



droplet microfluidics

for biology, food & cosmetics, drug discovery,
chemistry



Dolomite - a one-stop shop for microfluidic solutions

why choose Dolomite?

Dolomite offers a wide range of products for the production of highly monodisperse microfluidic droplets. These innovative products offer a range of benefits:

High monodispersity:

Microfluidic techniques offer extremely consistent size of droplets, particles or emulsions.

Wide range of fluids and droplet types:

Emulsions, particles, foams, gels, suspensions and sols can be made from aqueous, organic or fluorinated liquids and gases.

Rapid research or process optimization:

Parameters such as droplet size, flow rates, temperatures, mixing junctions, surface properties and order of additions can be quickly varied.

Straightforward scale up to production:

Conditions identified in the laboratory can be easily scaled up to a tonne per month.

Easy to use:

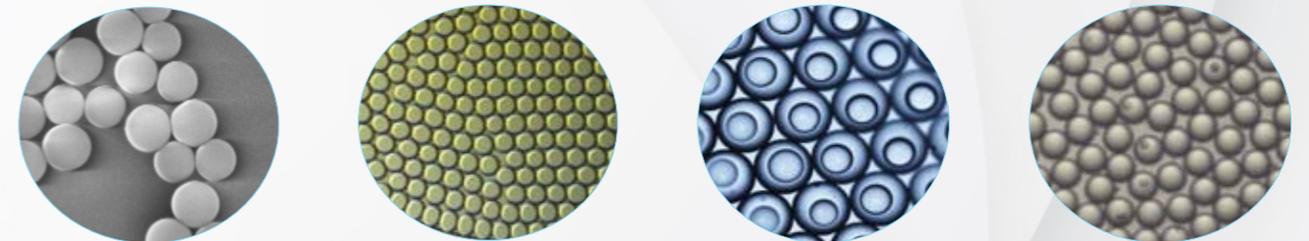
All of Dolomite's products are designed to quickly connect together without the need for tools.

microfluidic droplets

Microscopic droplets, particles and gas bubbles form some of today's most important products and experimental tools.

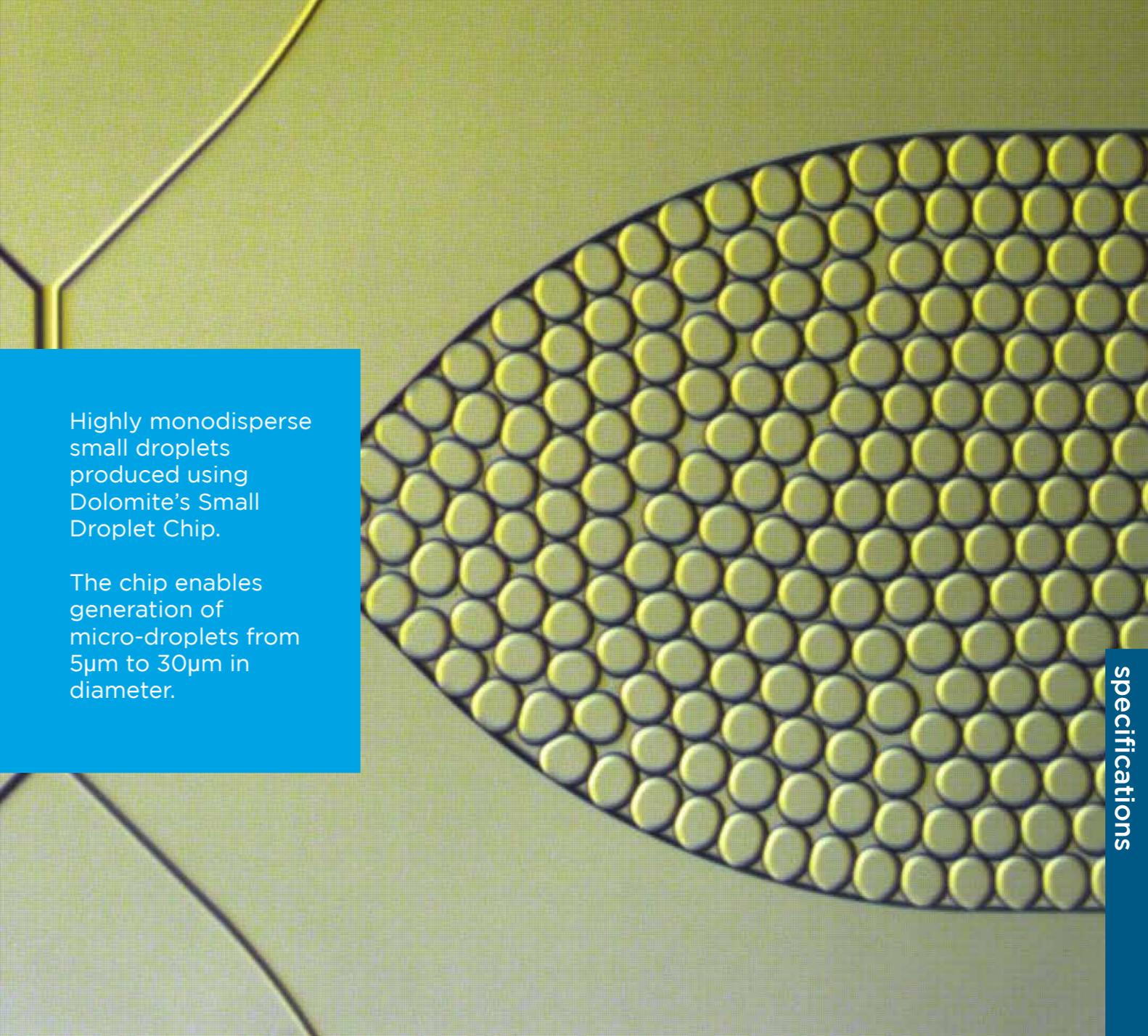
Applications for Dolomite's products include:

- **Encapsulation** of cells, DNA or magnetic beads for research, analysis and diagnostics
- **Droplet, emulsion, bubble or particle research**
- **Drug delivery** via polymer particles and drug formulation
- **Nanoparticles and polymer particles**
- **Bulk precision manufacturing** of emulsions and foams for foods and cosmetics
- **Protein crystallization**



specifications

Monodispersity:	1 - 5%
Size:	nm to 250 μ m
Throughput:	1 μ l to 30ml/min (1 tonne/month is 25ml/min)
Types:	Droplets, emulsions, double emulsions, encapsulations and Janus particles
Fluids:	Liquids (aqueous, organic, fluorinated) including solid suspensions and gases
Classes:	Emulsions, particles, foams, gels, sols and suspensions
Temperature control:	1°C to 300°C
Analysis:	Measure size, frequency and monodispersity
Surface coatings:	Hydrophobic: water-in-oil and oil-in-water-in-oil Hydrophilic: oil-in-water and water-in-oil-in-water Fluorophilic: water-in-fluorocarbon oil and fluorocarbon oil-in-water-in-fluorocarbon oil
Substrates:	Glass, quartz, polymer, customer PDMS chips can be used with our PDMS chip interface



Highly monodisperse small droplets produced using Dolomite's Small Droplet Chip.

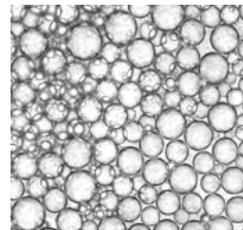
The chip enables generation of micro-droplets from 5 μ m to 30 μ m in diameter.

capabilities

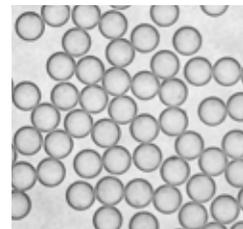
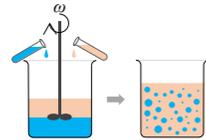
Dolomite products enable three types of droplet production methods: flow focusing, segmented flow and droplet on demand.

How to mix fluids to make the materials you need:

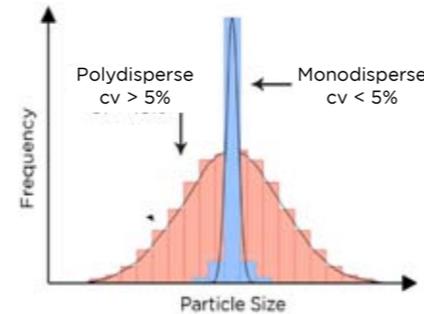
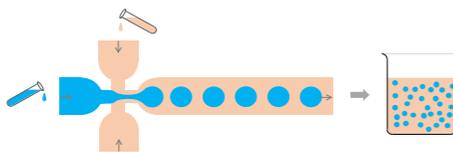
Material type	Dispersed phase	Continuous phase
Foam	Gas Bubbles	Liquid Medium
Solid Foam	Gas Bubbles	Liquid (later cured into solid)
Emulsion	Liquid Droplets	Liquid Medium
Gel	Liquid Droplets	Liquid (later cured into solid)
Sol / Suspension	Solid Particles	Liquid Medium
Solid Sol	Solid Particles	Liquid (later cured into solid)



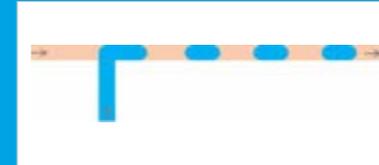
Batch method of emulsion production results in polydisperse droplets



Microfluidic continuous flow method results in monodisperse droplets

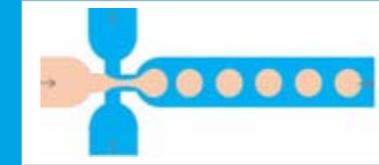


Segmented Flow



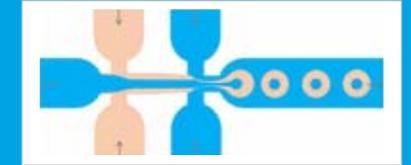
Forms slugs with size larger than junction size.

Droplets / Emulsions



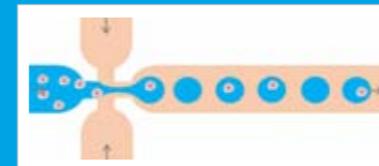
Forms droplets with a wide size range relative to junction size.

Double Emulsions



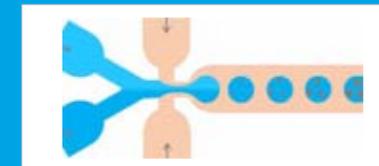
Forms droplets inside droplets over a wide size range.

Encapsulations



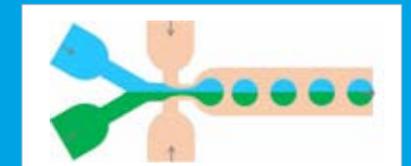
Placing one or a number of cells, particles, etc. inside the droplets.

Nanoparticles / Crystallization



Mixing of two streams, and subsequent isolation of reactants into droplets.

Janus Particles



Incomplete mixing of two streams, forming particles with heterogeneous surface property.

Droplet production is dependent on surface (hydrophobic/hydrophilic) and fluid interfacial tension. Shades of blue and green represent fluids (aqueous or organic liquid, and gas). Orange represents the other immiscible fluid.

After formation, droplets or particles can be processed by melting/freezing, solvent exchange, or photo/chemical polymerization.

R&D droplet systems

Dolomite offers a range of high-performance modular systems for production of highly monodisperse droplets, particles, emulsions, double emulsions or bubbles.

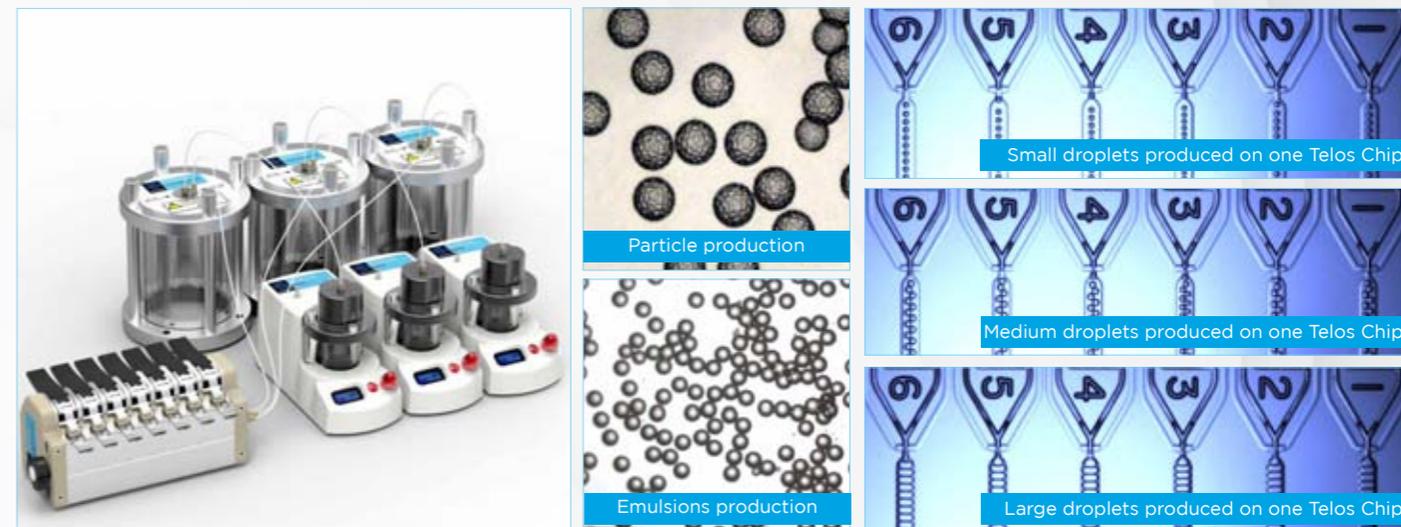


Benefits:

- **Excellent control:** Produce highly monodisperse droplets from nm to 250µm
- **Rapid research or process optimization:** Parameters such as flow rate, temperature, mixing junction, surface property and order of addition can be quickly varied and the effects analyzed and quantified automatically
- **Pressure based pumps (0 to 10bar):** The ultimate in smooth flow and control over droplet size

Telos[®] droplet production

Production of up to a tonne of highly uniform size 20µm to 150µm droplets, particles or emulsion a month. Ideal for scale-up, the system is modular and tool-free.



Benefits:

- **High-throughput:** Produce up to a tonne of highly monodisperse emulsions/month
- **Modular scalability:** One Telos clamp module allows a typical flow output of 3ml/min of droplets from 1 microfluidic chip with 7 junctions (scale up to 10 clamp modules i.e. 30ml/min)

droplets for biology

Individual cells, RNA or DNA molecules can be compartmentalized and optionally mixed with reagents such as lysis buffers and RT-PCR mix in tiny droplets, where each droplet behaves as a discrete micro-reactor. This enables analysis of many individual cells in populations, analysis of rare cells, high throughput sorting of libraries or single cell assays.

Isolating native antibodies or profiling T-cell receptors from blood samples

Natively paired antibody or T-cell receptor epitope binding sites can be isolated from samples by compartmentalizing individual cells with an RT-PCR mix; the amplicons from individual cells can be bar coded or linked by ligation or overlap PCR.

Compartmentalizing libraries for FACS sorting

Cells or expression libraries can be sorted by compartmentalizing individual cells or clones with a reaction mix, in small water-in-oil-in-water droplets that can be fed into a FACS machine.

High throughput RNA sequencing/expression profiling

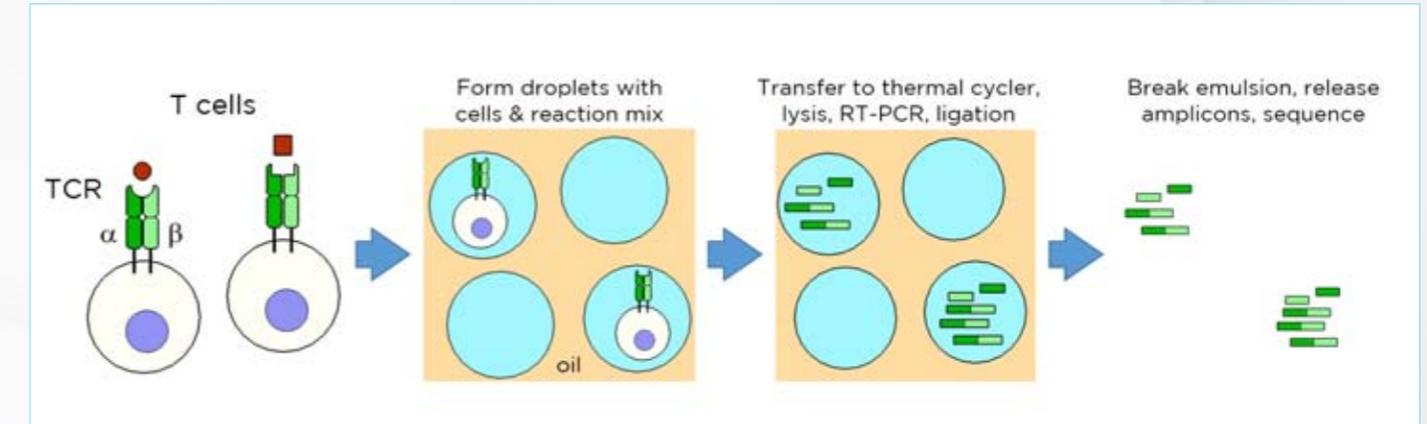
- The cDNAs from each cell in a population can be uniquely tagged by compartmentalizing each cell in a droplet with RT-PCR mix and a bar-coded bead.
- Libraries can be evenly amplified by emulsion amplification, where each droplet contains 1 template molecule or less.

Encapsulating cells in gel beads for cell therapies

Droplet chips enable encapsulating cells in gel beads that protect transplanted cells from the host immune system, while allowing nutrients to diffuse in.

Single cell-based assays in a highly reproducible micro-environment

Single cells can be compartmentalized in matrigel beads or with another cell, virus particle, labelling mix etc.



Case study: Abviro

AbViro develops new potential targets and therapies for a wide range of diseases by isolating complete functional antibodies from individual B or T cells, using a molecular barcoding technique.

"Most highly engineered, optimized and mature technology. Dolomite offers high quality pumps, flow sensors and microfluidics chips, all fully automated via their software. We can process in excess of a million cells per experiment, allowing us to obtain over 300,000 full-length, natively-paired antibodies from a single sample. This kind of throughput would be impossible with traditional methods."



Dr Adrian Briggs, Director of Molecular Biology R&D

droplets for chemistry

Highly monodisperse droplet technology benefits a range of chemistry related applications including nanoparticle synthesis, controlled crystallization, synthesis of polymer beads and biphasic reactions.

Nanoparticle synthesis

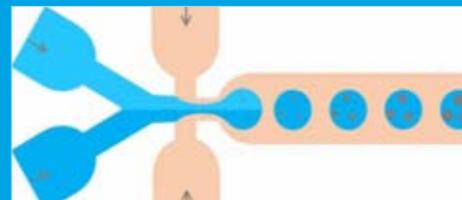
A wide range of nanoparticles, including core-shell and functionalized nanoparticles can be made from a broad range of materials including metals (Au, Ag, Pt, Ni, Fe, Co etc.), silica, organic materials and polymers.

Multi-step addition, temperature control and discrete control of the quantity of each reagent enables extremely consistent particle size.

Polymer Beads

Polymer beads such as PLGA, polystyrene and hydrogels can be synthesized with unrivalled size uniformity.

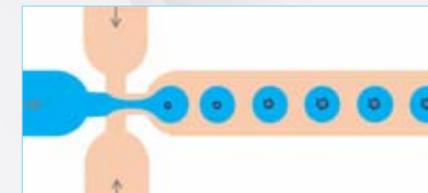
Typically a liquid phase (made up of one or many combined flow streams) is converted to uniform droplets in an immiscible liquid which are then polymerized by a range of techniques including photopolymerization, free radical polymerization, solvent extraction/displacement or melt cooling. This can be scaled to tonnes per month. Multiphase (e.g. gas filled) beads or particles with payloads can also be synthesized.



Controlled crystallization

Droplet technology offers narrower particle size distribution than traditional techniques such as milling or batch crystallization of bulk solutions.

By compartmentalizing a solution into identically sized droplets from $2\mu\text{m}$ (4fl) to $250\mu\text{m}$ (8nl) in an immiscible liquid, when crystallization occurs (e.g. activated by anti-solvent and/or cooling) the size of each crystal is tightly controlled.

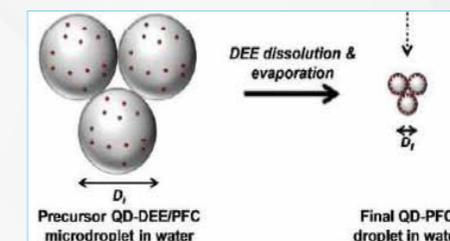


Biphasic reactions

Many chemical reactions are performed with two immiscible liquids. Microfluidic droplet technology offers an extremely high and reproducible surface area. Unlike batch processes, as this technology is scalable, reaction yields and impurity levels can be maintained from mg to tonne scale.

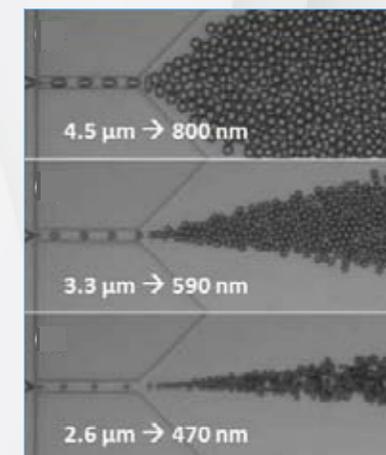
Case study: Nanoparticle production (solvent extraction)

The $14\mu\text{m}$ droplet chip was used to produce Quantum Dots by solvent evaporation from precursor microdroplets. Solvent removal from micron sized droplets results in sub-micron sized nanoparticles and is therefore ideal for production of new hybrid agents for medical imaging and therapy applications.



Images and source:

Department of Medical Imaging, University of Toronto

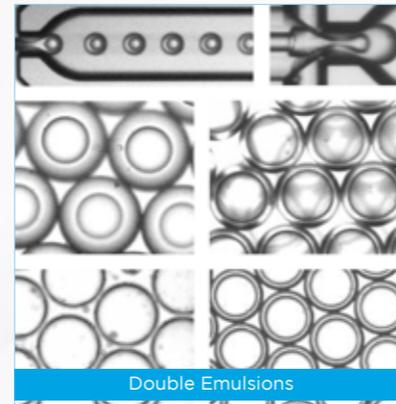


droplets for food & cosmetics

Droplet technology enables production of monodisperse particles, droplets, foams and emulsions with precise control of ingredients and sizes. Double emulsions with monodisperse outer and inner droplets are ideal for encapsulations of ingredients and novel formulations. Easy scale-up.

Microfluidics in food: new product design

- **Flavor/aroma enhancement:** Flavors can be encapsulated in droplet capsules with time controlled flavor release or different flavors/aromas created in a series of shells. Droplets can be precisely formulated and sizes controlled. Simple scale-up to kg/day.
- **Control of fat content:** Water droplets with an oil shell can be precisely engineered to tailor taste and product characteristics with lower oil and calorie content. Easy scale-up to kg/day for larger trials.



Typical food emulsions include: milk, cream, butter, coffee whiteners, margarine, mayonnaise, salad dressing, low calorie spreads, chocolate etc.

Encapsulations in cosmetics

Microfluidic encapsulations can protect/separate unstable (incompatible) ingredients or protect materials from oxidative degradation. Encapsulations can also be used for odour and taste containment in nutricosmetics or targeting of specific cells. The size, ingredients and monodispersity of particles, capsules, foams and emulsions can be precisely controlled enabling novel formulations. Ideal for development of face creams, hand creams, fragrances, make-up products etc.

Reliable water-in-oil-in-water double emulsions.

Droplets shown here are:

55 μ m droplets inside 200 μ m droplets

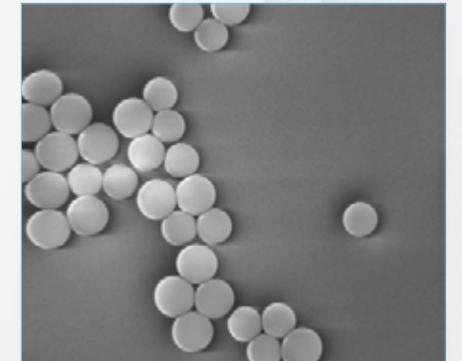
droplets for drug discovery

Dolomite's droplet technology enables production of precision engineered micro bubbles and complex particles with high control over particle size, monodispersity and ingredients. Easy scale-up to tonnes/month for trials and high value products. Ideal for drug delivery and those working with contrast reagents.

Particles and nanoparticles for drug delivery

It is possible to produce particles and micro bubbles e.g. suspension of solid particles with drug loaded inside, and is therefore ideal for localized drug release.

Dolomite's droplet technology enables precise formulations and ensures uniform particle sizes. Drug release rate may be varied by tailoring particle size. Easy scale-up to produce kg of product a day.



Contrast reagents

The solutions used for imaging in radiology, nuclear medicine, MRA and ultrasound contain air or gas micro bubbles which can efficiently reflect ultrasound beams used during investigations.

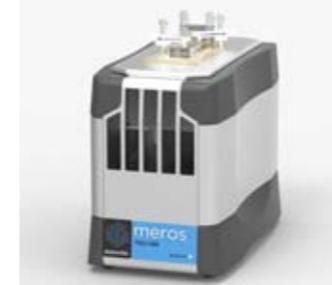
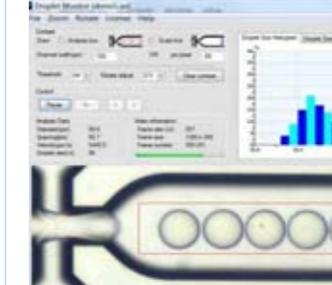
Droplet technology allows production of highly uniform micro bubbles with precise control over the size which improves product stability and quality, and ensures stable shelf life of microbubbles before and after injection.

Reliable particle production.

Particles shown here:

Monodisperse Fe_3O_4 particles of 10nm diameter.

Dolomite's technology

Pumps and Flow Sensors	Chips and Connectors	Droplet on Demand Technology	High Throughput Systems	Temperature Control	Specialist Droplet Chemicals	Analysis Software	Automation
							
<ul style="list-style-type: none"> • Ultra smooth flow • 0.07µl/min to 10ml/min • Chemically resistant • Up to 10 bar • Accurate • Closed loop flow control 	<ul style="list-style-type: none"> • Over 100 standard chip designs with various coatings, inputs, outputs, geometries, etch depths • Custom Chips • Quick, easy and reliable connectors 	<ul style="list-style-type: none"> • Generate droplets of up to 24 different samples and store up to 1000 droplets with sizes down to 25nl • Automated: software enables droplets on demand 	<ul style="list-style-type: none"> • Up to 1 tonne / month • 70 identical mixing junctions (7 junctions on one chip and up to 10 chips) • Precise flow control 	<ul style="list-style-type: none"> • Extremely accurate control of a fixed temperature from 1°C to 100°C, rapid temperature ramps or thermocycling • Microfluidic chips, slides, other devices 	<ul style="list-style-type: none"> • Bio-compatible surfactants and oils • For formation and stabilization of droplets • Wide temperature range 	<ul style="list-style-type: none"> • High speed camera microscope • Droplet Monitor Software measures droplets frequency, size and monodispersity 	<ul style="list-style-type: none"> • Software control • Control flow rate or pressure



Dolomite is the world leader in design and manufacture of high quality innovative microfluidic products. We offer:

- **Modular microfluidic systems, modules and components** such as pumps, chips, connectors, temperature controllers, sensors, accessories and software for analysis or automation.
- **Design, development and manufacture of custom-made components or modules**

Dolomite products are modular, easy to use, innovative and scalable and used in a wide range of applications in biology, drug discovery, chemistry, food, cosmetics and academia.

Dolomite is part of the Blacktrace group of companies, a world leader in Productizing Science® and has a worldwide network of offices and distributors.

www.dolomite-microfluidics.com



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