Chapter

# Droplet Microfluidic Device for Rapid and Efficient Metals Separation Using Host-Guest Chemistry

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## Abstract

Metals are pivotal elements in our daily life and industrial processes, to produce electronic devices, catalysts, smart materials and so on. However, they are mostly present as a mixture in the environment that makes their separation challenging over the past decade. Host-guest chemistry principle thoroughly has been used to design and synthesize thousands of organic receptors with high complexation ability and selectivity to certain metal ions. On the other hand, the droplet microfluidic device is well-known for its unique characteristics of fluid dynamics, such as large specific surface area and short diffusion distance making the process robust and efficient. Therefore, many reports of research employ host-guest chemistry of the droplet microfluidic system for the effective metal separation process. This chapter deals with up-to-date examples of the droplet microfluidic system application for separation of base and alkali metals, recovery of rare-earth and precious metals and removal of heavy metals either from the competitive metal system or from the real waste solution sample through solvent extraction techniques utilizing host-guest chemistry principle.

**Keywords:** droplet microfluidic device, host-guest chemistry, solvent extraction, recovery, metal separation

## 1. Introduction

Nowadays, smart and advanced technology researches have infiltrated on all aspects of human daily activities [1]. For example, smart devices containing metal elements have massively been applied in pharmaceutical and electronic fields [2]. In general, based on their properties and usage, metal elements can be divided into four groups, *i.e.* alkali and base metals (lithium, iron, cobalt, nickel, zinc, etc.), precious metals (silver, gold, palladium, platinum, rhodium, iridium, osmium and ruthenium), rare-earth metals (lanthanum, neodymium, europium, holmium, etc.) and heavy metals (cadmium, lead, mercury, chromium, etc.). Silver materials have been applied as an antimicrobial agent while lithium ones as well-known energy storage materials [3]. The demands for these smart materials have kept increasing, therefore, their supply has been depleting day-by-day. Global maldistribution of metals, furthermore, is worsened by the metal supplies in several countries. Over the past several years, researchers are putting their continuous efforts on metal recycling and recovery process from wastewater and other secondary resources [4].

Metal recycling is a process to recover metals either from generated solid waste/liquid metal waste or spent home appliances using several techniques for a constant supply to meet the demand. Many kinds of research have been conducted to evaluate the metal recycling process; however, the metal recycling is quite complicated due to the presence of other metals with similar physicochemical properties in varying concentrations [1]. Additionally, heavy metals removal from the environment is difficult because they usually exist in trace amounts compared with other elements [5]. Therefore, versatile techniques which exhibit high metal selectivity and high recovery percentage are highly required [6].

Solvent extraction or liquid-liquid extraction is one of the metal separation techniques where the metal extraction efficiency mainly depends on the nature of the extraction reagents used. For example, di(2-ethylhexyl)phosphoric acid (D2EHPA) extracted lead(II) from chloride aqueous solution, however, the selectivity against iron(III), zinc(II) and copper(II) ions is unsatisfied [7]. Meanwhile, a complete separation of lead(II) ions from iron(III), zinc(II) and copper(II) successfully achieved using an amide derivative of calix[4]arene due to its high and suitable host-guest interaction [8].

On the other hand, droplet microfluidic devices are popular in biology and analytical chemistry areas because of their unique characteristics and advantages [9–15]. Numerous research papers related to rapid and efficient metal separations reported recently, and their numbers keep increasing with time [16–20]. This chapter serves an up-to-date review on the application of the droplet microfluidic system for separation and recovery of metal elements using a combination of host-guest chemistry principle and solvent extraction technique.

## 2. Host-guest chemistry

Host-guest chemistry is one of the chemistry fields studies various non-covalent interactions between host and guest molecules [21]. Host molecule defined as a molecular entity that forms complexes with organic or inorganic guests, or a chemical species that can accommodate guests within cavities of its crystal structure. The guest molecule is a molecule having a complementary structure to the binding site of the host compound, thus generating a selective and strong interaction between them [22]. The non-covalent interactions between host and guest molecules are including size effect, hydrophobic, cation-π, π-π, electrostatic, and hard-soft acid-base interactions as well as hydrogen bonding. Because of these specific interactions, a selective complexation between host and guest molecules could be achieved [23].

Thousands of host molecules are being prepared and evaluated to find out the best suitable host candidate for metal separations. Among them, calixarenes are found to be interesting host molecules and they attracted a lot of attention for research works due to their special inclusion phenomena [24]. Calixarenes are macrocyclic compounds that are prepared from formaldehyde and $p$-alkylphenol as the repeating units. A single step preparation of calixarenes was firstly introduced by Prof. C.D. Gutsche in 1978, subsequently, it has grown rapidly due to some merits, such as large-scale synthesis, rigid structure, easy modification and stable host compound [25]. It is also interesting to note that, the ring size and conformation of calixarenes are controlled by using template and reaction temperature.

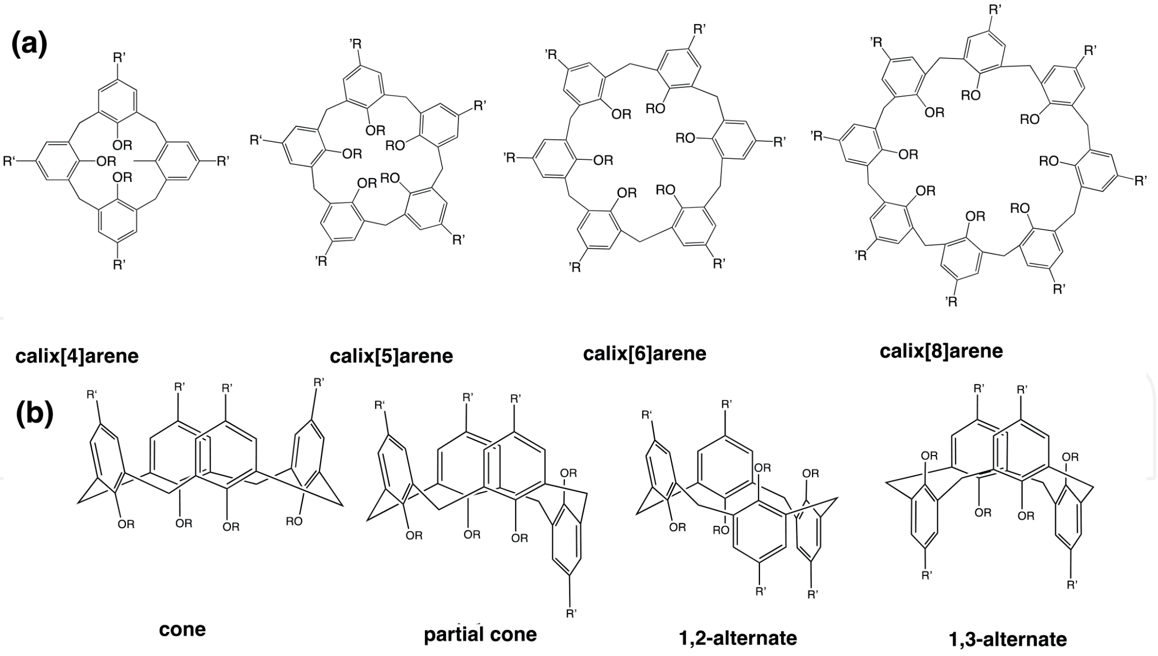

**Figure 1.**
*(a) The structures of calix[n]arenes and (b) the conformations of calix[4]arene.*

So far, there are four main subfamilies of calixarenes based on their ring size, *i.e.* calix[4]arene, calix[5]arene, calix[6]arene and calix[8]arene as displayed in **Figure 1(a)**. By increasing the ring size of calixarenes, their conformation could not easily be adjusted because of weaker hydrogen bonding on the calixarene structure [26].

Calix[4]arene is the most simple and special subfamily of calixarenes because it serves the most stable conformations. In general, there are four available conformations of calix[4]arene, *i.e.* the cone, partial cone, 1,2-alternate and 1,3-alternate conformations as shown in **Figure 1(b)**. Calix[4]arenes offer ideal frameworks for metal separation because of their size discrimination and chelating effects that contributed to high selectivity and high complexation ability with certain metal ions [27]. Furthermore, it is possible to change its sequence of metal selectivity by modifying their upper and lower rims [28]. Therefore, it is reasonable to understand that a lot of research works utilized calix[4]arenes for metal extraction, metal adsorption, and as chemosensor of metal ions, etc. [29–31].

## 3. Droplet microfluidic device

Microfluidic system is a miniaturized device that manipulates and controls fluids, usually in the range of microliters to femtoliters, in the channels with dimensions from tens to hundreds of micrometers [14]. The earliest microfluidic system was reported by Hodgson and Charles in 1963 while they investigated droplet generation when oil and water phases were introduced into the microchannel [32]. In 2001, Burns and Ramshaw firstly reported that the mass transfer of acetic acid from kerosene to aqueous phase was significantly enhanced by using droplet microfluidic device [33]. As of today, there are many types of microfluidic devices, such as continuous microfluidic devices, droplet microfluidic devices, paper microfluidic devices, and digital microfluidic devices have been fabricated and applied for many applications [34, 35]. Each of them serves as a unique platform for certain applications. Continuous microfluidic devices have been widely applied to particles and cell separation due to density differences. Droplet microfluidic devices serve as an ideal platform for metal separation, nanoparticle fabrication, drug delivery, and cell assay. Paper microfluidic devices have also been reported for routine chemical analysis and biochemical assays, while digital microfluidic devices are employed for immunoassays and chemical synthesis, etc. [36].

As the name indicates, the droplet microfluidic device generates droplets of two immiscible liquids such as organic and aqueous phases in the microchannel. Based on the liquids' intersection, there are 2 types of droplet microfluidic devices, *i.e.* T-type and Y-type of droplet microfluidic devices [9, 12]. A schematic representation of a droplet microfluidic device is shown in **Figure 2**. When the liquid is introduced into the microchannel through an inlet which is perpendicular to the main microchannel of a T-type droplet microfluidic device, it was defined as the dispersed phase, while, the continuous phase liquid that has introduced through an inlet which is in line with the main microchannel of a T-type droplet microfluidic device. However, both phases are equal to the Y-type of droplet microfluidic devices [13].

Kashid *et al.* have observed the droplets generation on both T-type and Y-type droplet microfluidic devices in 2010 [37]. For example, on the T-type droplet microfluidic device, first, the dispersed phase is entered the main microchannel and starting to block the flow of the continuous phase by exerting the pressure. The generated pressure squeezes the neck of the dispersed phase and the droplet of the dispersed phase is formed. Since both phases are immiscible, each droplet has a role as an individual reactor with a short diffusion distance. Furthermore, each droplet serves a large specific surface area. The combination of a short diffusion distance and a large specific surface area contribute to boosting the mass transfer process of chemicals from one phase to another phase [38].

Even though solvent extraction offers a selective and efficient technique for metal separation, the extraction kinetics rate in some processes is slow and time-consuming [38]. For comparison, **Figure 3** shows the obtained parameters and experimental data for silver(I) extraction using a tetramethylketonic derivative of calix[4]arene in batch-wise and microfluidic systems. In the batch-wise system, the extraction was carried out in a small glass vial with a diameter of 4 cm and height of each phase is about 1 cm. The extraction using a continuous microfluidic device was performed in a microchannel with 20 mm of length and 200 μm in depth and width while the extraction in a droplet microfluidic device was carried out in a microchannel with 73 mm of length and 200 μm of depth and widths. As shown in **Figure 3**, the diffusion distance of chemicals using batch-wise (20,000 μm) was a hundred times farther than both the microfluidic devices (200 μm). Furthermore, the total specific surface area of the droplet microfluidic device employed was ~550 times larger than that of the continuous microfluidic system while ~55,000 times larger than that of the batch-wise system. Because of that, it is reasonable to know that the required extraction time to reach an equilibrium state is 259,200 s (72 h), 15.0 s and 1.00 s for the batch-wise system, continuous microfluidic system, and droplet microfluidic system, respectively. This result demonstrates the remarkable advantage of using the droplet microfluidic device for metal extraction and separation process [39].

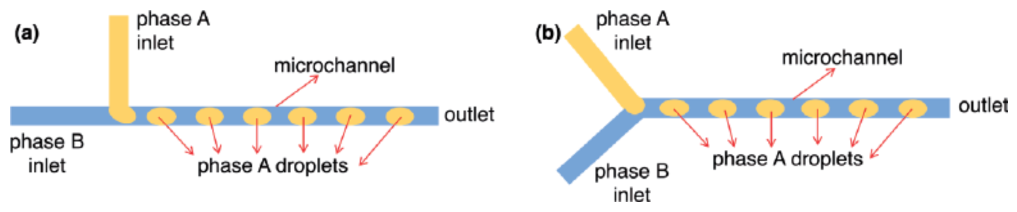

**Figure 2.**
*(a) T-type and (b) Y-type of droplet microfluidic devices.*

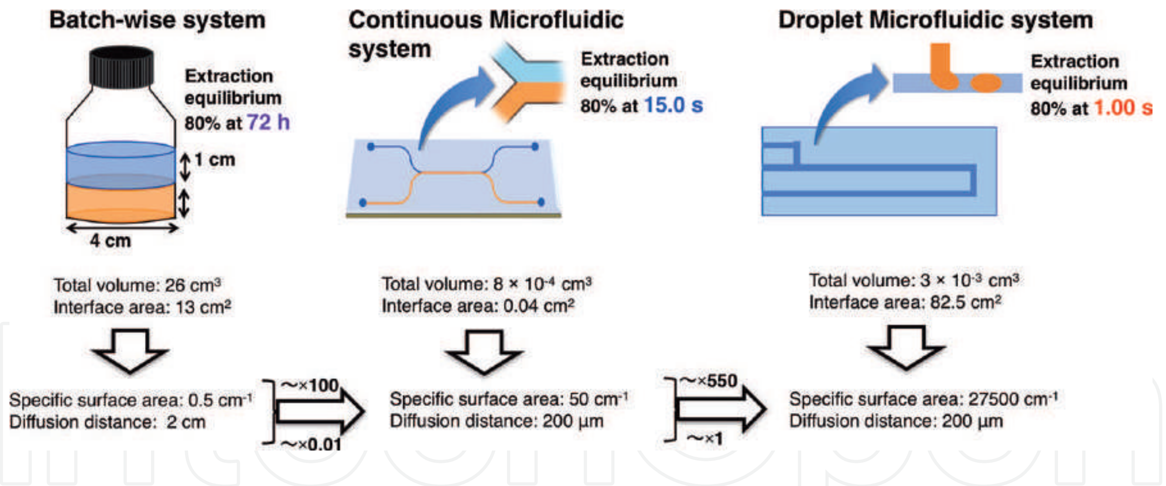

**Figure 3.**
*Comparison of batch-wise, continuous and droplet microfluidic systems for silver(I) extraction using a tetramethylketonic derivative of calix[4]arene [38].*

## 4. Metal separations using the droplet microfluidic device

Due to the significant enhancement of the extraction process, droplet microfluidic devices have been employed for metal ion separations through a solvent extraction technique [18–20]. The chemical structures of several extraction reagents employed in metal separations are shown in **Figure 4**. In general, metal ion concentrations were measured using either atomic absorption spectroscopy (AAS) or induced coupled plasma-atomic emission spectroscopy (ICP-AES) or induced coupled plasma-mass spectrometry (ICP-MS). The measured metal ion concentrations were further used to calculate extraction percentages (%*E*), distribution ratio (*D*) and separation factor ($\beta$) as mentioned in Eqs. (1)–(3) whereas $[metal\ ion]_{aqueous,0}$ is initial metal ion concentration in the aqueous phase before solvent extraction process, $[metal\ ion]_{aqueous,t}$ is the metal ion concentration in the aqueous phase after $t$ extraction time, and $[metal\ ion]_{organic,t}$ is the metal ion concentration in the organic phase after $t$ extraction time [26]. The metal extraction and separation processes are summarized and listed in **Table 1**.

$$\%Extraction = \frac{[metal\ ion]_{aqueous,0} - [metal\ ion]_{aqueous,t}}{[metal\ ion]_{aquoeus,0}} \times 100 \tag{1}$$

$$D = \frac{[metal\ ion]_{organic,t}}{[metal\ ion]_{aqueous,t}} \tag{2}$$

$$\beta = \frac{D_{metal\ ion\ A}}{D_{metal\ ion\ B}} \tag{3}$$

### 4.1 Alkali and base metals

Alkali and base metals are non-precious metals which are abundantly found in nature [40]. In this part, the example of utilization of droplet microfluidic system for extraction and separation of copper(II), iron(III), indium(III), calcium(II), cesium and lithium ions were discussed.

Evaluation of copper(II) extraction using Y-type microreactor was carried out by Yang *et al*. The commercially available extractant, AD-100 which consists of 70–75% (w/w) of 2-hydroxy-5-nonylbenzaldehyde oxime as the active reagent in 260# solvent oil as the organic diluent was used. The concentrations of AD-100 used influenced the copper(II) extraction percentage. Higher AD-100

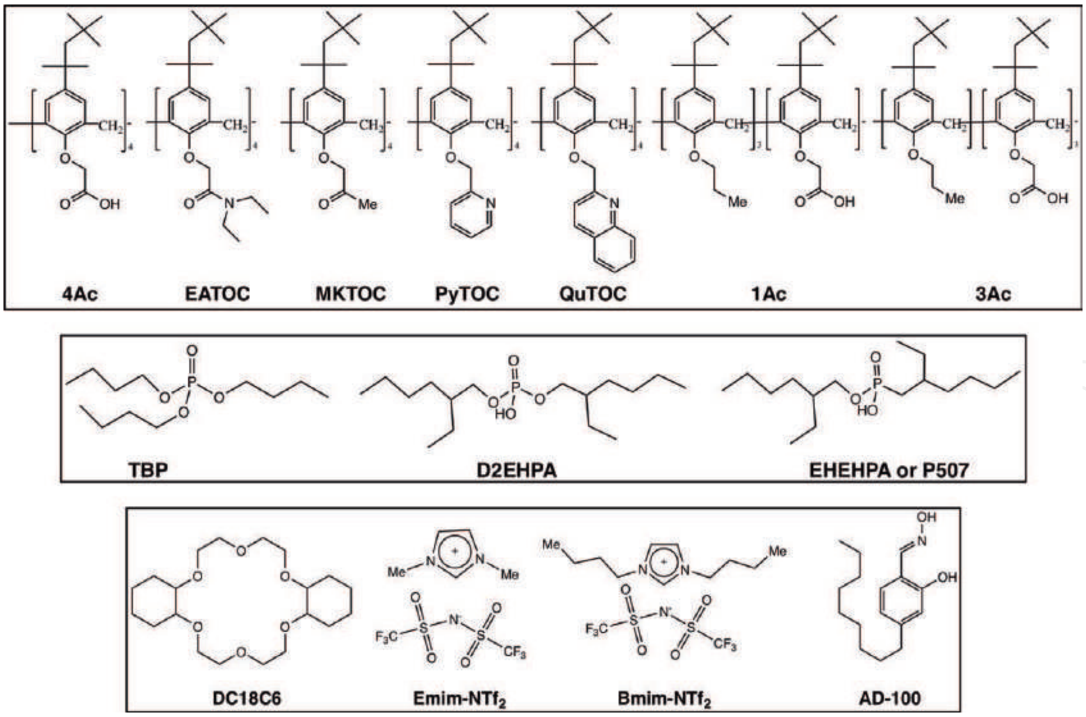

**Figure 4.**
*Host compounds and extraction reagents used for metal separations in this chapter.*

concentration gave higher extraction percentage while a higher concentration of copper(II) gave lower extraction percentage. The extraction percentages were also increased at longer extraction time, lower Reynolds number, higher pH of the aqueous phase, and higher temperature. Using the T-type of droplet microfluidic device, 96.0% copper(II) ions were extracted in 32.0 s extraction time [41]. On the other hand, Jiang *et al*. employed a Y-type microfluidic device to achieve an effective separation of copper(II) over iron(III) and zinc(II) with a mixture of 2-hydroxyl-5-nonyl acetophenoneoxime and 5-nonylsalicyladoxime in 1:1 volume ratio, called as DZ988N, as the extraction reagent. Using the microfluidic device, as much as 80.6% of copper(II) extracted at 0.78 s extraction time. While as much as 98.9% of copper(II) was stripped at 3.92 s by using 1.84 M of sulfuric acid solution in 2:1 organic to aqueous phase ratio. In a comparison of the microfluidic device to the batch-wise system, the separation factors of copper(II) over iron(III) and zinc(II) were significantly enhanced from 86.2 to 466 and 123 to 1089, respectively [42].

Iron(III) extraction kinetics using D2EHPA was investigated in a Y-type microfluidic device. The experimental results showed that the extraction of iron(III) was controlled by mixed reaction-diffusion resistance regime on a second-order extraction rate equation. Moreover, since the required extraction times for iron(III) and cobalt(II) are different, iron(III) could be separated from the cobalt(II) in the metal mixture solution, which may contribute to the real hydrometallurgical process [43].

Indium(III) separation from a metal mixture solution has been successfully achieved using a T-type of droplet microfluidic device. The metal mixture contains 23.0 mM of indium(III), 35.8 mM of iron(III), 44.2 mM of zinc(II), 153.8 mM of aluminum(III) and 141.5 mM of magnesium(II) ions [44]. It was found that indium(III) was extracted in 98.8%, while the other metal ions were hardly extracted (<5.00%). The separation process yielding that the separation factors of indium(III) over iron(III), zinc(II), aluminum(III) and magnesium(II) ions were 18,720, 266,373, 41,955 and 11,809, respectively, demonstrating that a high selective indium(III) separation was achieved within a minute.

| Sl. No | Metal ions | Extraction reagents | Microchannel | | | %E | β | $t$ (s) | Ref |
|---|---|---|---|---|---|---|---|---|---|
| | | | Length (mm) | Width (mm) | Type | | | | |
| **Base metals** | | | | | | | | | |
| 1 | Cu(II) | AD-100 | 900 | 0.6 | T | 96.0 | — | 32.0 | [41] |
| 2 | Cu(II) | DZ988N | 131 | 0.2 | Y | 80.6 | $466^{Fe(III)}$<br>$1250^{Zn(II)}$ | 0.78 | [42] |
| 3 | Fe(III) | D2EHPA | 3 | 0.1 | Y | 32.0 | — | — | [43] |
| 4 | Co(II) | D2EHPA-Na | 500 | 1.0 | Y | 92.0 | $3.54^{Li(I)}$ | 15.0 | [50] |
| 5 | In(III) | D2EHPA | 2000 | 0.8 | T | 98.8 | $18720^{Fe(III)}$<br>$266373^{Zn(II)}$<br>$41955^{Al(III)}$<br>$11809^{Mg(II)}$ | 60.0 | [44] |
| **Alkali metals** | | | | | | | | | |
| 6 | Ca(II) | DC18C6 | 20 | 0.5 | Y | 98.2 | — | 5.70 | [45] |
| 7 | Ca(II) | $EMIMNTf_2 + BMIMNTf_2$ | 130 | 0.4 | Y | 52.0 | — | 6.00 | [46] |
| 8 | Cs(I) | D2EHPA | 22 | 0.7 | Y | 100 | — | 40.0 | [47] |
| 9 | Li(I) | D2EHPA + TBP | 500 | 1.0 | Y | 50.0 | — | 5.00 | [49] |
| 10 | Li(I) | 1Ac | 73 | 0.2 | T | 100 | > 1000 | 4.00 | [51] |
| **Precious metals** | | | | | | | | | |
| 11 | Ag(I) | MKTOC | 73 | 0.2 | T | 100 | — | 4.00 | [52] |
| 12 | Pd(II) | QuTOC | 73 | 0.2 | T | 100 | — | 4.00 | [52] |
| 13 | Pt(IV) | PyTOC | 73 | 0.2 | T | 100 | — | 4.00 | [52] |
| **Rare-earth metals** | | | | | | | | | |
| 14 | La(III) | P507 | 120 | 0.1 | Y | 99.5 | — | 0.37 | [55] |
| 15 | La(III) | Phosphorus reagent | 100 | 1.0 | T | 90.0 | $3.50^{Eu(III)}$ | 10.0 | [56] |

| Sl. No | Metal ions | Extraction reagents | Microchannel | | | %E | β | t (s) | Ref |
|---|---|---|---|---|---|---|---|---|---|
| | | | Length (mm) | Width (mm) | Type | | | | |
| 16 | Nd(III) | P507 | 125 | 0.3–1.0 | Y | 88.0 | $2.23^{Pr(III)}$ | 12.0 | [58] |
| 17 | Ce(III) | P507 | 125 | 0.3 | Y | 76.5 | $3.25^{Pr(III)}$ | 12.0 | [57] |
| 18 | Sm(III) | P507 | 125 | 0.3 | T | 75.1 | — | 45.0 | [59] |
| 19 | U(IV) | TBP | 13 | 0.5 | T | 100 | — | 1.50 | [65] |
| **Heavy metals** | | | | | | | | | |
| 20 | Pb(II) | 4Ac | 73 | 0.2 | T | 96.0 | $14.2^{Fe(III)}$<br>$324^{Cu(II)}$<br>$296^{Zn(II)}$ | 4.00 | [66] |
| 21 | Pb(II) | EATOC | 73 | 0.2 | T | 100 | > 1000 | 2.00 | [8] |

**Table 1.**
*Summary of reports on metal ion extractions and separations carried out in the microfluidic devices at* t *extraction time.*

Jahromi *et al.* separated calcium(II) isotopes, $^{48}$calcium(II) and $^{40}$calcium(II) ions using dicyclohexano-18-crown-6 in a Y-type microfluidic device. Using a combination of the dicyclohexano-18-crown-6 and microfluidic device, $^{40}$calcium(II) was selectively extracted in 98.2% within 5.70 s. By using a continuous cycle extraction process, the amount of $^{40}$calcium(II) becomes lower in the aqueous phase, therefore, the concentration of $^{48}$calcium(II) ion was enriched [45]. Another experiment on calcium(II) extraction was carried out by using ionic liquids as the extraction reagent, named as 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide (EMIM NTf2) and 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide (BMIM NTf2) in a Y-type of droplet microfluidic device. The pH value of the aqueous phase did not affect the extraction percentage because the main extraction mechanism is not an ion-exchange mechanism. Even though some parameters were optimized, the highest extraction efficiency was only 52.0%, which was still unsatisfied [46].

On the other hand, cesium(I) extraction in a Y-type of droplet microfluidic system was studied by Tamagawa *et al*. Stable droplet generation was observed when the total flow rate of both phases is less than 100 mL h$^{-1}$. By using D2EHPA as the extraction reagent, the required times to reach the quantitative amount of extraction percentage (100%) were shortened 25 times from 1000 to 40.0 s using batch-wise and droplet microfluidic system, respectively [47].

Lithium metals are widely used as the main part of lithium-ion batteries and aircraft alloys, the continuous supply of lithium may become critical over time. Urban waste, especially from lithium-ion batteries and seawater, may serve as the potential secondary resource in the future. However, lithium-ion batteries contain lithium, cobalt(II) and manganese(II) ions, while seawater contains lithium and other metal ions, such as sodium, potassium, magnesium, and calcium ions in different concentrations, the lithium recovery from these resources poses to be a tough work [48].

Muto and co-workers investigated the extraction process of lithium using D2EHPA in a droplet microfluidic device. They found that a glass substrate gave higher extraction efficiency as well as the mass transfer coefficient due to stronger convection rate and larger specific surface area of the organic droplets. When 2.0 M D2EHPA was used as the extraction reagent for 1.0 mM of lithium ions in the aqueous phase, around 0.3 mM of lithium ions were extracted in 5.00 s as the extraction time. Furthermore, by the addition of 0.18 M tributyl phosphate (TBP), the amount of the extracted lithium can be improved to 0.5 mM at 5.00 s extraction time. Even though the extraction efficiency was only around 50%, the droplet microfluidic device serves as a potential platform for quick metal extraction compared with the conventional extraction process [49].

Hirayama *et al.* evaluated the separation of cobalt(II) over lithium from a model solution of lithium-ion battery waste. The mixture of 0.20 M of D2EHPA and 0.01 M of NaOH, called as D2EHPA-Na in cyclohexane was used as the organic phase while the model solution containing 1.0 mM of cobalt(II) and 1.0 mM of lithium ions was used as the aqueous phase. From the model solution, the extraction reagent extracted around 50 ppm of cobalt(II) and 1.5 ppm of lithium ions giving 3.54 as the separation factor for cobalt(II) over lithium ions. Furthermore, using the droplet microfluidic device, 98% purity of cobalt(II) solution was obtained within 4.50 s extraction time [50].

In our previous study, we investigated the possibility to extract lithium ions with monoacetic acid derivative of calix[4]arene using T-type of droplet microfluidic system [51]. At first, the droplet microfluidic device was fabricated from Tempax glass and the microchannel was produced utilizing a diamond-coated needle through a micromilling process. The microchannel dimensions were 73.0 mm in length and 200 μm in width and depth as confirmed by laser reflection microscope. The top and bottom parts of the T-type droplet microfluidic device were permanently bonds through a thermal fusion technique [52]. To prevent any disturbance of leaked sodium ions from the glass substrate, the microchannel was coated with SFE-X008 coating agent (1% of *m*-bis(trifluoromethyl)benzene in 94% of the ethyl perfluorobutyl ether). After coating, the wettability of the glass substrate was significantly changed from 20 to 120°, demonstrating a successful coating of the microchannel. From the preliminary investigation on lithium extraction using the monoacetic acid derivative of calix[4]arene (shown in **Figure 4** as 1 Ac) on the individual metal extraction, it was found that 100% of lithium ions were quantitatively extracted just within 2.00 s as the extraction time. Moreover, the complete stripping of lithium ions from the organic phase was easily achieved using 0.10 M HCl as the stripping agent.

Since the monoacetic acid derivative of calix[4]arene completely recovered (extraction and stripping efficiencies were 100%) the lithium ions, the competitive metal extraction was carried out using a mixture of metal ions as the aqueous phase. In a mixture of all alkali and alkaline earth metals (lithium, sodium, potassium, rubidium, cesium, magnesium, calcium, strontium, and barium ions) in 10.0 mM concentration each, the 5.00 mM of the monoacetic acid derivative of calix[4]arene extracted 4.99 mM of lithium ions showing a quantitative (99.8%) extraction percentage of lithium ions. By using 1.00 M of HCl, as much as 99.5% of lithium ions were successfully stripped from the ligand, which is remarkable. The results demonstrated that the lithium separation from seawater which mainly contains sodium, potassium, magnesium and calcium ions was successfully achieved using the monoacetic acid derivative of calix[4]arene in the droplet microfluidic system.

Seawater was sampled from Minatohama, Karatsu, Japan and filtered using Millipore membrane to prevent any blockage on the microchannel during the extraction process. The lithium concentration in the seawater was 0.03 mM while the sodium, potassium, magnesium and calcium ions concentration was 495, 10.1, 47.4 and 12.8 mM, respectively. Using a droplet microfluidic system, it was found that 31.6% of lithium (0.01 mM) and 1.00% of sodium ions (4.95 mM) were extracted from seawater, however, other metal ions were not extracted at all and remained in the aqueous phase. In this case, sodium ions were extracted due to the huge amount of existing sodium (~19,000 times higher) compared to lithium ions.

To achieve complete extraction of lithium ions from seawater, 20.0 mM of the monoacetic acid derivative of calix[4]arene in chloroform was used as the extraction reagent. As expected, 100% of lithium ions were successfully extracted. However, since the higher concentration of the extraction reagent was used, as much as 2.56% of sodium ions were also extracted. Both metal ions were completely stripped using HCl to obtain an aqueous phase containing 0.03 mM of lithium and 12.2 mM of sodium ions. To obtain a pure lithium solution, another type of calix[4]arene, named as triacetic acid derivative of calix[4]arene was used because it exhibits high sodium selectivity over lithium ions at the acidic condition. When the 10.0 mM of triacetic acid derivative of calix[4]arene (shown in **Figure 4** as 3Ac) was employed, 100% of the remained sodium ions were completely extracted leaving pure lithium ions in the aqueous phase. Similar to monoacetic acid derivative, triacetic acid derivative of calix[4]arene was also recycled. The scheme of recovery of lithium ions from seawater is shown in **Figure 5(a)**. From this experiment, a rapid and efficient lithium-ion recovery from the seawater was successfully achieved in the three-step process using calix[4]arene derivatives as the extraction reagents in a droplet microfluidic device [51].

### 4.2 Precious metals

Precious metals, *i.e.* silver, gold, palladium, platinum, rhodium, iridium, osmium and ruthenium metals are indispensable metals because of their high economic value

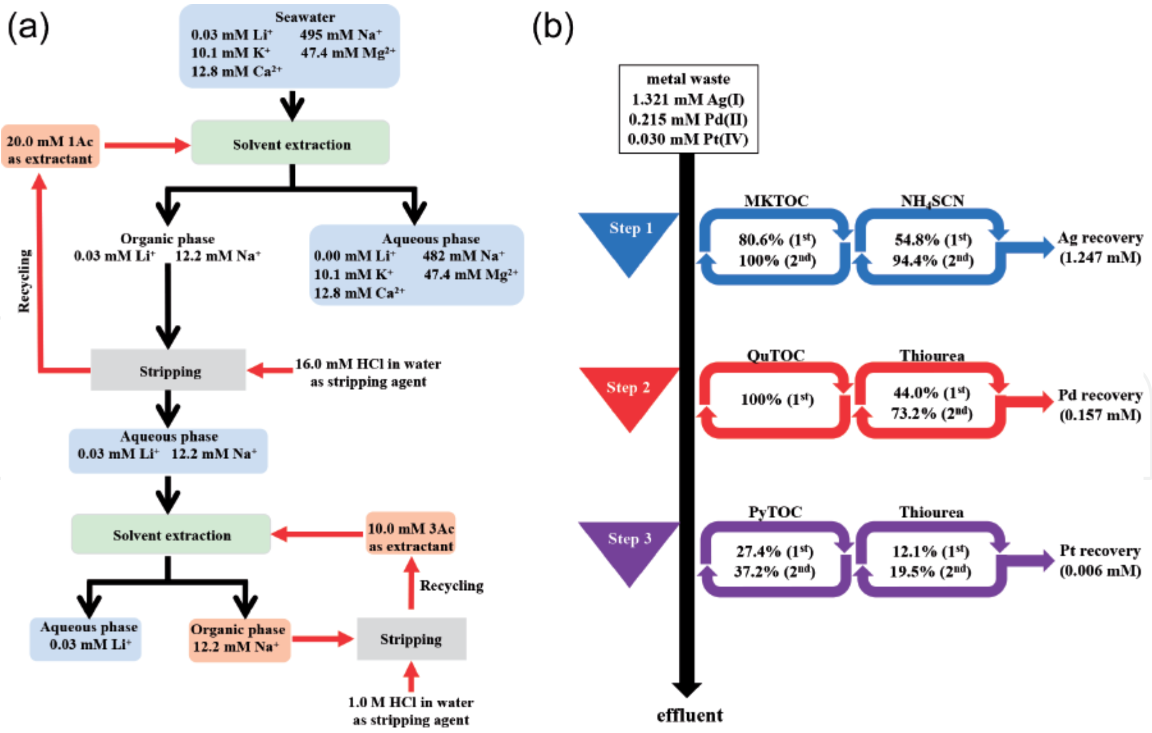

**Figure 5.**
*(a) A process of lithium separation from seawater [51] and (b) precious metals separation from a real metal waste [52] using the droplet-based microfluidic system.*

and their application for smart materials [53]. Bizzo *et al.* reported that silver(I), palladium(II) and platinum(IV) ions were found in the electronic waste serving as the secondary resource for precious metal ions [40]. Stepwise recovery of precious metals from electronic waste, therefore, must be established as an untapped resource for future precious metals supply. Even though the recovery process is complicated because of the presence of other metal ions with similar physicochemical properties, a stepwise recovery of precious metals from real metal waste using neutral type of calix[4]arene derivatives in a T-type of droplet microfluidic device was established [52]. Silver(I), palladium(II) and platinum(IV) ions extraction were carried out employing tetramethylketonic, tetraquinoyl and tetrapyridyl derivatives of calix[4]arene, respectively, as the extraction reagents. The chemical structure of tetramethylketonic, tetraquinoyl and tetrapyridyl derivatives of calix[4]arene were shown in **Figure 4** as MKTOC, QuTOC and PyTOC, respectively.

From the individual metal extraction experiment, it was found that as much as 99.9% of silver(I) was extracted at 2.00 s of extraction time from 0.10 mM of $AgNO_3$ solution in 0.10 M $HNO_3$ media using 5.0 mM of the tetramethylketonic derivative of calix[4]arene in a droplet microfluidic device. However, it required 72 h to achieve a similar extraction percentage of silver(I) using a batch-wise system showing that the droplet microfluidic device enhanced the required extraction time 130,000 times faster to reach the equilibrium stage of silver(I) ion extraction compared with the conventional batch-wise system. On the other hand, as much as 96.2% of palladium(II) ions was extracted at 4.00 s extraction time from 0.10 mM of $Pd(NO_3)_2$ solution in 0.10 M $HNO_3$ media using a tetraquinolyl derivative of calix[4]arene, and as much as 93.1% of platinum(IV) ions were extracted at 4.00 s extraction time from 0.10 mM of $H_2PtCl_6$ solution in 0.10 M HCl media using a tetrapyridyl derivative of calix[4]arene. The stripping of silver(I), palladium(II) and platinum(IV) ions were obtained in medium percentages using 2.00 M ammonium thiocyanate in water, 1.00 M thiourea in 1.00 M HCl and 1.00 M thiourea in water, respectively, from the metal-laden organic phase within 2.00 s only.

The evaluated real metal waste, mainly consisted of silver(I), palladium(II), platinum(IV), iron(III), copper(II), and nickel(II) ions at 1.32, 0.22, 0.03, 0.01, 0.82, and 0.01 M, respectively. To prevent any metal precipitations, the real metal waste was diluted 1000 times using 1.0 M $HNO_3$. Since the concentration of silver(I) was higher than palladium(II) and platinum(IV) ions, the silver(I) ions were extracted first and followed by palladium(II) and platinum(IV) ion extraction. The scheme of stepwise recovery of those precious metal ions from real metal waste is shown in **Figure 5(b)**. All extractions and stripping processes using a droplet microfluidic device were conducted at 4.00 s extraction time. Silver(I) ion extraction was carried out in two-cycle process due to high existed concentration. On the first cycle, 80.6% of silver(I) ions (1.064 mM) were extracted using 20.0 mM of the tetramethylketonic derivative of calix[4]arene. A complete extraction of silver(I) ions were achieved in the second cycle. Even though only 54.8% of silver(I) ions were stripped from the first cycle using 2.0 M ammonium thiocyanate, as much as 94.4% of silver(I) ions were recovered on the second cycle.

A complete palladium(II) ions recovery was achieved within a single cycle extraction process using 5.00 mM of the tetraquinolyl derivative of calix[4]arene, while the stripping percentages of palladium ions were 44.0 and 73.2% on the first and second cycle of stripping process using 1.00 M thiourea in 1.00 M HCl. On the other hand, 27.4 and 37.2% of platinum(IV) ions were extracted in the first and second cycles of extraction process using a tetrapyridyl derivative of calix[4]arene. Meanwhile, low stripping percentages of platinum(IV) ions, 12.1 and 19.5% of the first and second cycles of the stripping process, respectively, were obtained using 1.00 M thiourea in the water as stripping reagent. Even though platinum(IV) recovery still needs to be optimized, a stepwise and complete recovery of silver(I) and palladium(II) ions from real waste was established using a droplet microfluidic system at 4.00 s extraction time [52].

### 4.3 Rare-earth metals

Rare-earth metal separations leave a serious challenge due to astounding properties as well as their extensive applications in electronic and advanced materials [1]. Rare-earth metals including lanthanide and actinide groups which are classified as 4f and 5f elements in the Periodic Table. Their physicochemical properties are quite similar to each other, thus challenging many researchers to find the optimum separation process for hydrometallurgy field [30, 54]. In this part, lanthanum(III), praseodymium(III), neodymium(III), samarium(III) and uranium(VI) extraction and separation processes are described and discussed.

Lanthanum(III) extraction from a chloride solution was studied in a Y-type microfluidic device by Yin et al. By using phosphonic acid (2-ethylhexyl)-mono(2-ethylhexyl) ester (P507) as an extractant, high extraction percentage of lanthanum(III) ions was achieved within only 0.37 s [55]. Furthermore, the separation of lanthanum(III) and europium(III) ions using a T-type of droplet microfluidic device has been carried out. The separation factor of lanthanum(III) over europium(III) is in the range of 1.50 to 3.50 depends on the flow rate of the liquids [56].

Separation of praseodymium(III) and cerium(III) in a Y-type microfluidic device employing P507 as the extraction reagent was also investigated. At 12.0 s extraction time, as much as 75.0% of praseodymium(III) and 42.9% of cerium(III) ions were extracted into the organic phase yielding 3.25 as the separation factor. Even though the separation was not satisfied enough, the process could be recycled further to obtain pure cerium(III) ions as the remained aqueous phase [57].

On the other hand, neodymium(III) separation over praseodymium(III) was studied by He et al. using a Y-type droplet microfluidic device [58]. One and a half molar of P507 in sulfonated kerosene was used as the organic phase while praseodymium(III) and neodymium(III) in HCl and lactic acid media were used as the aqueous phase. At 12.0 s extraction time, it was found that P507 extracted 88.0% of neodymium(III) and 75.0% of praseodymium(III) yielding 2.23 as the separation factor of neodymium(III) over praseodymium(III). The similar separation factor was obtained using microfluidic at 12.0 s extraction time while the batch-wise system required 560 s extraction times. These findings initiated a rapid enrichment of neodymium from the wastewater sample within less than 600 s. From the wastewater containing 30–90 ppm of neodymium(III) ions, the neodymium(III) ions were enriched 200–450 times higher which is remarkable [58].

He et al. also investigated the extraction process of samarium(III) using P507 as the extraction reagent in a Y-type of droplet microfluidic device. Within 45.0 s, as much as 75.1% of samarium(III) can be extracted compared with the batch-wise system that requires 600 s to reach a similar extraction percentage [59]. Meanwhile, using a T-type of droplet microfluidic device, samarium(III) was extracted in 82.5% within 14.8 s, shorter than Y-type device. This phenomenon was caused by shorter diffusion distance and a larger specific surface area of T-type than Y-type of droplet microfluidic device [60].

Uranium(VI) extraction process was studied in a microfluidic device using several extraction reagents, such as phosphorus reagent, ionic liquids, and so on [61–64]. Among them, tributyl phosphate (TBP) exhibited as the best extraction reagent for uranium(VI) extraction process due to stable fluid dynamics, as well as, a possibility for large scale process through numbering-up the device. Darekar and coworkers investigated the extraction of uranium(VI) in 1.0 M $HNO_3$ using 30% v/v TBP in dodecane as the organic phase. It was found that quantitative (100%) extraction percentage was achieved at 1.50 s extraction time, however, the separation of uranium(VI) over other metal ions has not been reported yet [65].

### 4.4 Heavy metals

Heavy metals, especially lead(II) ions have been used in several industrial processes over the past several years and they get released into environment causing serious effects on environment and human health. A serious control monitoring of heavy metal ion concentration at industrial wastewater effluents should be comprehensively managed. So far, a lot of heavy metal removal techniques have been evaluated for wastewater treatment, however, they were unsatisfied because of heavy metals existed in trace amounts together with huge concentrations of base metal ions [5, 6]. In this part, two examples of a selective removal process of lead(II) removal using two derivatives of calix[4]arene, *i.e.* tetraacetic acid derivative (4Ac) and tetrakis(diethylamide) derivative of calix[4]arenes (EATOC) will be discussed.

In a conventional batch-wise system, the equilibrium state of lead(II) extraction using 4Ac reached after 24 h, however, it was shortened to 6.00 s using a droplet microfluidic device. The significant enhancement was observed by shorter diffusion distance and larger specific surface area aforementioned above. The lead(II) extraction percentages were increased from 73, 89 and 100% at 8.00 s for pH 2.00, 2.25 and 2.50, respectively, however, the separation of lead(II) and other metal ions was unsatisfied. As shown in **Figure 6(a)**, the extraction percentages of iron(III), copper(II), and zinc(II) were 60, 6.9 and 7.5%, respectively. This low selectivity of lead(II) extraction over Fe(III) was caused by the ion exchange mechanism in which the acetic acid groups of calix[4]arene were deprotonated and Fe(III) ions were easily extracted due to strong electrostatic interactions [66].

Another neutral calix[4]arene host molecule, EATOC was also evaluated to obtain a selective lead(II) separation from other metal ions mixture solution.

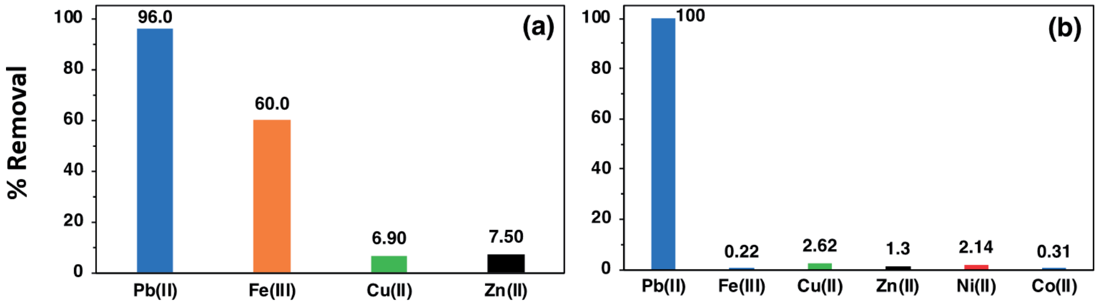

**Figure 6.**
*Lead(II) separation from other metal ions from a competitive metal mixture solution using (a) 4Ac [66] and (b) EATOC [8] as the extraction reagents in a droplet microfluidic systems.*

In this case, a neutral host molecule was used to achieve high metal selectivity. In 1.00 M $HNO_3$ media, one molecule tetrakis(diethylamide) derivative of calix[4]arene formed a 1:1 complex with one lead(II) ion revealed from the Job's plot experiment [8]. Using FTIR and $^1$H-NMR titration studies, it was elucidated that the lead(II) ion was chelated by EATOC through phenoxy oxygen atoms and carbonyl oxygen moieties. Since the lead(II)-EATOC complex was stable enough, a selective lead(II) extraction (100%) was achieved from a competitive metal system containing copper(II), zinc(II), nickel(II), iron(III) and cobalt(II) ions at 0.10 mM concentration of each metal ion [8]. A complete lead(II) removal was also successfully performed from a simulated wastewater effluent containing 0.10 mM of lead(II), 45.0 mM of iron(III), while copper(II), zinc(II), nickel(II) and cobalt(II) was in 30.0 mM concentration, respectively as shown in **Figure 6(b)**. Furthermore, the lead(II) ions was easily stripped in 98% using distilled water as the stripping reagent, which is a convenient and low-price process. These finding demonstrated that droplet microfluidic system is a promising device for a complete and efficient lead(II) removal from environmental samples [8].

## 5. Conclusions

Several successful reports on optimized separation and recovery of alkali and base metals, precious metals, rare-earth metals, and heavy metals using the droplet microfluidic system have been published. By employing the host-guest chemistry in a droplet microfluidic system offers a rapid and efficient metal separation from binary metal mixtures or real samples either from nature or industrial activities. In order to realize the true potential of droplet microfluidic devices for renewable metallurgical applications, the improved design of microfluidics addressing larger volumes with continuous operation along with effective utilization of host-guest chemistry are greatly needed to become a step forward in building a novel metallurgical technique for selective metal separations from a real sample, which otherwise not technically feasible to extraction using the conventional batch-wise system.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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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

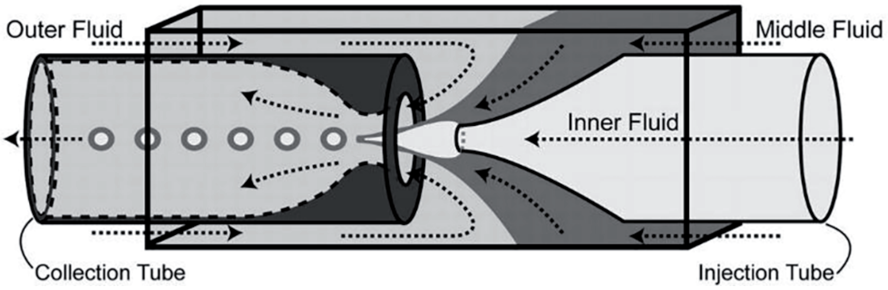

**Figure 1.**
*Glass capillary microfluidic device for double emulsion formation through coaxial jet [9].*

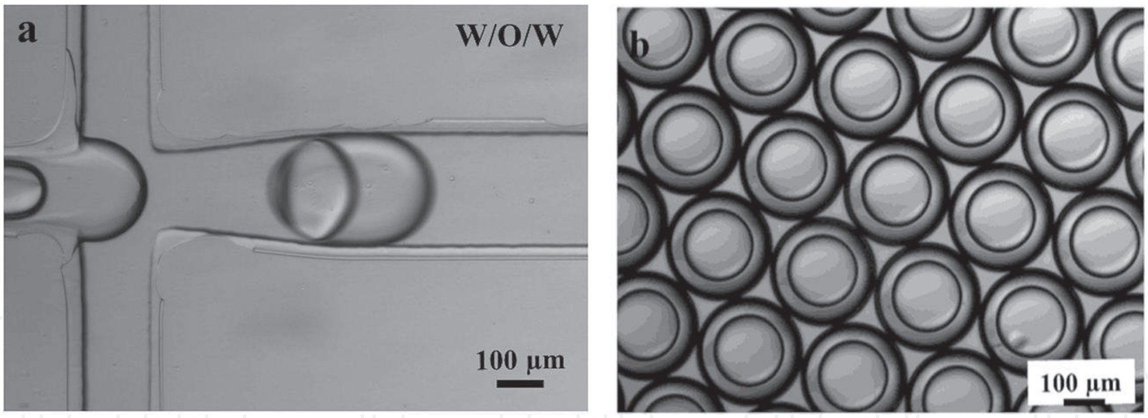

**Figure 2.**
*Double emulsions produced from a PDMS device replicated via soft lithography. Part of the device is subjected to plasma treatment to render it hydrophilic. (a) Optical image of a double emulsion forming at the second junction of device. (b) Double emulsions collected with high uniformity.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

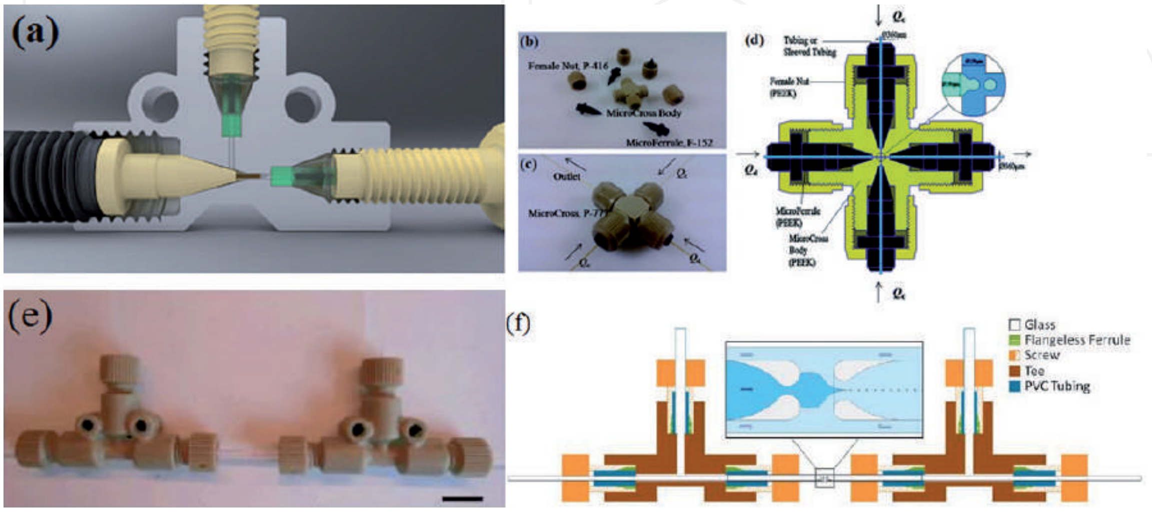

**Figure 3.**
*Microfluidic devices made from off-the-shelf components from commercial sources. (a) A 3D microfluidic nozzle for focusing and injecting of particulate samples. (b–d) Off-the-shelf components and the assembly of a micro-cross droplet generator. (e and f) Image and schematic of a reusable 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.

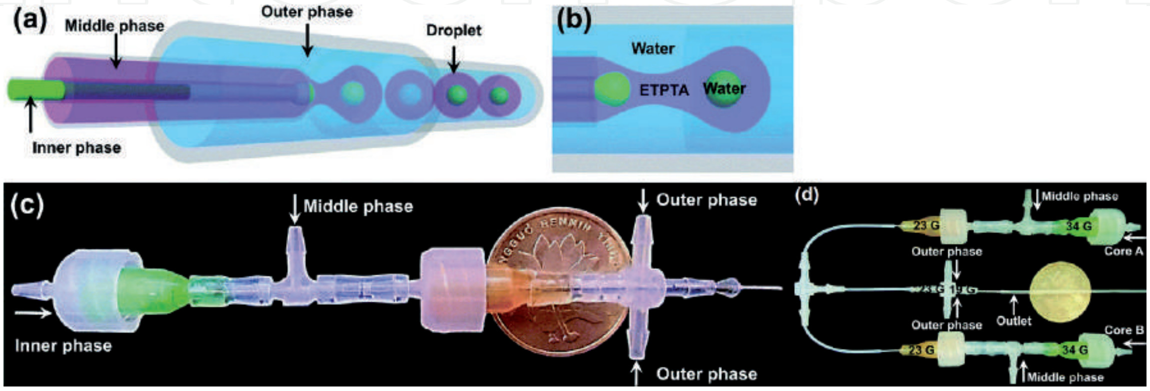

**Figure 4.**
*(a) Schematic illustration of generation of double emulsions from needle-based coaxial microfluidic device. (b) Clear depiction of production of W/O/W emulsions. (c) The assembly of the needle-based device with a coin for scale. (d) Extended configuration of needle-based microdevice for 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

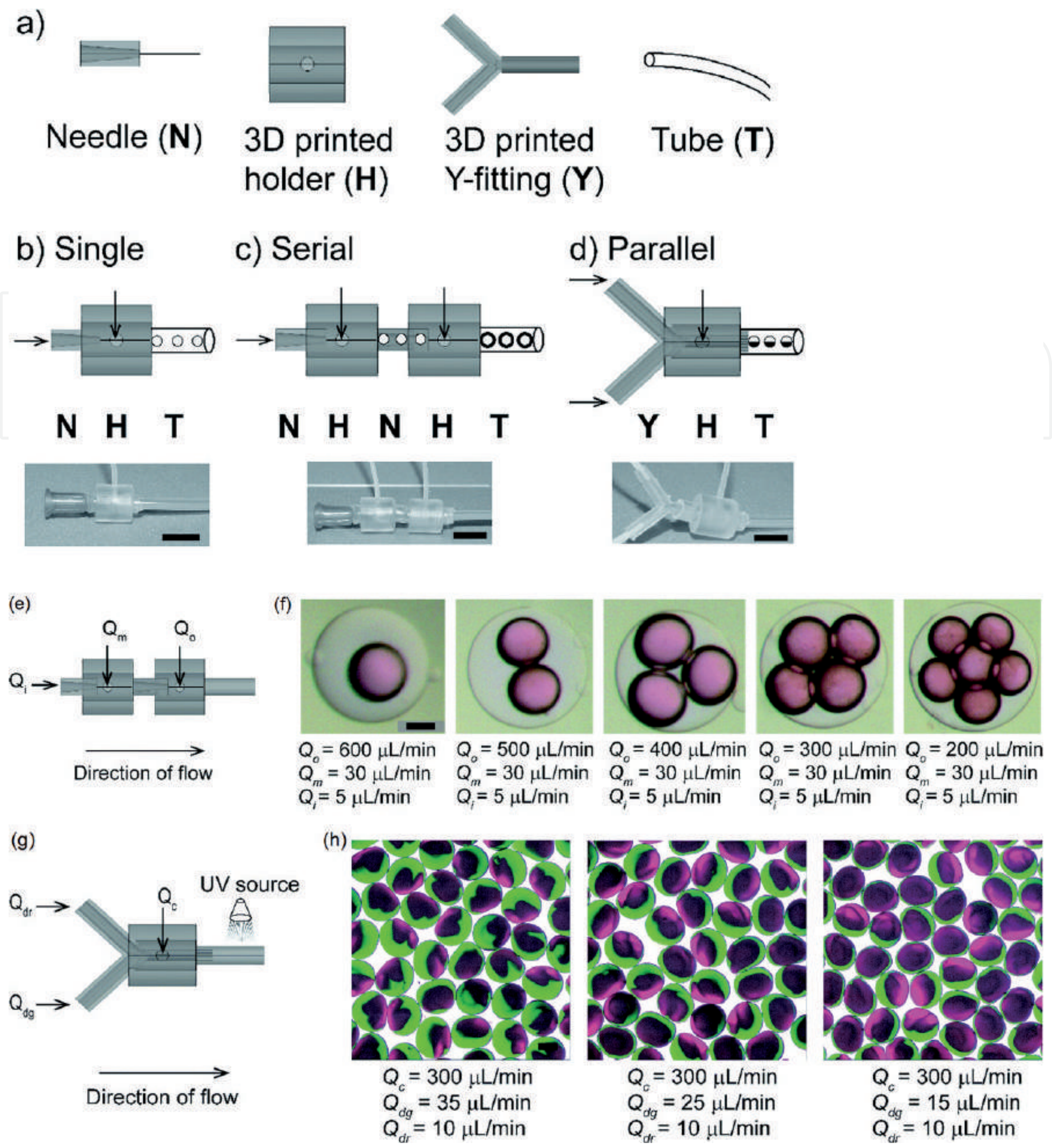

**Figure 5.**
*(a) 3D-printed modules and fittings for the fabrication of microfluidic axisymmetric flow-focusing device: needle (N), 3D-printed holder (H), 3D-printed Y-fitting (Y), and tube (T). Schematics and optical images of (b) a single flow-focusing device, (c) serially connected flow-focusing 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

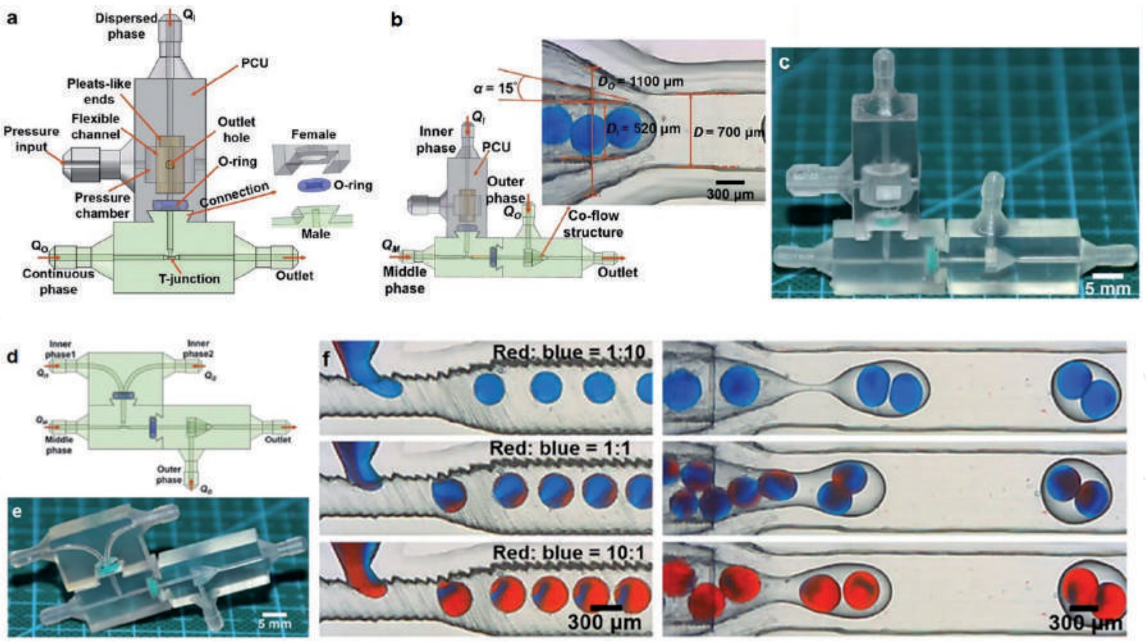

**Figure 6.**
*3D-printed modular device. (a) Schematic of a single droplet-generating pneumatic device consisting of a PCU and a T-junction. (b and c) Schematic and optical image of a pneumatic device for generation of double or multicore emulsions. (d and e) Schematic and optical image of modular device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

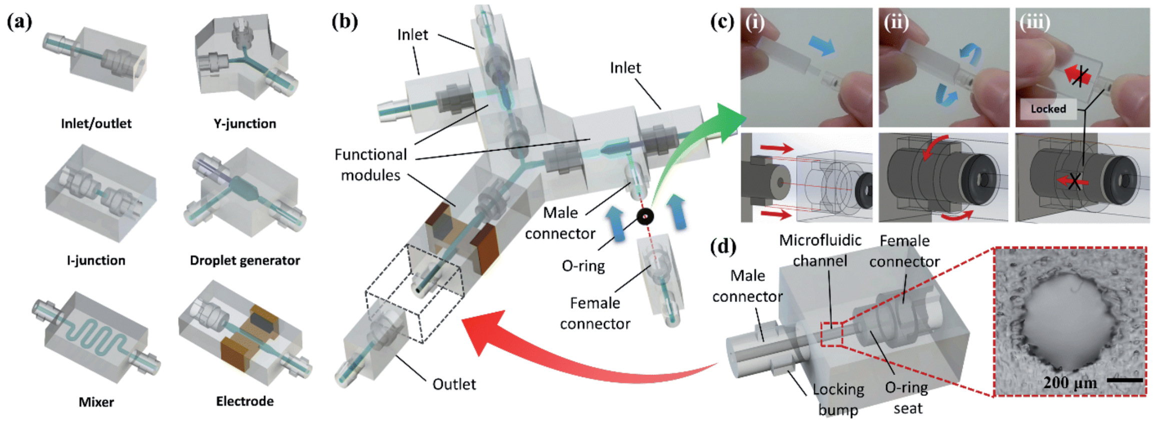

**Figure 7.**
*Schematic of 3D-printed modular microfluidic system. (a) 3D-printed modules of different functions and structures. (b) A full assembly of the modular device. (c) The design of the interlocking male and female connectors. (d) Male and female connectors printed on each module [33].*

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

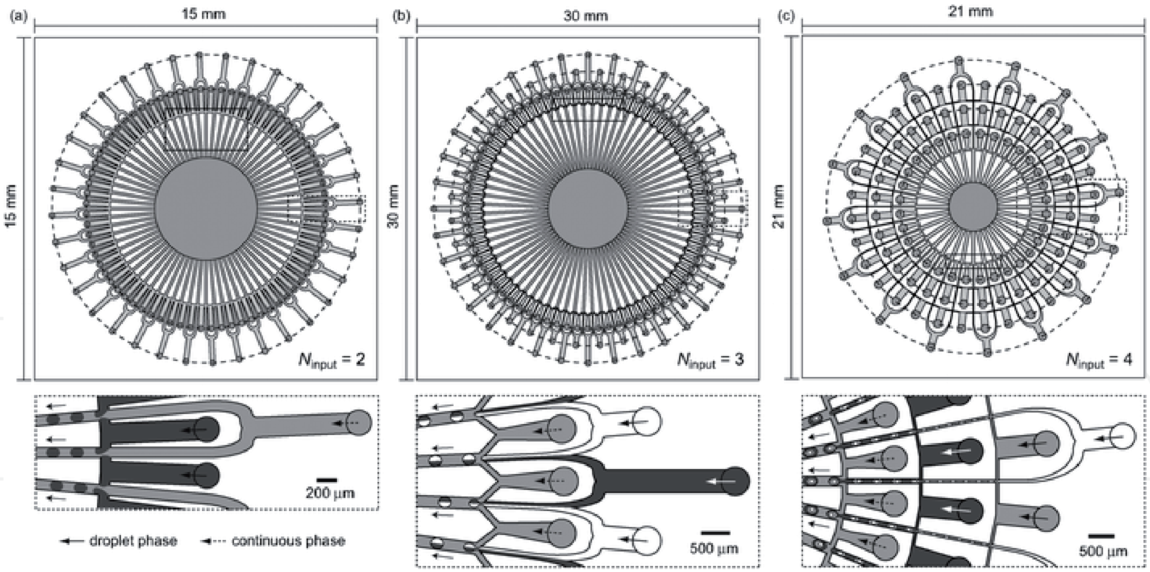

**Figure 8.**
*Designs of glass microfluidic chips with parallelized channels in circular arrangements. (a) 144 cross-flowing droplet generators on two concentric circles, (b) 72 droplet generators on three concentric circles, and (c) 32 emulsion generators in four concentric circles producing triple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

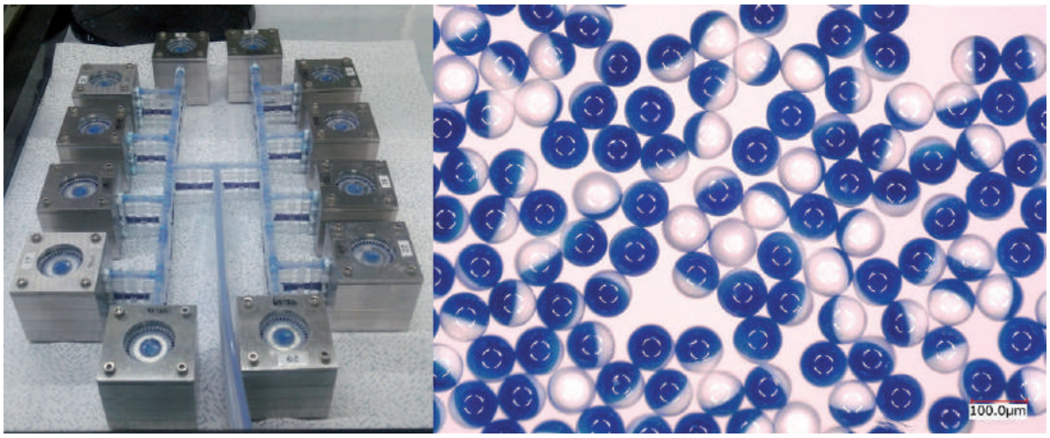

**Figure 9.**
*Parallelized devices are arranged in series to further scale up the production of Janus particles. Reproduced with permission [36].*

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

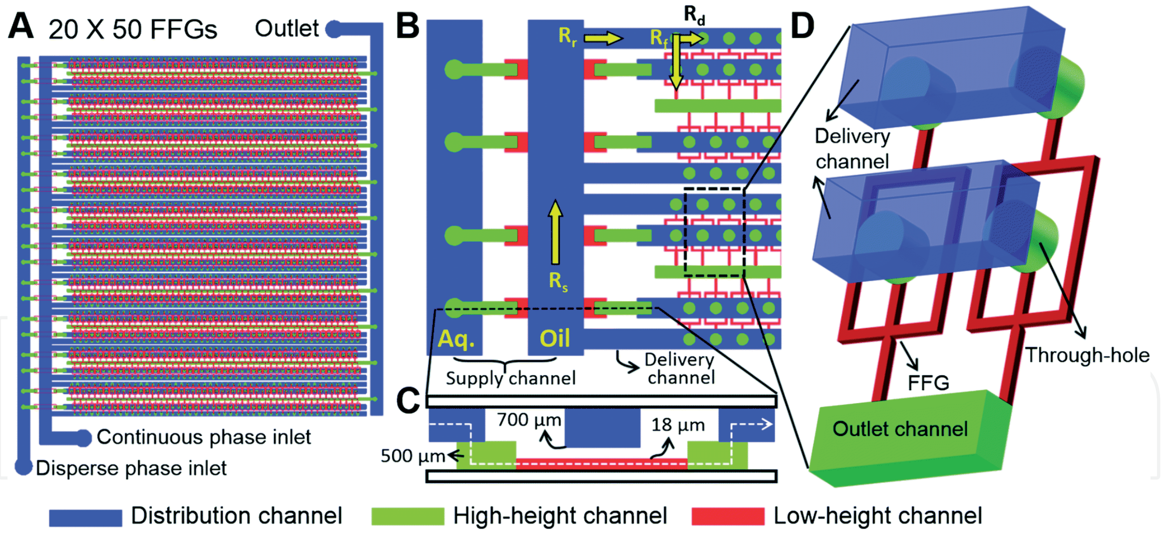

**Figure 10.**
*Schematic diagram of a PDMS parallelization device. (A) the channels are arranged in a 20 × 50 array. (B) The device has a ladderlike geometry, and solution is distributed evenly across the device. (C) Cross-section view of the 3D microchannel. (D) Schematic of the distribution of solution 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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Chapter

# Microfluidic Synthesis of Functional Materials as Potential Sorbents for Water Remediation and Resource Recovery

*Voon-Loong Wong, Chin-Ang Isaac Ng, Lui-Ruen Irene Teo and Ci-Wei Lee*

## Abstract

The advance of droplet-based microfluidics has enabled compartmentalization and controlled manipulation of monodispersed emulsions with high yield and incorporation efficiency. It has become a highly exotic platform in synthesizing functional material due to the presence of two immiscible liquids and the interface between them. With its intrinsic feature in high degree of product control, advanced emulsion-based synthesis of functional material is constituted as a template for effective water remediation and resource recovery. This chapter aims to provide an overview of recent advances in microfluidic technology for environmental remediation. More specifically, the facility of microemulsion-based functional materials for water remediation is reviewed. Moreover, the removal and recovery of pollutants, such as heavy metal, dye, pharmaceuticals, etc., from aquatic environment by the applications of adsorption on functional micro/nanomaterials are unfolded with respect to its potential for wastewater purification.

**Keywords:** microfluidics, remediation, functional sorbents, recovery, wastewater

## 1. Introduction

Over the past few years, tremendous growth in the manufacturing and widespread application of synthetic chemical compounds in industrial sectors has led to growing number of emerging contaminants in environmental matrices (air, wastewater, water, sediment, and soil), which poses a challenge for regulatory agencies. Apart from that, the environment has gradually suffered as a result of exposure to the emerging pollutants especially in water and wastewater. Various types of physical, chemical, and biochemical methodologies have been reported on effectively removing pollutants. These methods include membrane separation, biological degradation, advanced oxidation process, and adsorption as well [1]. Recent developments have indicated that the adsorption method is favorable due to its wide availability, lower cost, as well as its recyclability. As in terms of cost effectiveness, simplicity of construction, and easy adaptation of operating conditions, particle adsorption materials become the key for realizing various adsorption applications in environment remediation using fixed bed reactors, absorption columns, fluidized beds, and cyclone separators [2]. However, controlled shapes, size, and compartments are some of limitations for most conventional methods. Unlike conventional approaches, microfluidics is comparably conducive as it has improved and extended the possibilities to synthesize highly controlled size of microparticles with excellent adsorption capability and reusability [2].

Microfluidics is a multidisciplinary field stretch across engineering, physics, chemistry, microtechnology, and biotechnology. Microfluidic devices generally have two of the three geometric length scales in the order of microns. The micrometer length scale defines the most obvious but extremely important character of microfluidic devices especially their small size, which allows small sample volumes, low cost, and fast analysis, but with high resolution and sensitivity [3]. With the length scale associated with microfluidic devices, the flow within them tends to be laminar. Moreover, one characteristic of microscale miniaturization is the large surface area to volume ratio. Thus, this favorable aspect plays a major role in control and manipulation of fluid flow in microfluidics. Recent advances and innovations could make microfluidics technology ubiquitous and create microfluidic devices that are more functional, efficient, and cost effective than conventional techniques.

The development of microfluidic systems that allow for the formation of microdroplets inside microfluidic devices has gained greatly attention over the past 20 years. The rise in interest is due to the utilization of microfluidic devices in a broad range of biological and biomedical application areas including disease diagnosis, cell treatment, drug screening, single-cell analysis, and drug delivery. Liquid droplets dispersed in a second immiscible fluid are useful, particularly when the sizes and the size distribution of droplet can be prescribed on a few hundred nanometers to a few millimeters [4]. Microfluidic emulsification approach offers an alternate and versatile route to produce emulsions that are highly monodispersed and have high formation frequencies in multiphase fluid systems [5]. Additionally, the geometrical attributes and flow characteristics within these microfluidics system constitutes flexibility in producing complex structured emulsions, such as double-emulsions and multi-emulsions [6, 7]. Highly monodispersed single, double, or multi-emulsions can be used as a template to prepare micro- and nanoparticles with various structures and morphologies [7], as shown in **Figure 1**. As seen in **Figure 1**, the presence of different particle shapes, compartments, and microstructures is formed based on the flow and geometrical attributes in microfluidics. Consequently, the superior properties of droplet-based microfluidic device have become extremely promising and attractive platform that enables the production of functionalized monodisperse microparticles.

In order to fabricate micro- or nanoparticles, the analysis of droplet formation is imperative to understand the device operation and its process control to meet different application purposes. Additionally, other's droplet manipulation, such as fusion, fission, mixing, and sorting with high precision and flexibility constitutes essential issue, at which extensive investigations have been directed. Based on the sources of the driving force involved, there are five approaches to droplet manipulation: hydrodynamic stress, electro-hydrodynamics, thermos-capillary, magnetism, and acoustics [8]. Hydrodynamic stress is a simple and effective approach to accomplish droplet manipulation relating to the geometrical characteristics of microchannel [9]. In this mode of manipulation, various methods have been employed in the formation of droplets in microfluidics device, including co-flowing mechanisms, flow-focusing mechanisms as well as cross-flowing mechanisms [10]. These mechanisms enabled the formation of dispersions with highly attractive features, particularly the control over droplet and particle size distribution.

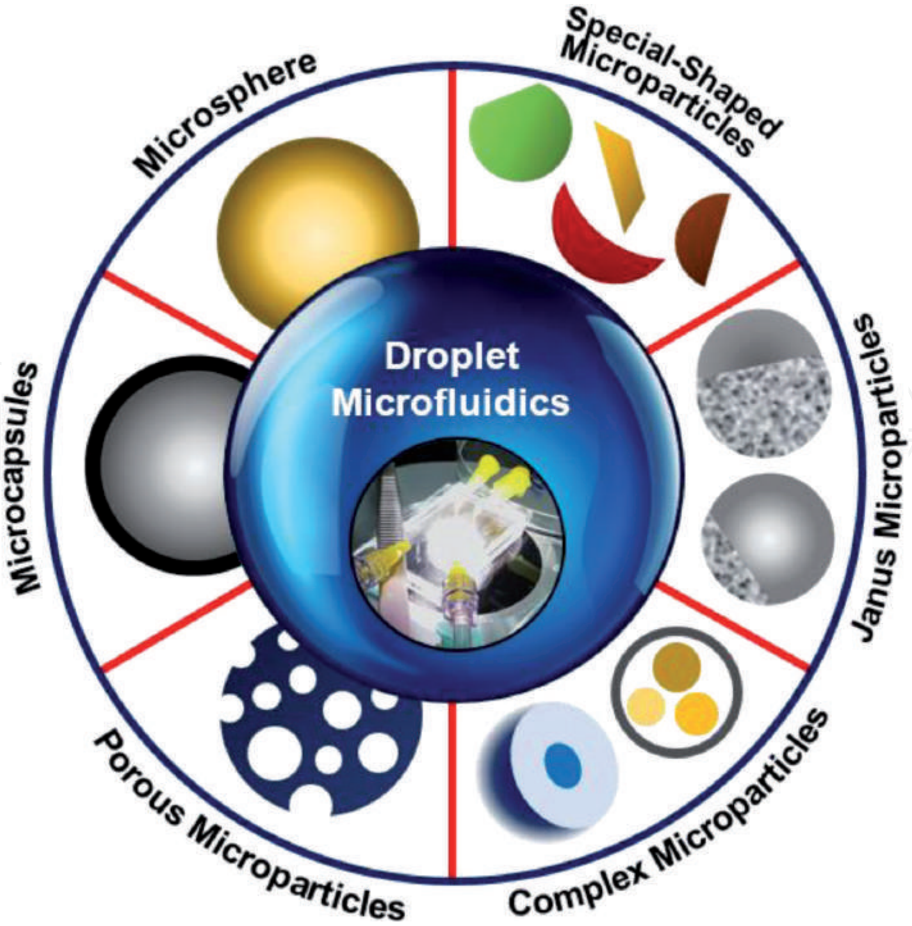

**Figure 1.**
*Classification of various structures of microparticles produced by droplet-based microfluidics.*

Over the years, microfluidic devices have been developed to synthesize particles for water remediation. For instance, Zhao et al. [11] synthesize graphene oxide microspheres using microfluidics technology for the removal of perfluorooctane sulfonate. Dong et al. studied the anionic dye adsorption using chitosan microparticles [2]. In addition, the performance of microcapsules for the $CO_2$ adsorption and permeability was investigated by Stolaroff et al. [12]. Hitherto, there are still little attempts that have been considered to use microfluidic platform as a selection scheme for large-scale industrial wastewater treatment. Toward practical and high capacity, microfluidic platforms generally suffer from the high cost and limited capacity for high throughput production of microfluidic synthesized particles. Nevertheless, it is possible to operate the production in parallel in order to realize continuous processes [13]. Moreover, the fundamental microfluidic research is still highly demanded to bridge the gap between the functional material synthesis and industrial perspective on exploring the possibilities and potential benefits of microfluidic processes [2, 13].

In this chapter, we will discuss the current trend of employing microfluidic technologies for environmental remediation, specifically for wastewater treatment and water remediation. Apart from that, we will also provide a general overview of the facility of microfluidics emulsification for the fabrication of various microparticles and nanoparticles as functional adsorbents. The sorption capacity and performance of the functional materials will be also evaluated in this review. Eventually, this chapter provides an impression of what are the consolidated fields of microfluidic formulation in functional material synthesis that will look like in about a decade from now.

## 2. Microfluidic technology for water remediation and resource recovery

Due to excessive discharges of harmful wastes and by-products to the environment, water contamination is the most prominent in which numerous organic and inorganic pollutants are found in the fresh water resources such as ponds, rivers, and underground water. Traditionally, there are various methods of water analysis including atomic adsorption, chemical analysis, chromatography, colorimetry, and spectrometry. Although these techniques have high sensitivity and accuracy, limitations such as expensive instrumentation, time consuming and requires manual operation in sampling process, causing the researchers to shift their interest toward microfluidics technology, which has a great potential to replace the traditional water analysis techniques [14].

### 2.1 Droplet microfluidic system

Droplet-based microfluidic technology involves the formation and manipulation of discrete droplets inside microdevices [15]. Droplet microfluidics is being widely used in different applications, such as chemical reactions, therapeutic agent delivery, imaging, biomolecule synthesis, diagnostic chips, and drug delivery [16]. The major concerns when creating droplet microfluidic device are the type of microfluidic chip fabrication materials used and the fluids used for droplet generation. Poly(dimethyl)siloxane (PDMS) is commonly used as fabrication material of microfluidic devices because PDMS is a relatively low cost and easily moldable elastomer. Nevertheless, PDMS has low solvent resistance, causing it to deform in the presence of strong organic solvents. Therefore, materials with higher solvent resistance, such as glass [17] and silicon, [18] are used. The pros and cons of the application of different microfluidic chip materials in droplet microfluidic system are shown in **Table 1**. The application of droplet microfluidics in the formation of functional materials for removal of pollutants will be discussed in Section 3 subsequently.

### 2.2 Microfluidic reactors

Microfluidic reactors, also known as microreactors, have been widely used in wastewater treatment because the development of microfluidics technology in this area helps to overcome some existing problems in bulk reactors. The two essential issues of bulk reactor are photon transfer limitations and mass transfer limitations [20]. Thus, great attention and interest have been shown in microfluidic system as microreactor inherits the merit of microfluidics. Recently, the technologies of microfluidics in advanced oxidation processes (AOPs) for wastewater treatment were studied and focused. AOPs involve the utilization

| Application | Glass/ silicon | Elastomers | Thermoset | Thermoplastics | Hydrogel | Paper |
|---|---|---|---|---|---|---|
| Droplets formation | Excellent | Moderate | Good | Good | N/A | N/A |
| Production cost | High | Medium | High | Low | Medium to high | Low |
| Reusability | Yes | No | Yes | Yes | No | No |

**Table 1.**
*Pros and cons of different microfluidic chip materials for different applications [19].*

of hydroxyl radicals ($OH^{\cdot}$) or sulfate radicals ($SO_4^{\cdot-}$) as a major oxidizing agent to effect water purification [21]. This is because these powerful radicals are extremely effective to destruct the organic and inorganic contaminants in wastewater and transform them to less or even non-toxic products [22]. The most popular AOPs that employ the technologies of microfluidics are photocatalysis and Fenton processes. The development and application of several AOP mechanisms will be discussed in the next sub-section. Then, a brief example of the application of different types of microreactors in water treatment and resource recovery is listed in **Table 2**.

### *2.2.1 Photocatalysis*

Heterogenous photoassisted catalysis, known as photocatalysis is one of the examples of hydroxyl radical-based AOPs which is of particular concern in wastewater treatment. It involves the utilization of light for decomposition or mineralization of organic pollutants into innocuous product, such as carbon dioxide and water, in the presence of catalysts [31]. The application of microfluidic technology offers a great number of advantages in photocatalytic water treatment. Microfluidic structures have larger surface-area-to-volume ratio, typically in the range of 10,000–50,000 $m^2/m^3$ [32], compared to bulk reactor in which the surface-area-to-volume ratio is typically below 600 $m^2/m^3$ [33]. The surface-area-to-volume ratio can be much larger if nanoporous photocatalyst

| Microfluidic device design | Application | Result | Ref. |
|---|---|---|---|
| Optofluidic planar reactor | Degradation of methylene blue | 30% of dye degraded within 5 min with a reaction rate constant two orders higher than bulk reactor | [23] |
| Microcapillary reactor | Reduction of methylene blue | Reduction rate of dye increased by >150 times compared to batch system | [24] |
| Tree-branched centimeter-scale reactor | Degradation of volatile organic compounds | 95% of pollutants (benzene, toluene, ethylbenzene, m-p xylenes and o-xylene) degraded in <5 s of residence time | [25] |
| Jet-aerated microfluidic flow-through reactor | Degradation of clopyralid as model organic pollutant | Clopyralid is eliminated effectively after 1 hour under several conditions | [26] |
| Microfluidic atmospheric-pressure plasma reactor | Degradation of methylene blue | >97% of dye degraded | [27] |
| Droplet microfluidic reactor | Extraction of lead (II) | Pb (II) ion was selectively and completely removed from the simulated wastewater effluent within 2.00 s | [28] |
| Microfluidic chip with polymethyl methacrylate (PMMA) plates | Adsorption of copper (II) | Adsorption capacity of 42.08 mg/g is achieved | [29] |
| Simple cross microchannel microfluidic device | Quantification of bacterial cells in potable water | Bacteria were accurately enumerated within 15 min after fluorescent staining | [30] |

**Table 2.**
*Application of microfluidic technology in water remediation and resource recovery.*

film is used. Thus, higher heat transfer performance can be achieved by using microreactors. Furthermore, the rate of reaction is significantly increased and consequently favors having higher throughputs [34]. With the enhancement of reaction rate, the reaction time is reduced. The time taken for degradation process in a microreactor takes only several to tens of seconds [35], whereas bulk reactor requires several hours [36]. Besides, microfluidic layer has short diffusion length, typically 10–100 μm to ease the diffusion of organic pollutants to the reaction surface [31]. In addition, microreactors usually contain an immobilized photocatalyst film under the thin layer of fluid. This can ensure a uniform irradiation on the reaction surface, resulting in higher photon efficiency [37]. Microreactor has self-refreshing effect as the running fluid can refresh the reaction surface naturally. This helps to move away the reaction products and stabilize the photocatalysts. According to journal by Wang et al. [35], the photocatalysts in microreactor can hold several hundred runs of photocatalytic reactions, whereas the activity of photocatalysts in bulk reactors starts to degrade after 10 runs of reactions [38].

### 2.2.2 Other mechanisms in AOPs

Electro-Fenton process is an efficient AOP that involves activation of hydrogen peroxide by metal salts, typically iron, to produce hydroxyl radicals [39]. Electro-Fenton process is extremely effective in water remediation of the effluents, which cannot be efficiently treated using biological technologies [39–41]. Besides, AOPs with plasma-based water treatment (PWT) have been widely studied as PWT have the potential to reduce organic contaminants in wastewater. The application of microfluidic technology in PWT gives the benefits of large surface-area-to-volume ratio and flow control, in low-cost and portable devices [27]. However, more researches and development are needed to validate PWT performance at macro-scale [42].

## 3. Droplet microfluidics for the production of micro- or nanofunctional sorbents

Droplet-based microfluidics is formed through fabricating emulsions of uniform size. There are two approaches to produce emulsions, which are active and passive. Unlike actively controlled microfluidic devices, the breakup of discrete phase in continuous phase driven is controlled in a fully passive manner, which is caused by flow instabilities and hydrodynamic pressure without external actuations, such as mechanical, electrical, thermal, and magnetic method [43]. In this section, passive formation of emulsion-based microparticles is mainly discussed. Emulsions can be produced and manipulated with micro device of different geometries forming different sizes and morphologies [44]. Monodisperse emulsions are produced in laminar flow region and generated drop-by-drop where the over size, shape, and morphologies of micro droplets can be control precisely [45].

The superior properties of droplet microfluidics are advantageous for precise microparticle manufacturing for wastewater treatment. Micro and nanofunctional particles with various morphologies are prepared using templates. In general, microfluidic device forms highly monodisperse emulsified droplets and forms microparticles via solidification, while nanoparticles are formed using photochemical, chemicals or physical methods [46]. The space structure of the emulsions is controlled while preparing the adsorbent with microfluidic devices. By changing the device structure of microfluidic device, complex structure of droplets can be produced such as single, double, and multiple emulsion [17, 47]. These emulsion droplets are classified according to the structures and the evolvement of the emulsion into different structures and morphologies. Single emulsion can be a template to solid particles including spheres and non-spheres, while double and multiple emulsions can be templates for Janus particles, microcapsules, vesicles, hollow spheres or core-shell spheres [48].

### 3.1 Emulsion template: single, double or multiple

Single emulsions are droplets of one phase fluid dispersed in another immiscible phase fluid. Flow focusing, cross-flow, co-flow are systems that are frequently

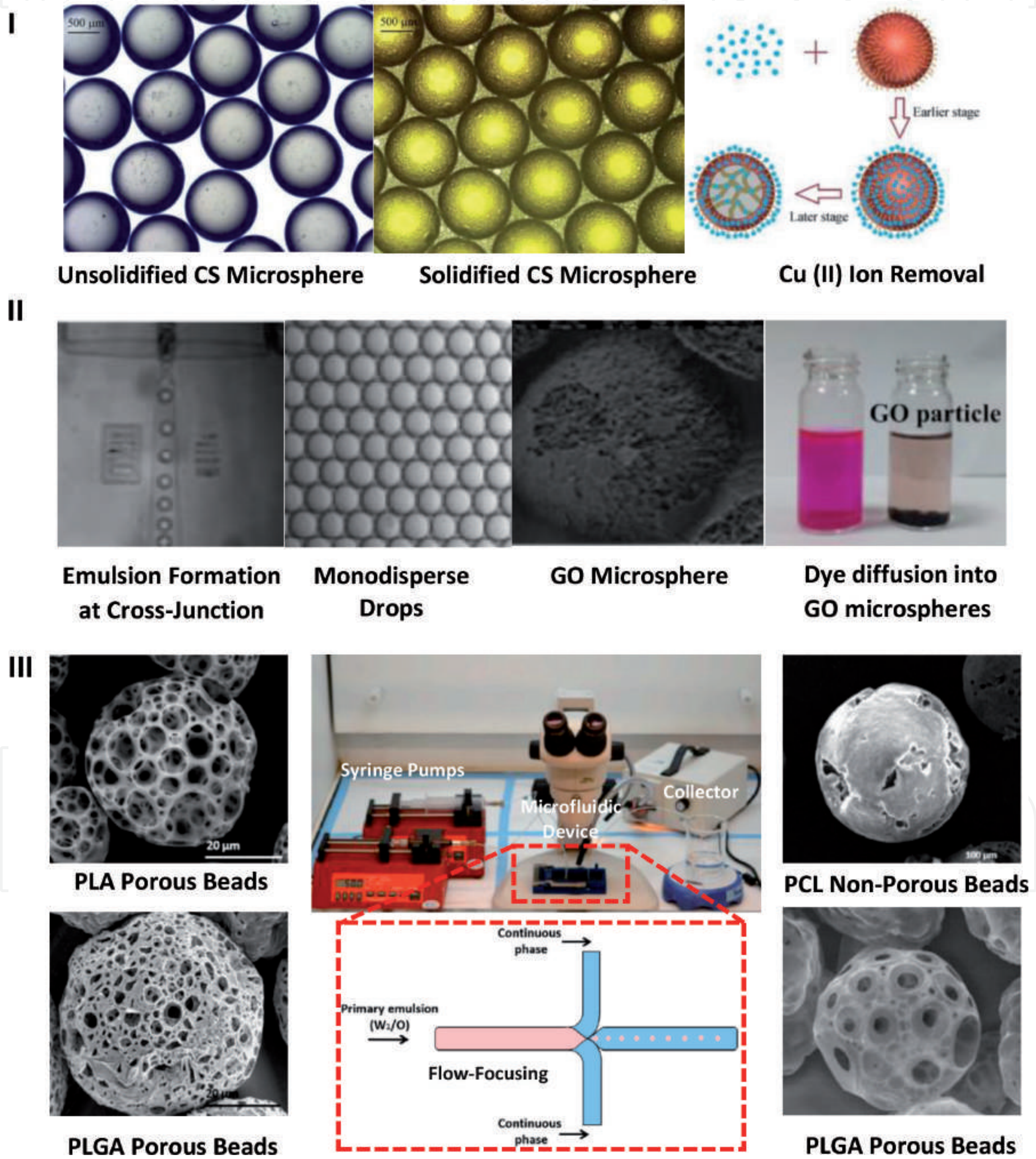

**Figure 2.**
*Wastewater treatment by adsorption method onto microfluidic synthesized microparticles. (I) The adsorption process of heavy metal copper (II) ions using solidified chitosan microspheres (CS-MS) synthesized via cross-flowing PMMA-based microfluidics [29]. (II) Absorption of fluorescent dye molecules using PEGDA-graphene oxide (GO) microspheres [11]. (III) Microfluidic-based synthesis of porous and non-porous PLA, PLGA, and PCL microspheres [54]. (I) is reproduced with permission from Zhu et al., 2017, Copyright 2017, Springer Nature. (II) is reproduced with permission from Zhao et al. [11], Copyright 2016, Springer Nature. (III) is reproduced with permission from Amoyav and Benny [54], Copyright 2019, MDPI.*

| Microsorbent | Device | Approach | Channel size | Emulsion solidification | Ref. |
|---|---|---|---|---|---|
| Chitosan/polyethylenimine-chitosan microspheres | Commercial membrane | Membrane emulsification | Dispersed: 20 µm pores | Chemical cross-linking, solvent extraction | [55] |
| Chitosan/chitosan-poly(acrylic acid) composite microspheres | PMMA plates (laser fabrication) | Flow-focusing | Dispersed: 160 µm wide<br>Continuous: 500 µm width | Chemical cross-linking, solvent extraction | [56] |
| Chitosan microspheres | PMMA plates (laser fabrication) | Cross-flowing | Dispersed: 1000 µm wide<br>Continuous: 1000 µm width | Chemical cross-linking, solvent extraction | [29] |
| Chitosan microsphere | PMMA plates (laser fabrication) | Cross-flowing | Dispersed: 1000 µm width<br>Continuous: 1000 µm width | Chemical cross-linking | [57] |
| Chitosan microparticles | PMMA plates (laser fabrication) | Flow-focusing | Dispersed: 500 µm width<br>Continuous: 500 µm width | Chemical cross-linking | [2] |
| Thiourea-modified chitosan | PMMA plates (laser fabrication) | Flow-focusing | Dispersed: 160 µm width<br>Continuous: 500 µm width | Chemical cross-linking, solvent extraction | [58] |
| Ion-imprinted chitosan microspheres | PMMA plates (laser fabrication) | Cross-flowing | Dispersed: 1000 µm width<br>Continuous: 1000 µm width | Chemical cross-linking | [59] |
| Chitosan/silica hybrid microspheres | PMMA plates (laser fabrication) | Cross-flowing | Dispersed: 1000 µm width<br>Continuous: 1000 µm width | Chemical cross-linking | [60] |
| Graphene oxide/$MgCl_2$-graphene oxide microspheres | PDMS chip (soft-lithography) | Cross-flowing | Not available | Photo-polymerization | [11] |
| Carbon nanotube microspheres | PDMS chip (3D printing/ soft-lithography) | Flow-focusing | Dispersed/Continuous: 900 µm width with a downstream constriction: 200 µm width | Decanting, solvent, cleaning, drying, pyrolysis | [61] |
| Hollow silica microspheres with ethyl butyrate | Glass microfluidic chip | Flow-focusing | Dispersed/continuous: 250 µm width | Hydrolyzation and condensation | [62] |
| PDMS microspheres | Off-the-shelf (needle-based) microfluidics | Flow-focusing | Dispersed: 510 µm width with downstream channel: 600 µm width | Photo-polymerization | [63] |

**Table 3.**
*Microfluidic synthesized spherical and functional microsorbents for water remediation and resource recovery.*

used to form monodisperse droplets, and the coefficient of variation of droplets is usually less than 5% [3]. There are five breaking modes in passive generation, which are squeezing, dripping, jetting, tip-streaming, and tip-multi-breaking. These five modes have its own characteristics, for example, the structure and component of the droplets can be changed to produce inorganic nanoparticles, metal particles, and polymer particles [49]. Double or multi-emulsions are droplets with smaller droplets encapsulated in larger drops [48]. These emulsions are produced with capillary micro devices that involve three fluid streams in different capillaries. Initially, single droplets are formed when inner fluid is sheared by the middle fluid, then double or multiple droplets are formed when the outer fluid pinched off the single droplets containing in the middle fluid. There are difficulties of precisely controlling the shell thickness, aggregation, and secondary nucleation.

### *3.1.1 Special-shaped particles*

Non-spherical particles have unique properties, and they are usually fabricated with many strategies such as seeded emulsion polymerization [50], template molding [51], and self-assembly [52]. However, a high quality, monodisperse, non-spherical particles with tailored geometries and shapes yet still difficult to produce using these methods. Droplets with different sizes and shapes in microfluidic channels are confined with microfluidic technologies for fabrication of non-spherical particles. The droplet will be deformed into ellipsoid, a disk, or a rod if the largest sphere can accommodate in the channel of a larger volume of droplet. Non-spherical droplet will be formed after they are solidified in the confined channel [53].

### *3.1.2 Spherical particles*

There are different types of spherical particles, such as polymer microspheres, inorganic microspheres, noble metal nanospheres, and semiconductor nanospheres [48]. Polymer microspheres are usually prepared through spray-drying, coacervation, and emulsification [48]. Inorganic microsphere, which is the composed of titanium, silica, and carbon, have potential application in biomolecules, sensor, catalyst, and drug deliver. Noble metal nanosphere, such as gold, silver, and platinum, has shape and size dependent properties. It is hard to obtain desired size and size distribution as this individual nanoparticle tends to precipitate and coagulate to lower the surface energy. For the synthesis of semiconductor nanospheres, the microfluidic reactor should be chemically and thermally stable; thus, the droplets and carrier fluid could be stable, non-volatile, non-interacting, and immiscible from ambient to reaction temperatures. Hitherto, these microparticles are widely applicable in biological, pharmaceutical, medical (such as tumor treatment, drug controlled-release, and multi drug loading), optical, electrical applications, and researches. Moreover, polymer microspheres and inorganic microspheres are of great interest due to their potentials in adsorption separation as adsorbent in wastewater treatment, as shown in **Figure 2** and **Table 3** [29].

## 4. Sorption performance of different functional micro-sorbents for pollutants removal

Pollution management is now one of the most challenging issue facing modern societies. Due to the increasing population as well as industrialization of most countries, some pollutants are being discharged into aquatic environment without further treatment. This has a negative impact on the environment. The advancement of microfluidic technologies has allowed the synthesis of functional sorbents with greater sorption capacity. This is because the structure of the sorbent can be easily modified during emulsion. Thus, microsorbents with different functional groups can be synthesized to remove certain pollutants. Chitosan is a material that is widely used to make adsorbent for pollutant removal due to its affinity in removing heavy metals. In this subsection, the sorption performance of different functional microsorbents will be discussed as well as the kinetic model and adsorption isotherm.

### 4.1 Application and sorption performance of chitosan-based microsorbents

Chitosan is a natural polymer material that is found in abundance. It is made from the chitin of crustaceans and shrimps. Due to its affinity with heavy metals, it is a material with great potential for biosorbent synthesis. For instance, polyethylenimine-chitosan microspheres are used to remove methyl orange and Congo red dyes. Based on empirical observations, the uptake of methyl orange dye ranges around 88–97%, whereas the uptake of Congo red dye ranges around 86–96% [55]. Zhai et al. [57] and Dong et al. [2] both have reported that the sorption performance of chitosan microspheres in the uptake of the common textile azo dyes. Apart from synthetic dyes, chitosan microspheres were also synthesized to remove copper (II) ions, the sorption performance was observed to be roughly 38.52 mg/g [29]. With the addition of polyacrylic acid, the sorption performance increased significantly [56]. Besides, Lv et al. [64] studied the sorption uptake of copper (II) ion with using polyethylenimine-poly(glycidylmethacrylate)-chitosan microsphere. Microfluidic synthesized ion-imprinted chitosan microspheres and thiourea-modified chitosan were also used to remove copper (II) ions. These studies have proved that microfluidic synthesized chitosan is a promising biosorbent for water remediation. Moreover, its mechanical intensity, sorption performance, and equilibrium adsorption amount of emerging contaminants are highly enhanced as compared to those conventional methods.

### 4.2 Application and sorption performance of non-chitosan-based microsorbents

Aside from chitosan, other microfluidic synthesized materials such as graphene oxide, silicon-based organic polymer, carbon, and silica were also used to be studied for wastewater treatment [11, 61–63, 65]. Copic et al. [61] reported that sodium dodecyl sulfate (SDS) and Congo red dye can be removed using carbon nanotubes microspheres. Li et al. [62] investigated that the synthesized hollow silica microspheres offer a much higher storage capacity as compared to conventional hollow nanospheres. Moreover, the drug detoxification capability of the hollow silica microspheres containing ethyl butyrate was tested on iodine removal [62]. The sorption capacity of iodine by silica microspheres goes up to 95% removal uptake. Lian et al. [63] studied the removal of toluene using polydimethylsiloxane microspheres synthesized via needle-based microfluidic devices. Ren et al. [65] synthesized anisotropic Janus microparticles loaded with $Fe_3O_4$ and $MnO_2$ nanoparticles for the adsorption of basic dyes in wastewater. The sorption performance of the dye uptake using Janus micromotors can be varied from 47 to 94%. Thus, the current adsorption isotherm, kinetic modeling studies, and sorption performance of each microfluidics generated micro-sorbents for different water applications have been listed in **Table 4**.

| **Microsorbents** | **Application** | **Sorption performance** | **Adsorption isotherm** | **Kinetic modeling** | **Ref.** |
|---|---|---|---|---|---|
| Chitosan/polyethylenimine-chitosan microspheres | Adsorption of methyl orange (MO) and Congo red (CR) | MO uptake: 88–97%<br>CR uptake: 86–96% | Not available | Pseudo-second-order | [55] |
| Polyethylenimine-poly(glycidyl methacrylate)-chitosan microspheres | Adsorption of copper (II) ions | $q_{max}$: 229 mg/g | Langmuir | Pseudo-second-order | [64] |
| Chitosan/chitosan-poly(acrylic acid) composite microspheres | Adsorption of copper (II) ions | Chitosan:<br>$q_{max}$: 50 mg/g<br>chitosan-poly(acrylic acid):<br>$q_{max}$: 66–72 mg/g | Langmuir | Pseudo-second-order | [56] |
| Chitosan microspheres | Adsorption of copper (II) ions | $q_{max}$: 38.52 mg/g | Langmuir | Pseudo-second-order | [29] |
| Chitosan microsphere | Adsorption of methyl orange | $q_{max}$: 207 mg/g | Langmuir | Pseudo-second-order | [57] |
| Chitosan microparticles | Adsorption of methyl orange | MO uptake: 15% to >95% (dosage from 1 to 7 mg).<br>$q_{max}$: 182 mg/g<br>(40 ppm) | Langmuir | Pseudo-second-order | [2] |
| Thiourea-modified chitosan | Adsorption of heavy metal copper (II) ions | $q_{max}$: 60.6 mg/g<br>(100 ppm) | Not available | Pseudo-second-order | [58] |
| Ion-imprinted chitosan microspheres | Adsorption of heavy metal copper (II) ions | $q_{max}$: 81.97 mg/g<br>(Ce < 400 ppm) | Langmuir | Pseudo-second-order | [59] |
| Chitosan/silica hybrid microspheres | Adsorption of heavy metal copper (II) ions | $q_{max}$: 53 mg/g (100 ppm) | Not available | Not available | [60] |
| Graphene oxide/$MgCl_2$-graphene oxide microspheres | Adsorption of perfluorooctane sulfonate (PFOS) | PFOS uptake:<br>>95–98% (in 2 min)<br>$q_{max}$: 5300 mg/g | Not available | Not available | [11] |
| Carbon nanotube microspheres | Adsorption of sodium dodecyl sulfate (SDS) and congo red (CR) | Filtration efficiency:<br>CR (84.7%), SDS (61.6%) | Not available | Not available | [61] |

| Microsorbents | Application | Sorption performance | Adsorption isotherm | Kinetic modeling | Ref. |
|---|---|---|---|---|---|
| Hollow silica microspheres with ethyl butyrate | Waste removal and drug detoxification/ iodine removal | Iodine uptake: 95% (in 30 seconds) | Not available | Not available | [62] |
| Poly(dimethylsiloxane) microspheres | Adsorption of toluene | Toluene uptake: 30–45% (350 ppm) | Not available | Not available | [63] |
| Poly-(ETPTA) /$Fe_3O_4$/$MnO_2$ bubble-propelled micromotors | Adsorption of methylene blue (MB) | MB uptake:<br>47–94% (6.67 ppm in 6.7% w/w $H_2O_2$) | Not available | Not available | [65] |

**Table 4.**
*Adsorption isotherm and kinetic modeling studies of microfluidics generated micro-sorbents on the uptake of each emerging contaminants.*

## 5. Conclusion

Certainly, microfluidic technologies are a relatively new research with great potential for development to enable more cost-effective synthesis of functional sorbents. Currently, the state-of-the-art microfluidic reactors for water remediation and resource recovery are being implemented in small-scale applications. Example of microfluidic reactors includes microfluidic atmospheric pressure plasma reactor, which is used to degrade methylene blue dyes. Furthermore, the advances in microfluidic technologies have improved the production of micro sorbents using microfluidic technology. Many efforts are also pouring into researching different functional sorbents for removal of different pollutants in wastewater. The results of such research have culminated in the discovery the adsorption capacity and isotherm model of different micro sorbents, which gives insight on the suitable sorbents required for different pollutants.

At present, the need of highly effective water remediation and resource recovery has brought about mounting interest in the research of microfluidic technologies. Many breakthroughs had been achieved in such research which enabled highly specific and controlled synthesis of functional sorbents using microfluidic systems. However, there are still many barriers that prevent the implementation of microfluidic technologies on an industrial scale. The greatest challenge against microfluidic technologies is the economical aspect. Due to the highly specific characteristics of sorbents used in wastewater treatment, most microfluidic systems are highly specific as well. Sorbents used in different applications would require different microfluidic systems to synthesize. Thus, more research will need to be done in order for such problems to be overcome. Of course, environmental problem such as water remediation and resource recovery cannot be solved by microfluidic technology alone and will need other technologies to complement it.

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## Conflict of interest

The authors declare that they have no conflicts of interest.

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