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Chapter

Advances in Droplet Microfluidics with Off-the-Shelf Devices and Other Novel Designs

Maxine Yew, Kaiseng Koh and Yong Ren

Abstract

For the past three decades since the dawn of the concept of scaling down fluidic processes and systems, various microfabrication techniques have been significantly explored and developed. Glass and elastomers, as first-generation microfluidic device materials, are still widely used, while other alternatives have emerged. We have seen a rise in novel and innovative device designs and fabrication in droplet microfluidics which enable easier and more cost-effective approach of generating droplets, such as the use of commercially available "off-the-shelf" components, plug-and-play modular devices, and 3D-printed droplet generators. This chapter aims to review some of these facile approaches for droplet generation and discuss the versatility and functionability of these designs for possible commercial formulations. Discussions of rationales for and challenges of the development of these conceptual devices are included.

Keywords: off-the-shelf, 3D printing, droplet generator, modular, parallelization

1. Introduction

Microfluidics defines the science and engineering of a small-scale fluid system. It is a study of design, fabrication, and operation of a system conducting fluids in microscopic channels of widths or diameters ranging from 10 to 500 micrometers (μm). Gañán-Calvo first introduced the use of micron-scale capillaries later established by Thorsen et al. who demonstrated the use of a simple T-junction microfluidic device to control the flow of immiscible liquids, forming monodisperse droplets [1, 2]. The manipulation of discrete fluid packets in microdroplets provides benefits in large reduction of reagent volume, size of sample, and the equipment [3]. This opened a completely new wave of interest in microfluidic systems in a broad range of fields such as biochemical, engineering, and pharmaceutical benefits from the advantages of small and precise.

Droplet-based microfluidics, one subcategory of microfluidics, focuses on the discrete volume creation with the use of immiscible fluids and allows the handling of fluids under confined spatial and temporal control. Applications of droplet microfluidics are largely distinguished into two aspects: droplet reactors for biochemical reactions and analysis [4] and droplet-templated material synthesis. The proverbial use of lab-on-a-chip (LOC) in various biochemical analyses is driven by the time and cost-efficiency of performing automated high-throughput analysis with small volume

of reagents, especially in the areas of genomic study, point-of-care (POC) diagnostic, drug discovery, etc. To date, only a handful of selected microchips have been commercialized [5]. Compared to conventional bulk methods, microfluidic techniques provide a power platform that enables the creation of highly controllable emulsion droplets in which the size, shape, and composition of the droplet can be manipulated. This allows the synthesis of functional droplets such as microcapsules for drug delivery and cell encapsulation, microparticles, and various types of Janus particles.

With the rapid development in microfluidic systems and its applications, different selections of techniques and materials are increasingly accessible for fabrication of microsystems (especially for those who are just starting out in the field). Some of these fabrication techniques require high-priced tools and machineries with skilled workers to produce intricate designs of microchannels and microchambers in which droplets are generated and manipulated, while simple assemblies of microdevices with commercially available components have also been reported. To produce emulsions, which are droplets in immiscible phase, the selection of materials with compatible surface wettability is important.

The huge potential of droplet-based microfluidics has stimulated rapid development of flexible platforms to generate highly monodispersed droplets with diverse structures. The recent years see a soaring number of researches and publications on life sciences and material synthesis applications based on microfluidic approach. Likewise, there has also been a rise in novel and innovative device designs and fabrication in droplet microfluidics which supposedly enable easier and more cost-effective approach of generating droplets, such as the use of commercially available "off-the-shelf" components, plug-and-play modular devices, and 3D-printed droplet generators. While this signifies a positive outlook on the development of microfluidics, the ultimate reception of the technology depends primarily on the end users. Different applications where microfluidic approach is employed have different prerequisites for commercialization, for instance, for material synthesis such as catalyst preparation or drug formulations, high throughput is expected to generate sufficient materials, whereas for chemical/biological assays, throughput might not be a focal criterion, instead development of chip-to-world interfaces for stable connection to analytical units would be crucial. Up until now, the successfully commercialized microfluidic products are mainly for POC diagnostics, genotyping and sequencing, and other biomedical-related applications [5].

2. Summary of existing droplet-based microfluidic technology

As the standard material interface used in the field of microelectronics which pioneered microfluidics, glass and silicon are naturally the first-generation materials for microfluidic devices [6]. Originally, glass and silicon substrates are processed via standard photolithography which mainly comprises three steps: (i) lithography or pattern transfer onto a substrate, (ii) etching of microchannels, and (iii) lastly bonding to create an enclosed structure [6]. The process of photolithography has been well documented. Devices fabricated via lithographic methods generally have quasi-two-dimensional (2D) planar flow [7]. Umbanhowar et al. and Utada et al. both introduced three-dimensional (3D) co-flow and hydrodynamic flow-focusing devices with tapered capillaries to produce monodisperse single and multiple emulsions, respectively [8, 9]. Both dispersed and continuous phase fluids meet in parallel streams in the co-flow geometry, while for the flow-focusing device, the dispersed and continuous phases are introduced in opposite directions, whereby the flow is eventually focused through an orifice. By combining both geometries, monodisperse multi-emulsions could be generated via single-step emulsification

(see **Figure 1**). 3D axisymmetric flow-focusing devices circumvent the wetting of channel walls by the dispersed phase as the effect of wall channel is of less concern and droplet formation frequency is higher [10–12]. Microgrooves can also be formed on glass substrates via deep reactive ion etching (DRIE). Nisisako and Torii have produced a planar synthesis silica glass chip with 256 parallel generators formed by DRIE which could produce emulsions up to a rate of 320 mL/h [13, 14]. However, micromachining of glass is very expensive, and it gets even more difficult and costly to fabricate elaborated and complex designs on a glass chip.

Soft lithography, an extension from conventional photolithography, allows the lithographic master to be used for rapid prototyping of elastomeric material such as polydimethylsiloxane (PDMS). PDMS has been and is still a popular option because it is cheap and elastic and it is easy to work with high flexibility [15]. Its intrinsic properties such as high permeability to gases and optical transparency have even greatly extended its use in biomedical researches such as cell culturing and tissue analysis [16]. PDMS devices (see **Figure 2**) manufactured via soft lithography are inherently 2D; however, fabrication of 3D microfluidic devices is now possible with advances in 3D printing, whereby 3D PDMS microchannel can be casted from 3D-printed molds [17].

With the vast selections available, researchers often establish their choices for the development of microfluidic systems based on the applications, material compatibility, ease of fabrication, as well as the start-up cost incurred; many methods/techniques remain underdeveloped or ceased to be developed presumably due to high start-up cost. While glass and PDMS have been extensively used in pioneering many microfluidic researches and applications, the known disadvantages associated with the fabrication and use of these materials have often been deliberately overlooked by the microfluidic community. As PDMS is inherently hydrophobic, small hydrophobic nonpolar molecules tend to be absorbed into the polymer, which could significantly disrupt the microenvironment at which biological studies are carried out [15]. Economy-wise, it would be very costly to work with glass due to laborious procedures and difficulty in reproducing, while expansion of PDMS for industrial work will be less viable. Apart from glass and PDMS, plastic has also been a popular option and one that is believed to play a major role in translating microfluidic research into commercialized technologies [19]. There has been an increasing interest in developing materials such as polymethymethacrylate (PMMA), polycarbonate, and cyclic olefin (co)polymers through microfabrication techniques such as hot embossing, injection molding, micromilling, and stereolithography [20, 21]. Plastics are more rigid and hence more collapse resistant than PDMS, and they generally have good compatibility for biological applications [19].

Hot embossing and injection molding are both replicating techniques akin to soft lithography, with the use of thermoplastic materials. With hot embossing, a thermoplastic film is patterned against a master, and a cast is formed as the molds

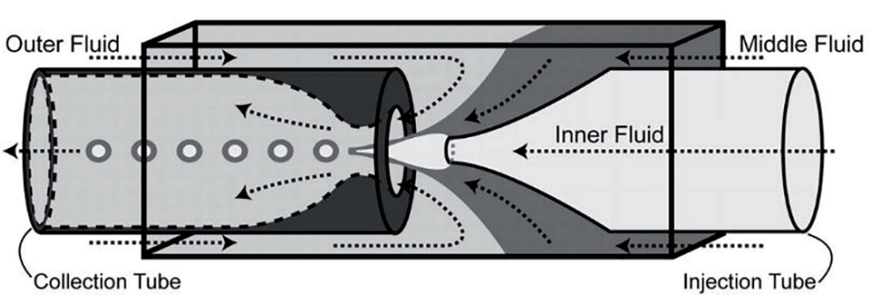


Figure 1.
Glass capillary microfluidic device for double emulsion formation through coaxial jet [9].

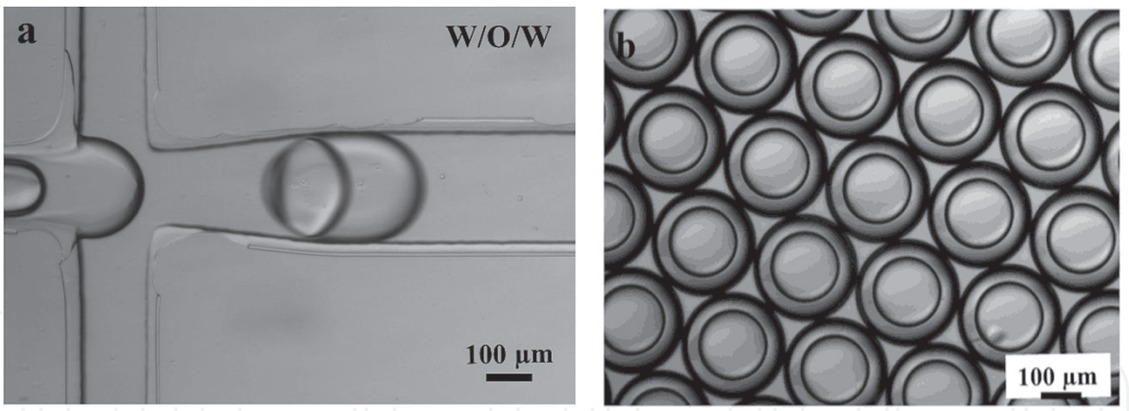


Figure 2.
Double emulsions produced from a PDMS device replicated via soft lithography. Part of the device is subjected to plasma treatment to render it hydrophilic. (a) Optical image of a double emulsion forming at the second junction of device. (b) Double emulsions collected with high uniformity. Reproduced from Ref. [18] with permission from the Royal Society of Chemistry.

are heated and compressed [22]. Injection molding involves the heating and subsequent injection of a thermoplastic melt into mold cavity, after which the cast will be removed from the mold once cooled down. While the resolution of molds and casts for both methods is subject to the methods used to make the mold inserts, especially complex three-dimensional structures, such replicating techniques are promising for rapid prototyping of microdevices. Micromilling, which has been a less popular alternative compared to mold replicating, is a conventional machining approach of incising features on workpieces. Advances in the milling technology now allow 3D computer-aided design (CAD) models to be prototyped on automation through computer numerical control (CNC) mills with microscale resolution [19]. Micromilling can also be used to fabricate molds to be used in replicating devices.

While these microfabrication techniques are more established now than two decades ago, ongoing researches are directed at reducing the cost of the prototyping techniques with cheaper materials. Currently, hot embossing and injection molding are limited to thermoplastics only, while the main concern for micromilling would be whether the quality of micromilled devices would suffice for practical use.

3. Some novel and innovative designs of droplet generators

3.1 Off-the-shelf devices

With rapid development in droplet emulsification, there has been much consideration in the use of "off-the-shelf" devices. While the term "off-the-shelf microdevice" might be ambiguous and may refer to already commercialized microchips, here it is defined as droplet generators assembled using commercially available components. Some of these components include medical dispensing needles, laboratory tubing, and tiny plastic fittings (such as ferrules and flanges) that might have been used as universal fluidic fittings or connectors to, for instance, laboratory analytical units. These easily assembled 3D devices are seen as cheap yet practical alternatives to conventional droplet generators requiring laborious effort to be fabricated. Simply said there could be no need for lithographical pattern transfers, microforging of fine glass capillaries, or any other hefty microfabrication units for the synthesis of these devices. Such robust and disposable devices from quick assembly of commercially available components are also useful and cost-saving when hazardous experiments are conducted [23]. Unsurprisingly, there have been

some publications that explore and incorporate the use of such droplet generators for production of functional materials such as microcapsules for drug delivery or gas sorption [24, 25]. Apart from being highly cost-effective and easy-to-make, some have reported that their off-the-shelf devices could also be easily disassembled for cleaning and there is also higher flexibility in droplet generation as the device can be reconfigured for desired formation [26].

Figure 3 shows the different devices assembled with components from commercial microfluidic sources, IDEX Health & Science. In **Figure 3a**, a 3D microfluidic nozzle is formed using a micrometering valve assembly and other fluidic fittings in an effort to focus and inject particulate samples into a downstream fused silica microfluidic device [27]. A silica capillary with a cone shape tip is used as the delivering nozzle and is sealed to the microferrule with a 5-min epoxy. **Figure 3e** and **f** shows a capillary microfluidic device with two polyetheretherketone (PEEK) chromatography tees, while **Figure 3d** shows a micro-cross droplet generator with high-pressure PEEK adapters [26, 28]. Microferrules and female nuts are used to secure the capillaries in place. According to Benson et al., the device can produce both oil-in-water (O/W) and water-in-oil (W/O) emulsions by just flushing with ethanol before the formation of the other, and the device is also reusable and could be disassembled for cleaning. The tips of two glass capillaries are flamed to create two orifices: one for the injection of the inner fluid and the other for the focusing of the flow. With the flamed-tip design, there is no need to modify the wettability of the capillary, allowing changeable formation of O/W and W/O. The distance between the orifices of the two aligned capillaries can also be adjusted, and the flow regime in the device changes even when the flow rates are maintained. Wu et al. compared the synthesis of droplets in the micro-cross droplet generator to that from a planar PDMS chip having a similar geometry. The former has a higher droplet formation frequency due to faster 3D fluid thread collapse than in the 2D flow. The micro-cross droplet generator is also able to operate under high flow pressure of up to 400 psi [28].

Steinbacher et al. demonstrated an assembly of a simplified mesofluidic device entirely from off-the-shelf components, small-diameter tubing, barbed tubing adapters, and needles, into droplet-forming devices and particle concentrator [23]. The readily available components can be arranged into a T-junction

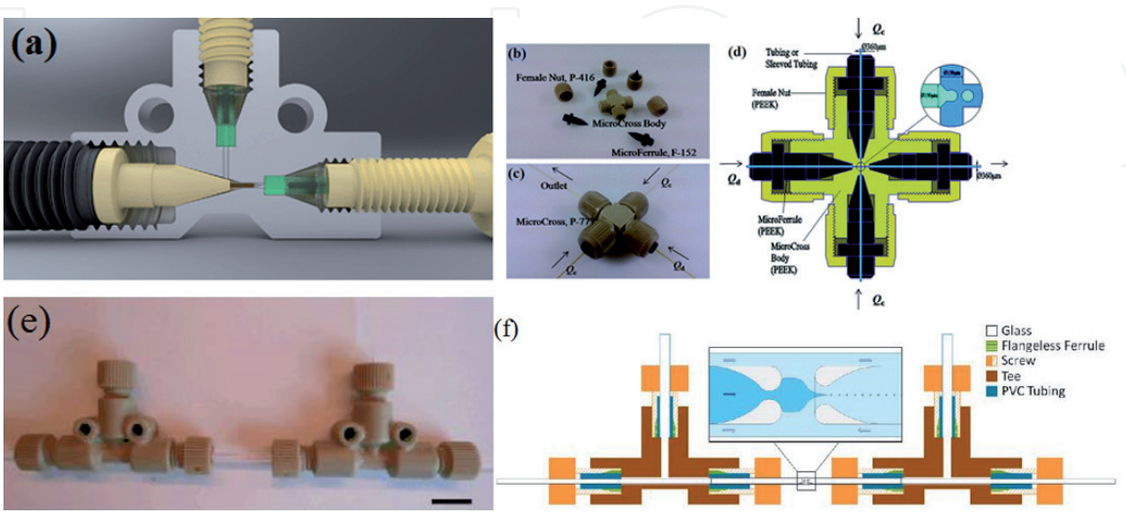


Figure 3.
Microfluidic devices made from off-the-shelf components from commercial sources. (a) A 3D microfluidic nozzle for focusing and injecting of particulate samples. (b–d) Off-the-shelf components and the assembly of a micro-cross droplet generator. (e and f) Image and schematic of a reusable modular glass capillary device assembled from commercial materials. Scale bar = 1 cm. Reproduced from Refs. [26-28] with permission from the Royal Society of Chemistry.

device or a flow-focusing configuration, and the formation of monodisperse droplets, microcapsules, and Janus particles has been reported to be successful, with the results comparable to those synthesized with more complicated devices. Li et al. also reported the assembly of yet another entirely off-the-shelf microdevice with flexible designs [29]. The device is mainly composed of dispensing needles of different sizes (60–1550 μm) and assembled with mini tee- and cross-links as shown in **Figure 4**. The stainless-steel dispensing needles are arranged and aligned to form microchannels for the flow of the immiscible phases. The assembling of the device is made using plastic tubing as well as UV curable glue. Monodisperse single and multiple droplets have been successfully formed using the needle-based microdevice by reconfiguring the device. The size of the droplets can be controlled by varying the needle used as well as the flow rates of each phase.

The past few decades have seen a myriad of microfluidic device designs, yet the innovative assemblies of off-the-shelf devices have shown that the basic modalities of a droplet generator could be substituted by commercially available components, tee-link for a T-junction, cross-link for a cross-channel, dispensing needles and glass capillaries as the inlet and flow channels, and other structures that could also be replaced by commercially available parts, which greatly reduce the fabrication cost to as low as 3USD per device. Assemblies of such devices have also shown that without sealing the droplet generators onto rigid substrates, the devices are recyclable and can be reconfigured for versatile droplet generation. The development of such microdevices has seemingly negated the need for complicated microfabrication techniques such as those listed previously. However, the need for manual assembly as well as the difficulty in aligning glass capillaries remains an issue in the fabrication of these devices as most of them still adopt the use of glass capillaries, especially when nontransparent fittings are used, it poses an obstacle for clear observation of droplet formation. Alas, there has not been many further researches reported following successful demonstrations of the use of these devices, and it is questionable if these devices would stand any chance to be commercialized. To the best of the author's knowledge, there has yet to be any work reported on the parallelization of off-the-shelf devices. In the meantime, such devices remain a short-term solution for preliminary droplet generation studies and a conceptual proving tool for new droplet-based applications. Nonetheless they would be useful for applications in detection or quick analyses, given their versatility to be connected or integrated to other existing units.

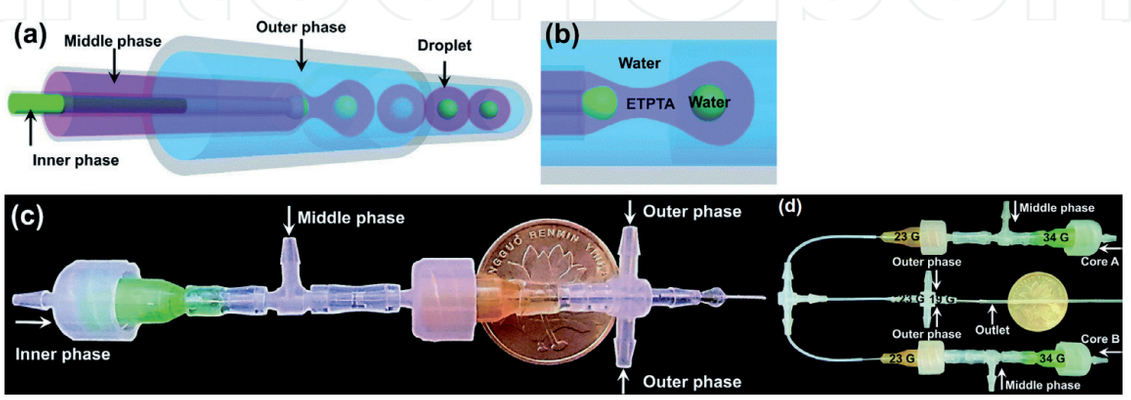


Figure 4.
(a) Schematic illustration of generation of double emulsions from needle-based coaxial microfluidic device. (b) Clear depiction of production of W/O/W emulsions. (c) The assembly of the needle-based device with a coin for scale. (d) Extended configuration of needle-based microdevice for complex emulsion production. Reproduced from Ref. [29] with permission from the Royal Society of Chemistry.

3.2 3D-printed devices

Additive manufacturing (3D printing) has been vastly adopted in fabrication of microfluidic devices with the advance of the technology in generating structures at increasingly high precision. 3D printing is a layer-by-layer manufacturing technology that now allows an extensive range of materials to be printed, such as various types of plastics and even glass [20, 30]. As is it largely automated and assembly-free, rapid prototyping can be achieved for microdevices. There are different types of 3D printing techniques, but they are primarily categorized into (i) extrusion-based 3D printing, (ii) stereolithography, and (iii) multijet (or polyjet) modeling printing [17]. 3D printing of microfluidic devices with elaborated and complex designs is now possible with the advances in the resolution and accessibility of 3D printers. In this section, an emphasis is given to 3D-printed modular devices, to introduce and highlight the versatility of droplet generators with "plug-and-play" functionality, which could be a good solution for chip-to-world integration and development.

Vijayan and Hashimoto developed 3D-printed fittings to form axisymmetric flow-focusing droplet generators with other readily available materials such as needles and elastic tubes [31]. While monolithic 3D-printed device is now possible with the rapid development in 3D printing technology, the authors have opted to print the device in parts and assemble with other commercially available parts, as they claim that this gives more customizability to the device's configuration, allowing for the generation of higher order and complex emulsions. Akin to the off-the-shelf needle device by Li et al., commercially available dispensing needles of varying inner diameters (60–250 μm) are used to produce droplets of a larger range of sizes, while for fully 3D-printed microchannels, the minimum channel features achievable are a few hundred micrometers [32]. Multiple emulsions and Janus particles can also be formed by connecting the device in series or incorporating a 3D-printed branched Y-channel such as that shown in **Figure 5g**.

For stereolithography and polyjet 3D printing, post-processing is needed to remove support materials or nonpolymerized resins from narrow channels; and it is even more challenging and time-consuming to do so for monolithically printed devices [31, 32]. Modularly printed microfluidic devices, however, allow easy removal of uncured materials and surface treatment onto different modules to facilitate generation of complex emulsions, and external active components may also be incorporated to the device as individual modules. Such modular plug-and-play units would also be useful in chip-to-world interface to existing systems requiring microfluidic solutions. Many have produced comprehensive reviews on the advances of 3D-printed devices, including works on plug-and-play modular devices, and the works included in the following discussion merely demonstrate the potential of 3D printing in microfluidics and hence are far from exhaustive.

Ji et al. presented a modular multimaterial 3D-printed device that allows both passive and active (pneumatic control) generations of various emulsions [11]. Three modules have been printed, a function module, a T-junction module, and a co-flow module, of which at least two modules are needed for the assembly of a functional device. There are three switchable modes for the function modules, namely, single-inlet and dual-inlet modules, depending on the type of emulsions to be generated or a pneumatic control unit (PCU), for active control of droplet generation by controlling the deformation of the flexible channel. A multimaterial polyjet 3D printer is used to print the PCU module which consists of both elastic (orange) and rigid (gray) parts, as indicated in **Figure 6a**, while the T-junction and co-flow modules are printed with a stereolithography printer using a clear resin. Surface treatment is carried out on individual modules to render the surface hydrophobic/hydrophilic. **Figure 6d–f** shows passive generation of single and multiple emulsions in the differently configured device. Likewise, single and double emulsions can be generated by

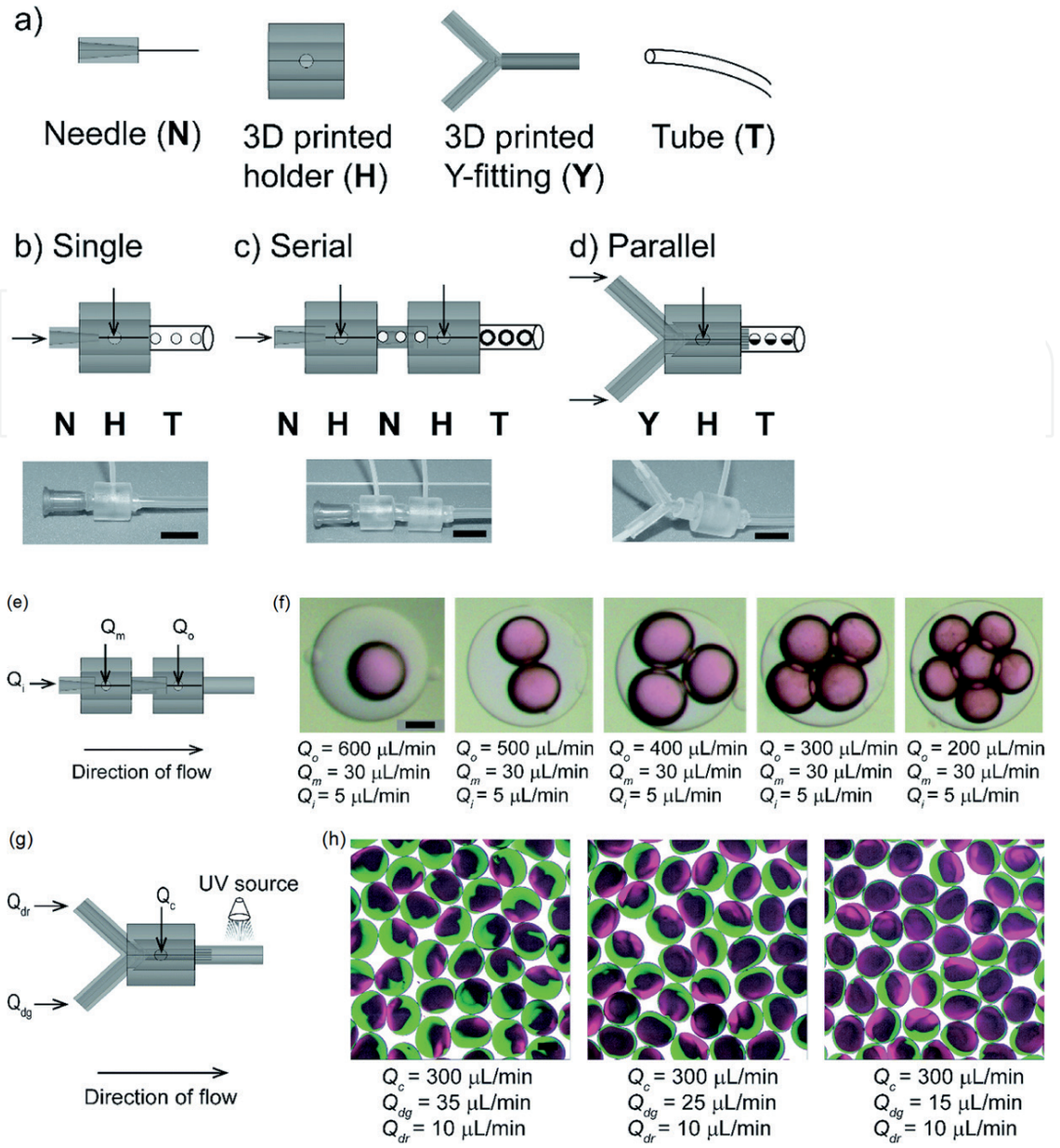


Figure 5.
(a) 3D-printed modules and fittings for the fabrication of microfluidic axisymmetric flow-focusing device: needle (N), 3D-printed holder (H), 3D-printed Y-fitting (Y), and tube (T). Schematics and optical images of (b) a single flow-focusing device, (c) serially connected flow-focusing devices to produce double emulsions, and a (d) flow-focusing device with a Y-shaped parallel laminar flow to produce compartmented particles. Scale bar = 10 mm. (e) a schematic illustration of serially connected flow-focusing devices for producing double emulsions. (f) W/O/W double emulsions with varying numbers of inner droplets. Scale bar = 600 µm. (g) Schematic illustration of production of bi-compartmented Janus particles with a Y-channel as inlet. (h) Optical micrographs of produced compartmented particles at different flow conditions. Scale bar = 300 µm [31]. Published by the Royal Society of Chemistry.

replacing the single—/dual-inlet module with a PCU, and under different applied air pressure, the flexible channel undergoes deformation through pneumatic excitation, and regimes of unstable and stable droplet generations are identified. The modules are connected through snap-fit joints printed to the modules with an O-ring, and no leakage is detected during the experiment even at a pressure of 4 bar.

Song et al. also fabricated a modular microfluidic system that allows both passive and active generation and manipulation of complex emulsion droplets [33]. Various modules such as inlet/outlet, I-junction, Y-junction, co-flow droplet generator, mixer, and a module containing electrode are printed with an i3DP printer with clear transparent UV curable polymer; however, the visibility of the modules is slightly reduced

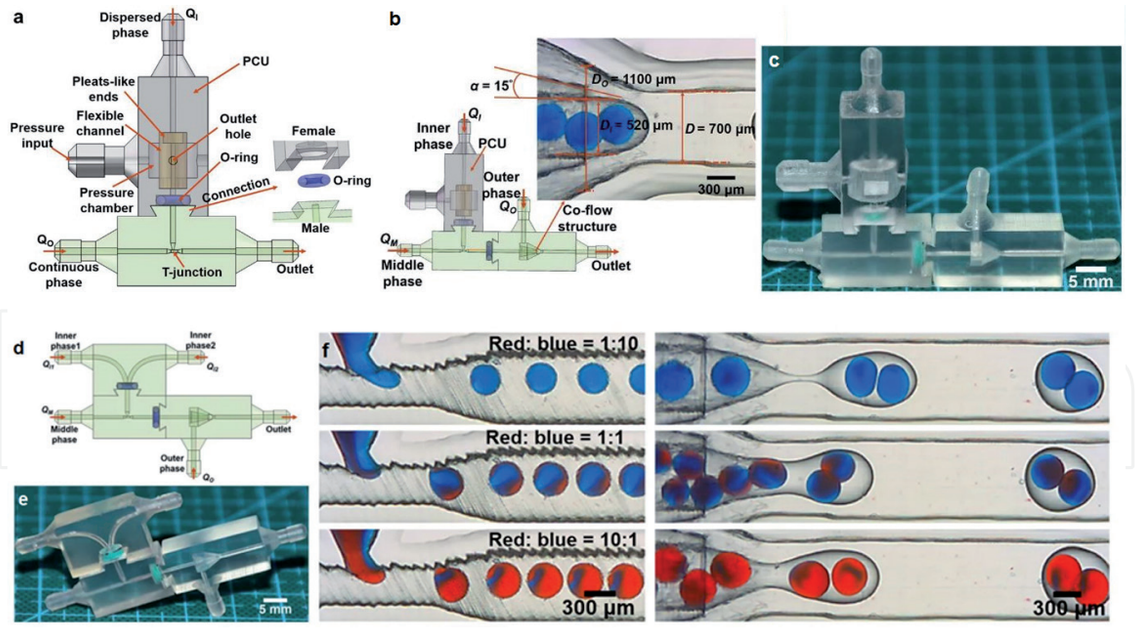


Figure 6.
3D-printed modular device. (a) Schematic of a single droplet-generating pneumatic device consisting of a PCU and a T-junction. (b and c) Schematic and optical image of a pneumatic device for generation of double or multicore emulsions. (d and e) Schematic and optical image of modular device with dual inlet. (f) Frames from high-speed recording showing complex emulsions produced via dual-inlet device [11].

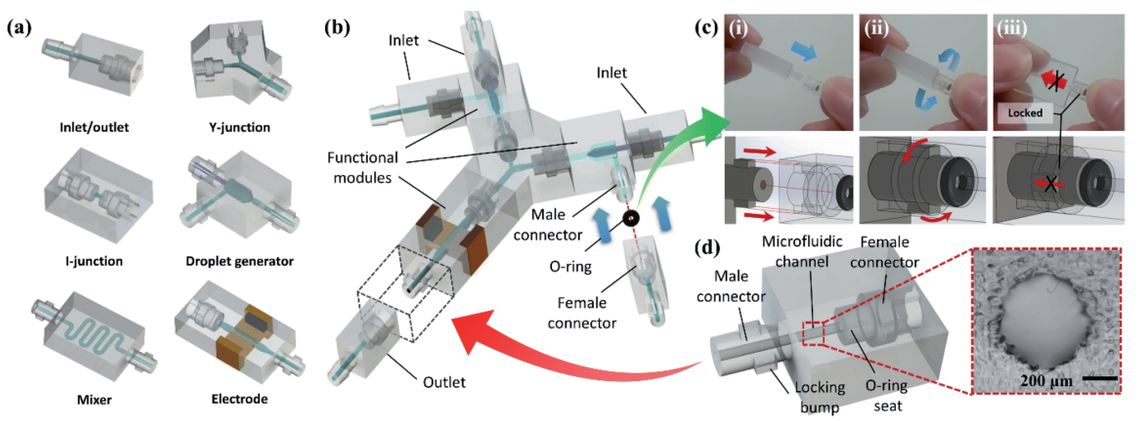


Figure 7.
Schematic of 3D-printed modular microfluidic system. (a) 3D-printed modules of different functions and structures. (b) A full assembly of the modular device. (c) The design of the interlocking male and female connectors. (d) Male and female connectors printed on each module [33].

due to surface roughness. The modules have interlocking male and female connectors that secure the assembly, and an inherently printed O-ring groove around the female connectors circumvents the leakage around the joint. An assembly of all the modules into an operative device is depicted in **Figure 7**. When the generated droplets reached the electrode module, they experience an electric field in a direction perpendicular to the flow direction. The shape of the droplet is distorted as an effect to the electrohydrodynamic flow patterns within and outside the droplet. Again, by reconfiguring the device, versatile range of droplets has been formed such as alternating droplets and single- and dual-core double emulsions. Under the influence of the electric field, the droplets are subjected to electrocoalescence to form Janus structure.

Unlike other methods, 3D printing is an additive technique, and 3D parts are formed layer by layer without requiring molds. A variety of 3D printing methods has been developed; likewise, a wider range of choices of polymer-based printing materials are available, although some are proprietary materials limited to

certain printing techniques. At present, 3D-printed devices are limited by the minimum achievable channel dimensions, subject to the printing resolution. The printing time of a device is also subject to the complexity of its design structure. Nonetheless, given the current development trajectory in additive manufacturing, there is high anticipation on 3D printing to resolve challenges with current existing microfabrication techniques such as high start-up cost, low channel resolution, and manual assembly of devices. The demonstration of plug-and-play modular devices is believed to be able to partly resolve the long-standing chip-to-world issues.

4. Droplet-based microfluidics: now and then

Droplet microfluidics is an enabling platform that is now widely recognized and adopted in many research disciplines. The past few decades have seen a rapid evolution in microfluidic-based technologies, especially in contributing to life science-related researches and gradually into material sciences. Much could be benefitted and have been realized from the subscale world of micros and nanos, attributed to rapid analyses and fast reactions, high precision, and good control of droplet size and compositions. Progressively, droplet-based platforms have been used for the synthesis of functional materials such as drug delivery vehicles and nanomaterials [34]. Conversely, the low production rate of droplets at 0.1–10 mL/h hinders the extensive use of the technology for high-volume production [35]. The direct solution to addressing low throughput of droplets is to increase the number of droplet generators to scale up production of droplets within a single chip.

4.1 Microfluidic emulsification: toward parallelization

Such effort to scale up the production of chip-based emulsions has been reported as early as 2008 by Nisisako and Torii who demonstrated parallelization of up to 128 and 256 droplet generators on planar glass chips to achieve throughput of 128.0 and 320.0 mL/h of Janus droplets and single emulsions, respectively [14]. Microgrooves are etched onto synthesis silica glass substrate by DRIE to form different droplet generator geometries such as cross-junction, Y-shape co-flow, and even three-consecutive cross-junctions, joint in a circular manner for the production of various emulsions [13, 14]. The etched chip is sealed with another glass substrate, and the microfluidic chip is mounted on a stainless-steel holder connected to the inlets of different liquids. Some of the designs are illustrated in **Figure 8**, while **Figure 9** shows the arrangement of commercialized modules sharing a single set of infusion pumps, for generation of Janus microparticles of a few hundred kilograms per month [36].

Other parallelization devices have also been reported, especially for mass production of single-phase emulsions. The channels in the parallelization devices are commonly distributed in a ladderlike geometry, in a treelike branched geometry, or in a row, while different layers are needed for the introduction of all liquid phases through through holes to be distributed into the microchannels [35, 36]. Apart from DRIE, parallel channels can also be micromachined onto PMMA substrate, replicated onto PDMS via lithography, or 3D printed [37, 38]. A PDMS millipede device is also reported, with more than 500 nozzles arranged in 2 rows, and droplets are formed through the nozzles and break under static instability [39]. Jeong et al. demonstrated the mass production of W/O emulsions at kilo-scale using 1000 parallel flow-focusing drop generators arranged in a 20 × 50 dense array on a PDMS device which is currently the highest degree of parallelization ever achieved (see **Figure 10**) [40]. Currently only Nisisako's team has demonstrated mass-production of Janus

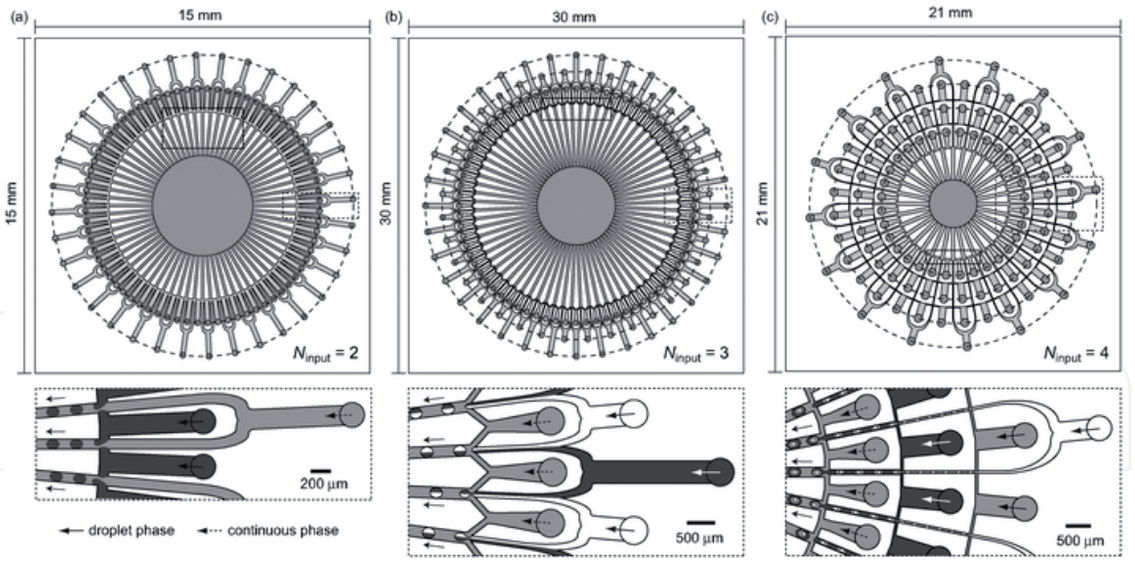


Figure 8.
Designs of glass microfluidic chips with parallelized channels in circular arrangements. (a) 144 cross-flowing droplet generators on two concentric circles, (b) 72 droplet generators on three concentric circles, and (c) 32 emulsion generators in four concentric circles producing triple emulsions. Reproduced from Ref. [13] with permission from the Royal Society of Chemistry.

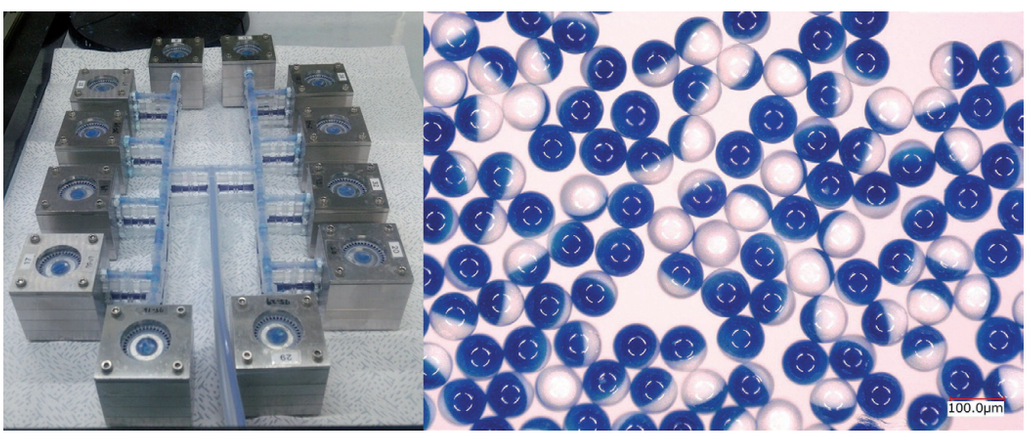


Figure 9.
Parallelized devices are arranged in series to further scale up the production of Janus particles. Reproduced with permission [36].

particles for commercial applications; however, there is no other information on the status of the parallelized device, whether the technology has been commercialized.

4.2 From "proof of concept" to commercialization

Inkjet printing is a classic example of commercialized microfluidic application to date, having been developed in the 1950s and largely commercialized and manufactured in the 1970s for digital image printing, through impelling droplets onto papers. The inkjet technology is subsequently adopted as a patterning tool for material deposition onto a wider range of substrates, for applications such as direct printing of electronic and optical devices [41]. More recently, studies have been conducted on the synthesis of microparticles via emulsion solvent evaporation following inkjet printing of droplets on substrates [42]. Following the debut of inkjet printing, notably only a limited number of microfluidic applications successfully made their way into the market in the following years, mainly in the areas of microfluidic genotyping and POC diagnostics. Chin et al. and Volpatti et al. summarized the commercialization of

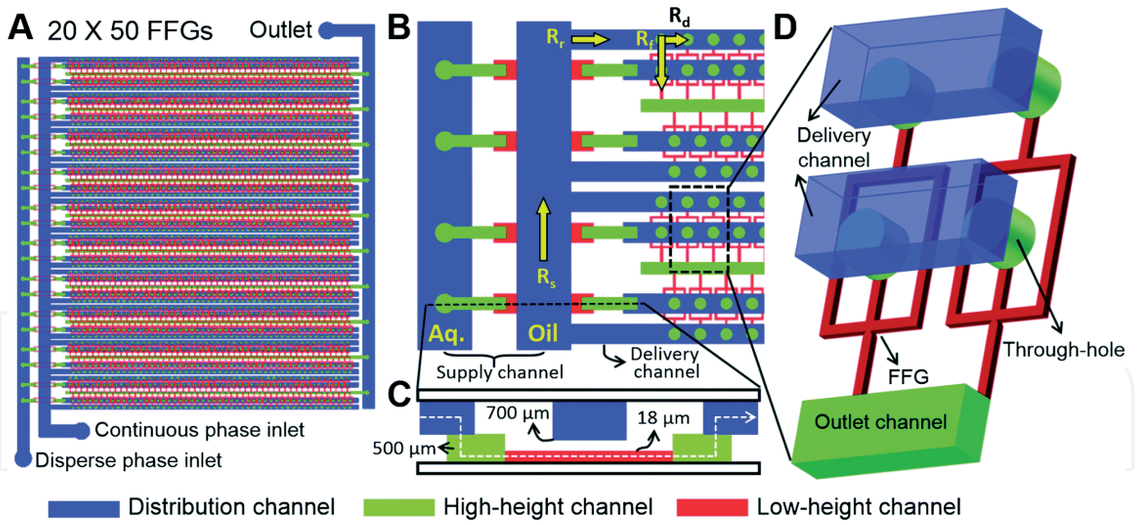


Figure 10.
Schematic diagram of a PDMS parallelization device. (A) the channels are arranged in a 20 × 50 array. (B) The device has a ladderlike geometry, and solution is distributed evenly across the device. (C) Cross-section view of the 3D microchannel. (D) Schematic of the distribution of solution from the delivery channel to the through holes and then the droplet generator; droplets are formed and then exit through the outlet channel. Reproduced from Ref. [40] with permission from the Royal Society of Chemistry.

microfluidic devices of which most are LOC-based POC diagnostic devices, reportedly commercialized by a few companies [5, 43]. These POC devices developed by individual companies cover a vast range of purposes, ranging from flu, cardiovascular diseases, malaria and *E. coli* detection to blood chemistry analysis. Devices for cancer detection and DNA and RNA signatures are still under development. These devices come in different forms such as disposable cards or cartridges containing preloaded test solutions and capillary-driven test strips, and the entire analysis could be performed on-chip or off-chip with handheld analyzers or benchtop instruments. More conventional POC devices are expected to adapt LOC concepts and functions in order to improve diagnosis and to meet greater clinical needs.

Alas, the overwhelming accomplishments in microfluidic research and development are not reflected in the slow uptake of microfluidic technology in the market. The industrial realization of microfluidic innovations is most often held back by the inflexibility of microfluidic components for integration, economic non-viability, and the lack of standardization. A complete microfluidic system usually entails many different fluidic components, and a single manufacturing process is not possible at current stage without the intervention and support from manual labor. Automated and assembly-free prototyping of simple devices is perceived to be a goal that is not attainable in the near future. Most importantly, with many deemed "promising" innovations, the challenge is to ensure that such innovations can be adapted and integrated to other existing appliances, technologies, or systems. Chin et al., Volpatti et al., and Mohammed et al. have all echoed the same concern that the focus should be on practical, marketable devices that are readily integrable, instead of unending development of single microfluidic component with niche function. Such is the demerit of introducing microfluidic-formulated solutions; they are too unique to be adapted; hence, the issue of chip-to-world interface should also be addressed and resolved even from the initial design phase [44]. And unless a minimum volume demand is met and a reasonable margin is secured, it is both uneconomic and unsustainable for mass production of microdevices, a risk that no stakeholders would bear [45].

The translation of the technology seems more challenging as it appears that academic researchers are more interested in publishing their inventions rather than developing them into commercially viable products. Many successful inventions remain a "proof

of concept" and ceased to be developed. In fact, many of the microfluidic systems are limited to "one design one application" which are applicable only to niche research areas, rendering them less appealing for further development. The voluminous lateral development of microfluidic researches and lack of standardization on methods and materials instead become the stumbling block for a standard microfluidic solution to reach mainstream uses, hence slowing the commercial uptake of the technology [5, 44].

5. Conclusion

Microfluidic-based researches are growing in an unprecedented pace with more research disciplines adopting the technology, techniques, and tools that are now much established. At present, novel microfluidic platforms offering diverse functionalities and solutions are surfacing each day, and there seems to be no limit to what the microscale technology could offer, be it in clinical technologies or the manufacturing sector. While researches are flourishing in the academic perspective, the ambiguity surrounding the commercialization of microfluidic applications did not go unnoticed. The interest of much of the microfluidic community is in lateral development of microfluidic solutions with only a small amount ongoing researches targeting at resolving technical challenges for innovation-to-market translation: the technologies and economy for mass productions. Despite the continuous effort and enthusiasm for more microfluidic solutions to be realized industrially, the path to commercialization and industrialization for more microfluidic solutions depends potently on the joint effort and commitment from the researching teams and their industrial counterparts.

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