200 + 0.4, 0.8, 300 (flow sensor adaptor)	0.25, 1.6, 200 + 0.4, 0.8, 300 (flow sensor adaptor)	0.25, 1.6, 200 + 0.4, 0.8, 300 (flow sensor adaptor)
Flow sensor to In-line valve	0.4, 0.8, 300 (flow sensor adaptor)	0.4, 0.8, 300 (flow sensor adaptor)	0.4, 0.8, 300 (flow sensor adaptor)
In line valve to T-Connector	-	0.25, 1.6, 300	0.25, 1.6, 300
T-Connector to Chip	0.1, 0.8, 4410 (~ F3 resistor*)	0.1, 0.8, 441 (~ F30 resistor)	0.1, 0.8, 441 (~ F30 resistor)
	0.1, 0.8, 147 (~ F100 resistor)	0.1, 0.8, 147 (~ F100 resistor)	0.1, 0.8, 147 (~ F100 resistor)

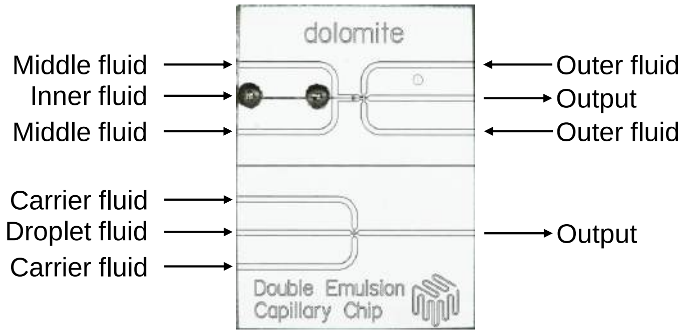
The table shows details of tubing used to make fluidic connections. Numbers are written in triplets denoting tubing inner diameter in mm, tubing outer diameter in mm, and tubing length in mm.

* Flow resistances (3200269 and 3200270) may be approximated by an equivalent length of standard FEP tubing. This has been indicated in the table above. Eg. 0.1, 0.8, 4410 (~ F3 resistor). In the Microfluidic calculator on the Dolomite website, a tubing of ID 0.1mm and length 4410mm pumping water at a pressure of 1 bar results in a flow rate of 3µL/min. This is the reasoning behind the naming of flow resistors (F3). 3200269 and 3200270 are made of fused silica with higher size tolerance than the FEP (or PTFE) tubing, and are thus recommended for accuracy of flow rates compared with FEP.

Production of double emulsions is carried out using Dolomite's Double Emulsion Chip (100µm etch depth) (Part No. 3200342), and Dolomite's Mitos P-Pumps (Part No. 3200016). The P-Pumps provide pulseless liquid flow with a precise pressure driven pumping mechanism, delivering pneumatic pressure at a 1 mbar resolution. They use compressed air or inert gas to drive the fluid by displacement. This enables ultra-smooth flow, which is a unique feature of the Mitos P-Pumps, and is a critical requirement for achieving monodispersity. Occasionally, issues arise with dissolved gases which can normally be resolved by using helium, which has a very low solubility in liquids.

Additional components such as flow sensors and fluidic accessories make the system easier to use. Mitos Flow Rate Sensors (Part No. 3200098 and 3200099) and the Mitos Sensor Display (Part No. 3200095) enable monitoring of flow rates, as well as detecting instances of backflow. The F10 Flow Resistor (Part No. 3200269) and the F30 Flow Resistor (Part No. 3200270) can be used to insert additional flow resistance into the system. Flow resistances are used with some knowledge of the fluidic viscosities to equalize the pressure at the chip junction. The use of flow resistances enables a wider operating range, and lends greater control on adjusting flow ratios.

Fluid accessories such as the 2-way In-line Valve (Part No. 3200087) and the T-Connector ETFE (Part No. 3000397) enable fluids to be introduced sequentially onto the chip. This is useful during start-up, when exploring optimal pressures and flow rates. A High Speed Camera and Microscope System (Part No. 3200050) is used to view the chip junction. Reducing the pixel size of the image enables frame grabbing at higher frequencies of up to 1.5 kHz. Videos are recorded, and later analysed with Dolomite's Droplet Monitor software to estimate outer droplet size and droplet production rates. When connecting tubing of differing inner diameters, a useful guide is to use larger ID tubing upstream, and smaller ID tubing downstream leading to the chip.



Schematic of the Double Emulsion Chip. There are two fluidic junctions – the upper junction is useful for producing double emulsions, and the lower junction is useful for producing single emulsions. This application note focusses on the use of the upper junction.

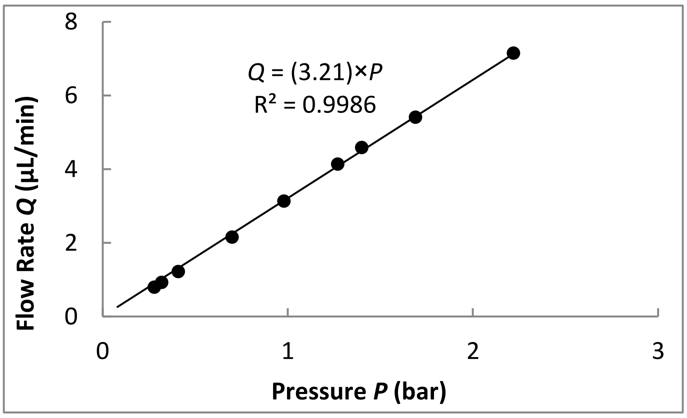
The schematic of the chip above shows the fluidic connections. Only one of the two junctions available on the chip is used in this application note. Three different fluids are pumped to the chip – 1% SDS in water as the inner fluid, 2 % PGPR in mineral oil as the middle fluid, and 2% Tween 80 in water as the outer continuous fluid. The solutions are freshly prepared beforehand, and degassed to prevent incidents of bubble production in the system. They are additionally filtered through a 0.2µm pore size filter. Care is taken during assembly on the system to ensure that minimal dust is introduced into the system.

Where possible, at least one Ferrule with Integrated Filter (Part No. 3200245) is used as an in-line ferrule in each of the fluidic tubing leading to the chip.

Results & Analysis

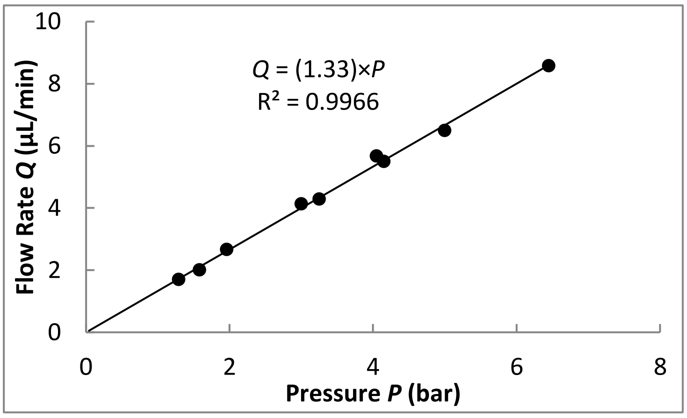
Flow characteristics of the system

With pressure pumping, the flow rate Q is proportional to the pressure P set in the P-Pump and inversely proportional to the fluid resistance R_f. The fluidic resistance depends upon structural aspects such as cross sectional area of the flow and length of tubing, and fluid properties such as viscosity. The graphs below show the flow rates at various pumping pressures, where the slope of the graph is the inverse of the fluidic resistance (R_f^{-1}) of that particular fluid line (inner, middle or outer). These data points are a collection of all data points observed when successfully producing double emulsions.

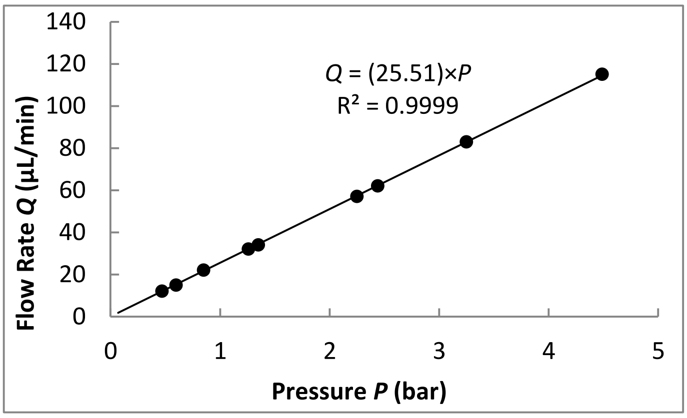


Inner phase – 1% SDS in water

The three fluids are coupled in their fluidic resistance via the interaction at the chip junction – this is the reason for the slight drift ($R^2 < 1$) in the data points off the straight line. These slopes are fluidic resistance, and while are fixed for fluid combinations, can be tweaked advantageously by the use of flow resistors.



Middle phase – 2 % PGPR in Mineral Oil

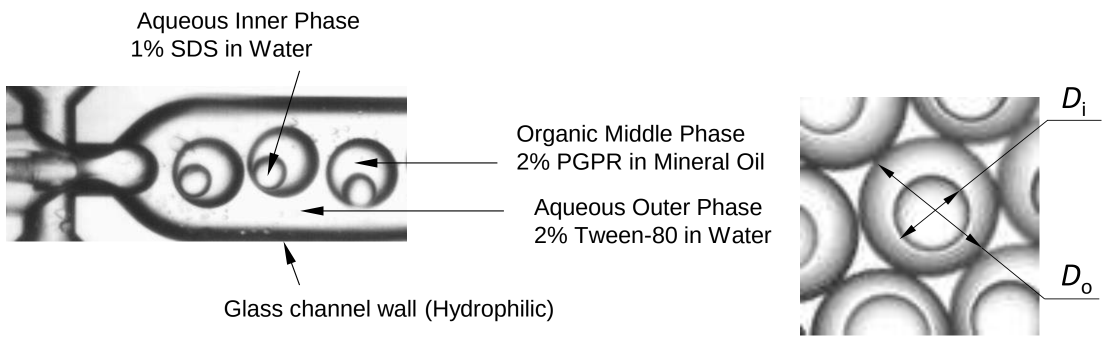


Outer phase – 2% Tween 80 in water

The outer fluid has been set up with the least fluidic resistance, and has the largest volumetric flow rate. This is essential for it to form the continuous phase. The inner fluid and the middle fluid have been set up with comparable fluidic resistances and hence their volumetric flow rates are comparable. When producing thin shelled double emulsions, the middle phase flows slower than the inner phase, and vice versa.

Droplet production and mechanism of droplet breakup

Care should be taken that none of the input streams should flow backwards. If not corrected in time, one of the fluids is liable to flow backwards all the way to the fluid reservoir causing contamination. This is checked by the use of the 2-way In-line Valves and ensuring that flow rates are always positive. Once flows are set-up, the imaging system is used to observe droplet production at the junction. A typical image of double emulsion production using bright field microscopy at the junction is shown below.

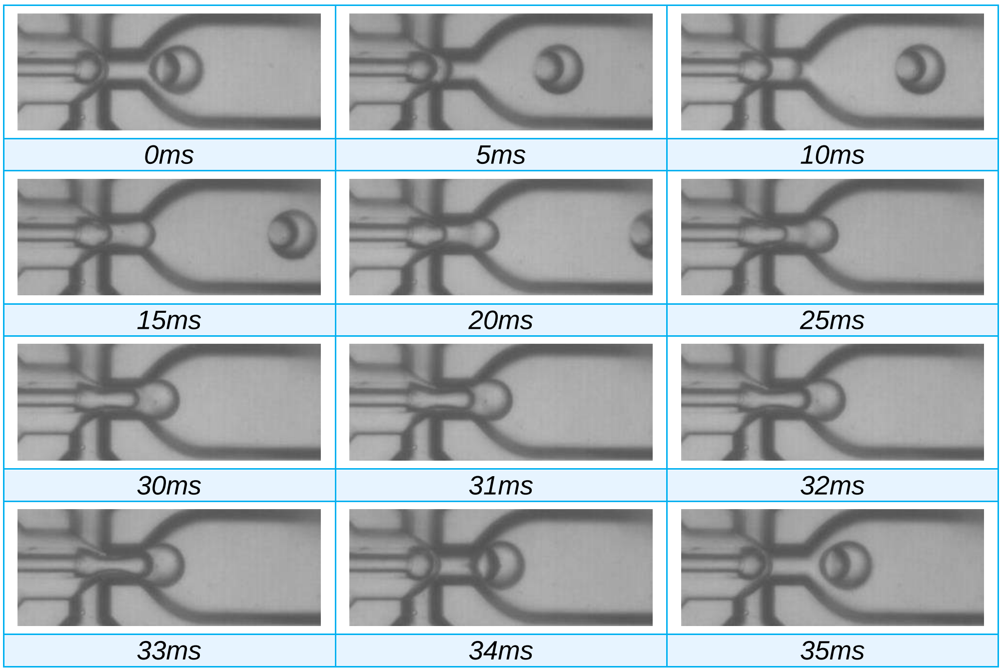


Left: Typical image of double emulsion produced at chip junction; droplets move left to right. Right: Scheme for measuring droplet sizes – D_i is inner droplet apparent diameter†, and D_o is outer droplet apparent diameter.

A 1 second duration video at high frame rate of the droplet production is recorded, and decomposed into frames. These are shown in the table below along with respective time stamps to indicate timeline of droplet breakup. A double droplet pinch-off occurs on the

† When visualizing double emulsions, it should be noted that the refractive index mismatch due to differential material properties gives inexact droplet sizes from direct visual measurements. All sizes reported here are apparent sizes, and not corrected due to the refraction.

timescale of a few milliseconds. The image corresponding to 0ms shows a droplet that has just pinched off. Subsequently, the two immiscible fluid streams continue to fill the junction and extend towards the right as the pinched-off droplet flows downstream to the right. At 33ms, the two immiscible fluids extend as an elongated shell. In the next image at 34ms, ‘necking’ appears on the inner fluid shell, constricting further and resulting in inner fluid breakup, thereby creating the inner droplet. The middle fluid continues to ‘neck’ and also pinches-off. The inner fluid always breaks off before the middle fluid, and at times breaks up multiple times, creating many inner droplets in a larger outer droplet.



Sequence of images depicting the pinch-off during production of double emulsions. Droplets flow from left to right. A timescale of 35ms corresponds to a droplet production frequency of about 28 per second.

The successful production of double emulsions depends strongly on the fluid properties and surfactant chemistry.

Producing double emulsions with variable inner/outer droplet size – 3 Illustrative cases

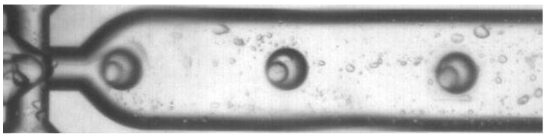
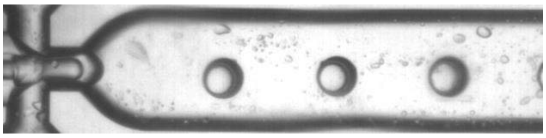
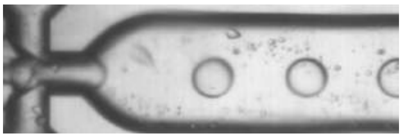
Test	Outer Droplet Size (μm)
1	100
2	125
3	150

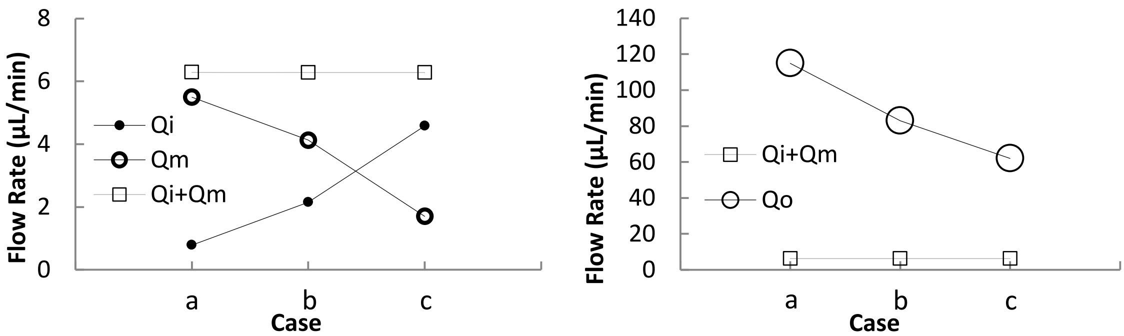
In each of the tests, the outer droplet size is kept constant, while the inner droplet size is varied. As the three fluids involved are coupled via fluidic resistance, all three pressures are required to be changed to keep the outer droplet size constant while changing the inner droplet size.

In order to study the effect of varying flow ratio, three different outer droplet sizes were taken as starting points. These are shown in the table above, and are typical droplet sizes obtained on a 100μm etch depth chip. For each of these cases, the flows are further varied to be able to tune the size of the inner droplet so that a tuneable volume percentage of the inner versus outer droplet is achieved.

Droplets with diameter larger than the channel depth of 100μm will appear larger than they really are because they will be flattened. Sizes of all droplets on-chip are estimations only, and should be specifically calibrated for shape distortion. When collected off-chip, droplets are spherical, and can then be measured accurately.

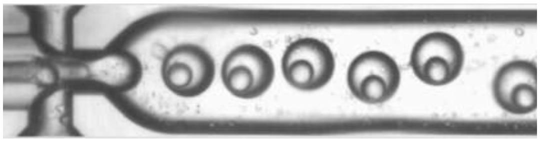
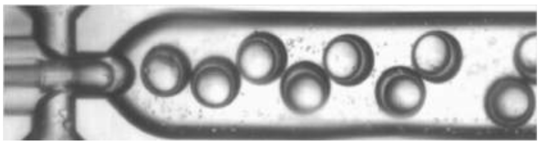
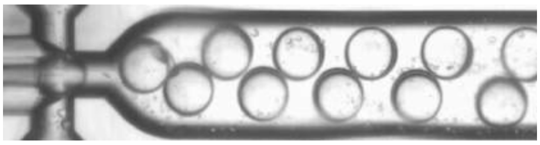
Test 1: Outer Droplet Size 100µm with droplet production at 200 per second

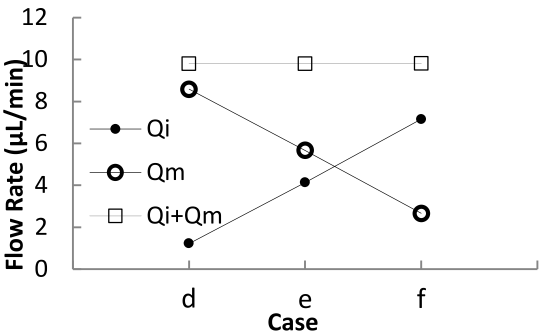
	Pressure			Flow Rate			Droplet Dia.		Junction Image
	Inner P_i	Middle P_m	Outer P_o	Inner Q_i	Middle Q_m	Outer Q_o	Inner D_i	Outer D_o	
Case	[mbar]	[mbar]	[mbar]	[µL/min]	[µL/min]	[µL/min]	[µm]	[µm]	
a	0.28	4.15	4.49	0.79	5.5	115	50	100	
b	0.70	3.00	3.25	2.15	4.13	83	70	100	
c	1.40	1.29	2.44	4.58	1.70	62	90	100	

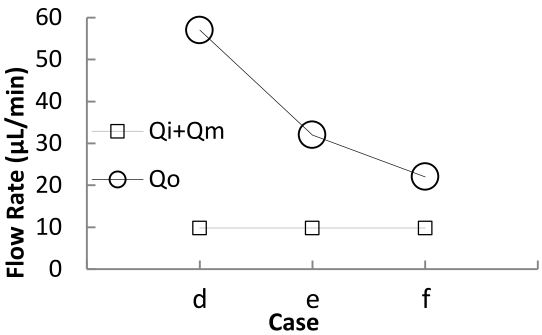


Left: The ratio between the inner fluid flow rate Q_i and the middle fluid flow rate Q_m varied while ensuring that the total of the two remains constant. Right: The ratio between the outer fluid flow rate Q_o and the combination of the inner and middle fluid flow rate ($Q_i + Q_m$).

Test 2: Outer Droplet Size 125µm with droplet production at 160 per second

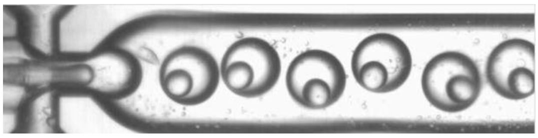
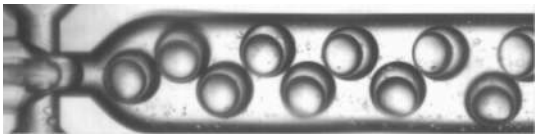
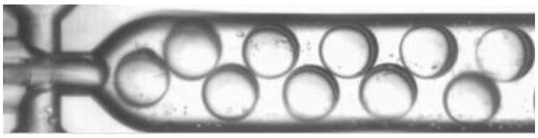
	Pressure			Flow Rate			Droplet Dia.		Junction Image
	Inner P_i	Middle P_m	Outer P_o	Inner Q_i	Middle Q_m	Outer Q_o	Inner D_i	Outer D_o	
Case	[mbar]	[mbar]	[mbar]	[µL/min]	[µL/min]	[µL/min]	[µm]	[µm]	
d	0.41	6.45	2.25	1.22	8.58	57	62.5	125	
e	1.27	4.05	1.26	4.13	5.67	32	93.7	125	
f	2.22	1.96	0.85	7.15	2.66	22	112.5	125	

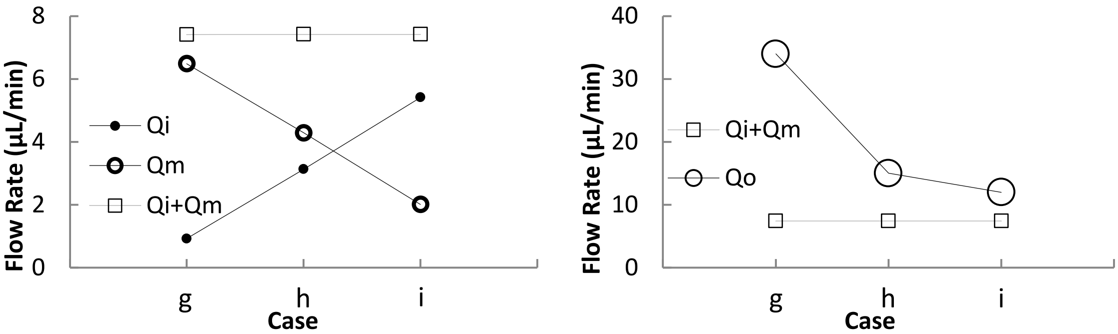




Left: The ratio between the inner fluid flow rate Q_i and the middle fluid flow rate Q_m varied while ensuring that the total of the two remains constant. Right: The ratio between the outer fluid flow rate Q_o and the combination of the inner and middle fluid flow rate ($Q_i + Q_m$).

Test 3: Outer Droplet Size 150µm with droplet production at 70 per second

	Pressure			Flow Rate			Droplet Dia.		Junction Image
	Inner P_i	Middle P_m	Outer P_o	Inner Q_i	Middle Q_m	Outer Q_o	Inner D_i	Outer D_o	
Case	[mbar]	[mbar]	[mbar]	[µL/min]	[µL/min]	[µL/min]	[µm]	[µm]	
g	0.32	5.00	1.35	0.92	6.49	34	75	150	
h	0.98	3.25	0.60	3.13	4.29	15	112.5	150	
i	1.69	1.58	0.47	5.41	2.01	12	135	150	

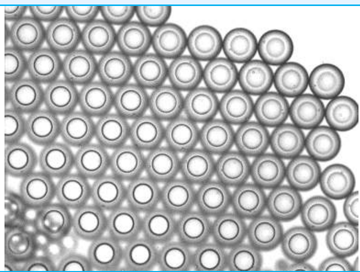
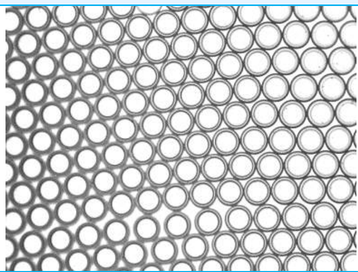
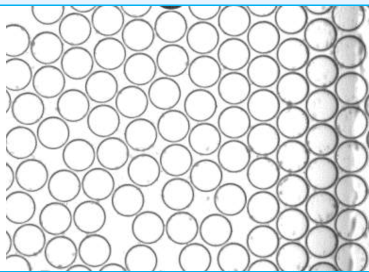
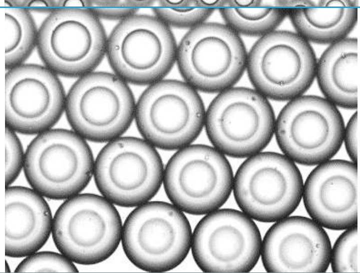
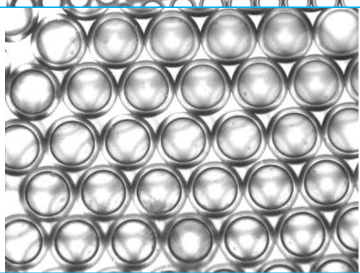
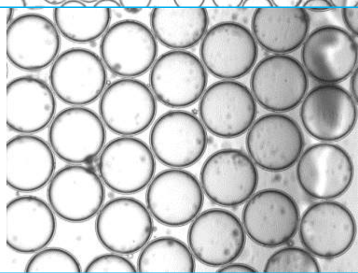
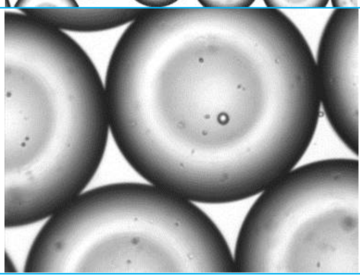
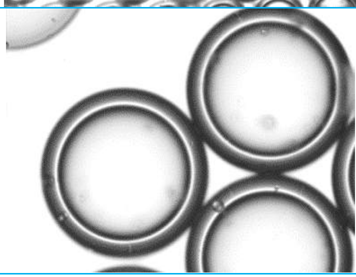
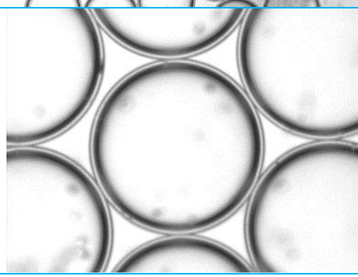


Left: The ratio between the inner fluid flow rate Q_i and the middle fluid flow rate Q_m varied while ensuring that the total of the two remains constant. Right: The ratio between the outer fluid flow rate Q_o and the combination of the inner and middle fluid flow rate ($Q_i + Q_m$).

Collection off-chip

The selection of the collection vessel is critical to the stability of the emulsion. In the present test, generated w-o-w emulsion requires the surface of the collection vessel to be hydrophilic, therefore a glass vessel with unmodified walls was chosen. For visualization, a plain glass slide is used on which 50µL of emulsion is placed. High magnification images (obtained at 3 magnifications of 5×, 10× and 30×) are presented in the table below. The parameters used to quantify the collected double emulsions are:

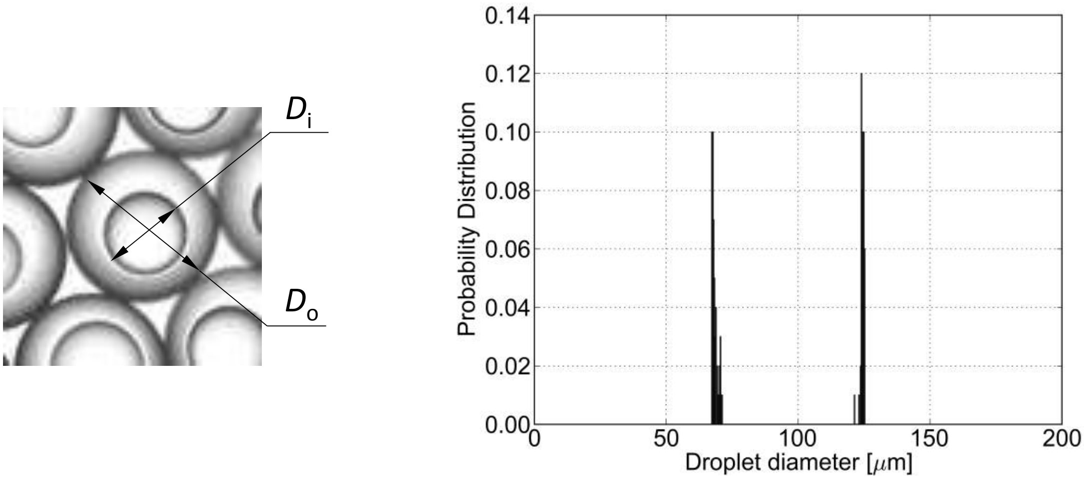
- The outer droplet size in all cases is 100µm.
- Size Ratio $D\% = (Di/Do \times 100)$.
- Volume Ratio $V\% = (Vi/Vo \times 100) = (Di^3/Do^3 \times 100)$.

	Test 1a	**Test 1b**	**Test 1c**
	Di = 50µm, *Do* = 100µm	*Di* = 70µm, *Do* = 100µm	*Di* = 90µm, *Do* = 100µm
D%	50%	70%	90%
V%	12.5 %	34.3%	72.9%
5×			
10×			
30×			

Close packed monolayers of sample on a collection glass slide. These images are representative of Test 1, case a, b and c respectively.

Monodispersity of collected sample

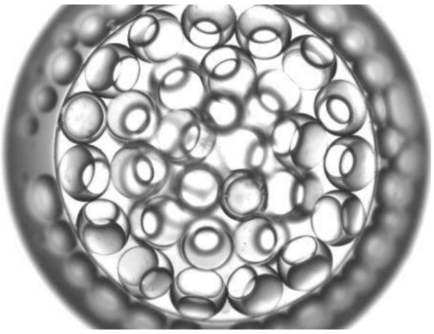
A droplet size-analysis was performed recording droplet diameters over 15 minutes using a low frame rate. These images were then processed using Dolomite's Droplet Monitor Software to extract size information. This gives the temporal information on shifts in droplet sizes. The information is presented in the distribution based histogram shown below.



Left: Two dimensions characterize double emulsions. Right: Droplet diameter distribution of the w/o/w double emulsion, revealing the monodispersity of the sample both for the inner water and the outer oil droplets. Data represents a sample size of 5000 droplets.

The sample was found be highly monodisperse and consistent. Test case 2(d) is presented as an illustration. The droplet diameter distribution, determined for 125µm double emulsion droplets, is extremely narrow for both the inner water and the outer oil droplets and exhibits mean values seen as two distinct peaks at 62.5 and the second at 125µm respectively. As the standard deviations – 0.9µm for the inner and 1.8µm for the outer droplets – are only 1.3% and 1.4% of the corresponding mean diameters, the double emulsion sample is considered monodisperse regarding both the inner and the outer droplets.

Conclusion



A microfluidic method for the production of monodisperse double emulsions is demonstrated using Dolomite's Double Emulsion System composed of the Double Emulsion Chip, Mitos P-Pumps, flow accessories and imaging system.

The system was found to be easy and quick to install, and required no custom parts using three P-Pumps, it was possible to set the flow of the three input fluids streams independently, allowing control of the outer droplet size, inner droplet size and production frequency.

As well as measuring the droplet size generated on-chip, a sample was collected off-chip and analysed, confirming that the droplets were highly monodisperse.

Three outer droplet sizes were generated during the experiment along with three inner droplet sizes giving a total of nine sets of flow conditions. The size ratio between inner and outer droplets was shown to be readily controlled by varying the system input pressures. Rates of production can potentially be adjusted higher or lower by an order of magnitude by using different flow resistors.

The work presented in this article has particular relevance to applications in the area of invitro compartmentalization, drug encapsulation and biomolecular screening.

Appendix A: System Component List

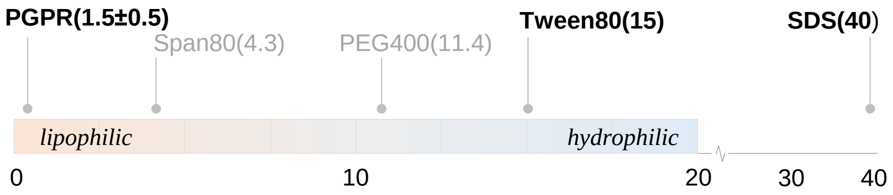
Part No.	Part Description	#
3200342	Double Emulsion Chip (100µm etch depth), W/O/W	1
3200016	Mitos P-Pump	3
3200095	Mitos Sensor Display	3
3200098	Mitos Flow Rate Sensor (1 - 50µl/min)	1
3200099	Mitos Flow Rate Sensor (0.4 - 7µl/min)	2
3200269	F10 Flow Resistor	1
3200270	F30 Flow Resistor	1
3200063	FEP Tubing, 1/16" x 0.25mm, 10 metres	1
3200304	FEP Tubing, 0.8 x 0.1mm, 10 metres	1
3200087	2-way In-line Valve	3
3200245	Ferrule with Integrated Filter (pack of 10)	1
3000399	1/4 - 28 Straight Female Coupling, ECTFE	1
3200306	Flangeless Ferrule 0.8mm, ETFE (pack of 10)	1
3000477	End Fittings and Ferrules for 1.6mm Tubing (pack of 10)	1
3200148	Linear Connector 7-way	2
3200050	High Speed Camera and Microscope System	1
3200017	Mitos P-Pump Vessel Holders Kit	3
3000397	T-Connector ETFE	2
3200379	H Interface 7-way (11.25mm)	1

Appendix B: Surfactant Action

In the production of double emulsions, there is an implicit instability issue which must be addressed through the use of appropriate surfactants. Compared with simple emulsions consisting of only two phases, complex destabilization processes need to be taken into consideration for multiple emulsions. These can be coalescence of the internal aqueous droplets, coalescence of the oil droplets, rupture of the oil film resulting in the loss of the internal aqueous droplets, or passage of the water and water-soluble substances through the oil layer between both water phases. This can occur in two various ways: via reverse micellar transport created by the lipophilic emulsifier and by simple diffusion across the oil phase connected with osmotic differences between both water phases.

Stability can be increased by the use of high viscous oil in order to prevent diffusion of water and water-soluble substances between the inner and outer water phase, the polymerization of interfacially adsorbed surfactant molecules, and the gelation of the oily or aqueous phases of the emulsions to create solid shells.

The chemistry challenge as regards stability is the presence of two thermodynamically unstable interfaces. At least two different emulsifiers are necessary for their stabilization: one with a low HLB (Hydrophilic–Lipophilic Balance) for the W/O interface and a second one with a high HLB for the O/W interface.



HLB's of surfactants PGPR, Tween 80, and SDS used for producing double emulsions. SPAN 80 and PEG 400 are some other commonly used surfactants, marked on the scale bar for perspective.

The aim of the emulsifier is to stabilize the W/O interface of the primary emulsion. When the multiple emulsion is created, a part of the lipophilic emulsifier migrates to the external O/W interface and will, together with hydrophilic emulsifier, influence the formation of multiple droplets. The HLB value of emulsifiers on the O/W interface is therefore not only the HLB value of hydrophilic emulsifiers, but the sum of the HLB values of hydrophilic and lipophilic emulsifiers. However, this value is difficult to estimate due to the fact that the amount of lipophilic emulsifier on the external interface is not fully known. Its amount on the O/W interface is dependent on several factors such as: its total amount in the emulsion, it's W/O fraction in the multiple emulsion and its droplet size in the primary and multiple emulsion. To link the effect of both emulsifiers on the formation of multiple emulsions, a ‘‘weighted HLB” is considered which weights the HLB according to the W/O fraction. At a weighted HLB > 10, multiple emulsions are less preferential, but rather simple O/W emulsions are formed. On the other hand, at a very low weighted HLB value, W/O emulsions will be formed.

The second important factor for emulsion stability is the chemical compatibility of the emulsifier with other emulsion ingredients. The suitability of the emulsifier is determined primarily by experimental means. Tween 80 is very often used in combination with Span

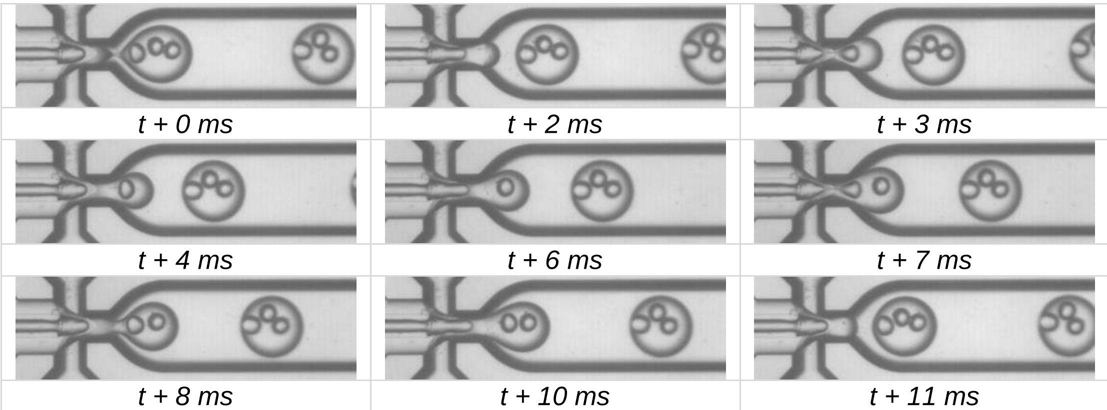
80 in multiple W/O/W emulsions because they have similar chemical structures. It has been found in the majority of cases that the most stable emulsions are formed when both emulsifying agents are of the same hydrocarbon chain length.

The use of emulsifiers, although quantified via HLB score, is still largely empirically motivated. A combination of these for the use of double emulsions remains a field of high scientific interest with progressively larger scientific publications devoted to exploring in greater detail.

Appendix C: FAQ's & Helpful Tips

Q: Is it possible to encapsulate more than 1 droplet per droplet?

A: Yes, as shown below, this usually occurs at high flow rate ratios where the middle phase is flowing relatively faster than the inner phase. The inner phase undergoes droplet breakup as shown in the image sequence shown below.

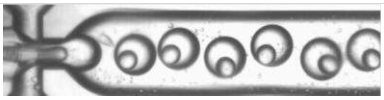
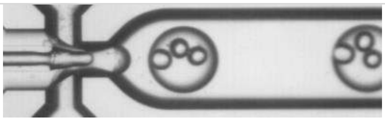
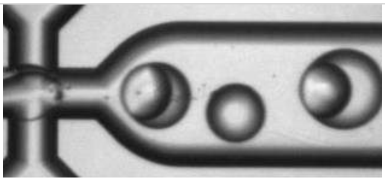
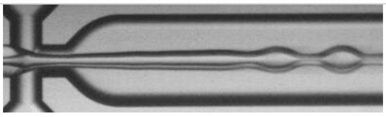


Time sequence images extracted from a video showing three aqueous droplets inside an organic fluid droplet, which in turn is surrounded by a continuous aqueous fluid. Fluid flow is from left to right.

Hazy appearance an optical artefact due to fast moving droplets captured at low frame rate.

Q: Despite a proper selection of flow resistors, is it still possible to get chaotic flow?

A: Yes, the below table shows some situations where double emulsions are not produced, and some remedial suggestions not involving chemistry changes.

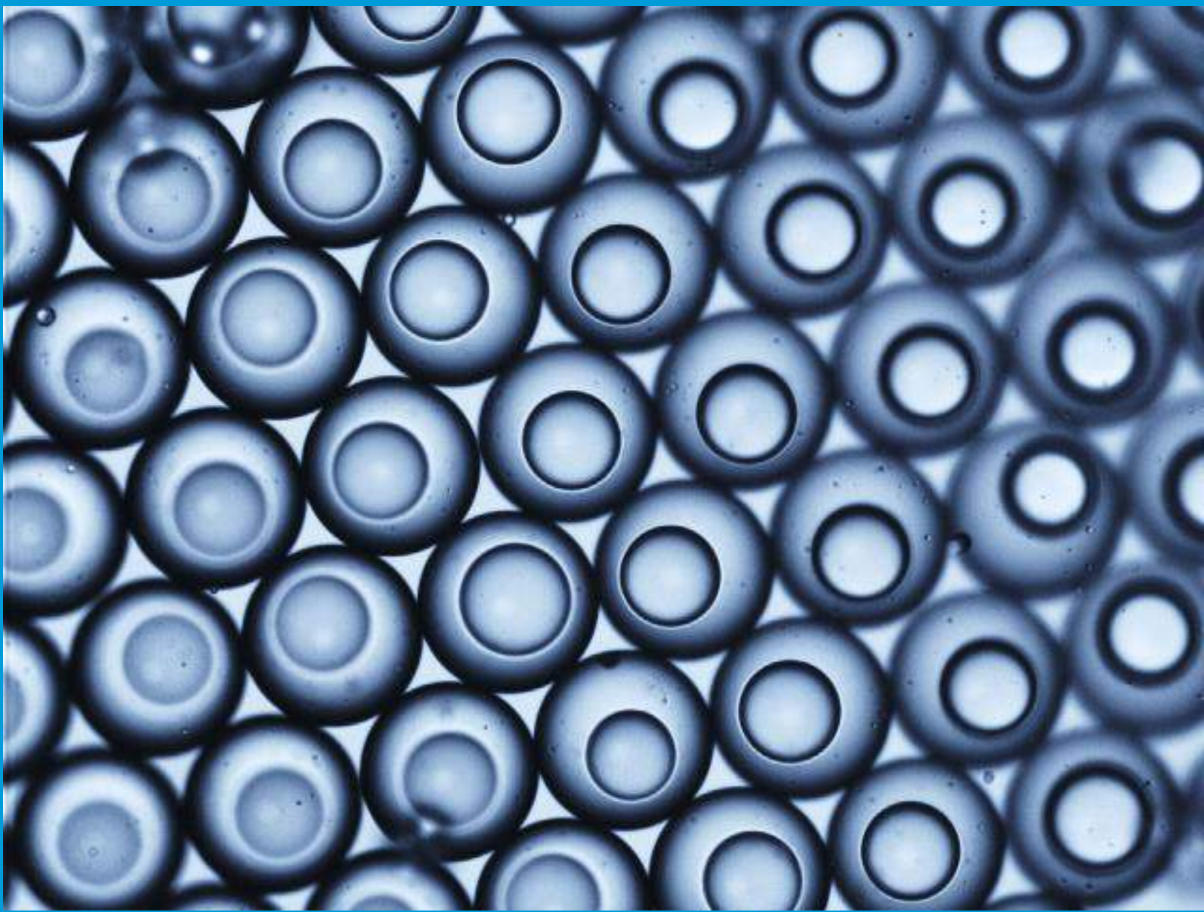
Outcome	Outcome	Possible mitigation
Double emulsions (1 in 1)		-
Double emulsions (many in 1)		Increase middle phase fluid flow
Missed droplets		Adjust flow ratios – Increase inner fluid flow
Inner fluid dripping, middle fluid jetting		Reduce middle fluid flow
Inner and outer fluid jetting		Reduce Inner and middle fluid flow, OR Increase outer fluid flow

IP License

Dolomite is a licensee of Japan Science and Technology Agency (“JST”) under JST’s microdroplet generation technology.

This enables our customers to purchase and use our droplet chips for R&D purposes without any restriction from this comprehensive IP family.

Contact us for more information about licensing this IP for your custom application or chip design.



The Dolomite Centre Ltd.
Unit 1, Anglian Business Park, Royston,
Hertfordshire, SG8 5TW, United Kingdom

T: +44 (0)1763 242491
F: +44 (0)1763 246125
E: info@dolomite-microfluidics.com
W: www.dolomite-microfluidics.com

Dolomite Microfluidics
29 Albion Place
Charlestown, MA 02129

F: 617 848 1211
F: 617 500 0136
E: salesus@dolomite-microfluidics.com
W: www.dolomite-microfluidics.com