We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Microdroplets Advancement in Newtonian and Non-Newtonian Microfluidic Multiphase System

Kai Seng Koh, Voon Loong Wong and Yong Ren

Additional information is available at the end of the chapter

Abstract

With recent advancement in droplet microfluidics for both microdroplet encapsulation and fission, it is of paramount importance to understand the flow physics for both Newtonian and non-Newtonian fluids in microdroplet encapsulation and fission as the development of the field is approaching to its maturity. The chapter aims to review and discuss the fluid flow behavior of the multiphase system, mathematical models as well as the fundamental phenomena driving force of microdroplet encapsulation and fission multiphase system. Together, the recent advances in technologies that enable fabrication and application of droplets encapsulation and fission from both Newtonian and non-Newtonian microfluidic multiphase system will be reviewed as well.

Keywords: Newtonian fluids, non-Newtonian fluids, microfluidic, multiphase system, microdroplet encapsulation, microdroplet fission

1. Introduction

Emulsion is a fine dispersion of small droplet made from two immiscible liquids, where one liquid phase is dispersed into another continuous flow of liquid phase in which both liquids are not soluble with one another [1]. The fundamental liquids combination for emulsion to form is rather simple, i.e., where the multiphase system usually have large liquids density difference (at least >100 kg/m^3) using the example of water and cooking oil; the larger the density difference, the better the emulsion can be formed. In addition, the multiphase system of the liquids selection can be classified into Newtonian fluid systems and non-Newtonian fluid systems. In the case of Newtonian fluids such as water, oil, glycerol and salt solutions with low molecular weight, due to the independent of fluid viscosity from shear rate and fluid
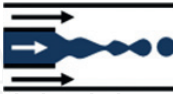
velocity flow, the shear stress in a steady, laminar flow condition is having a linear relationship with its shear rate. In contrast, non-Newtonian fluids, examples of which in daily life including chocolate, toothpaste, lubricating oils experience a non-linear relationship for its shear stress versus shear rate curve due to the fact that the fluid viscosity is a variable at any given flow condition, i.e., temperature and pressure. Such fluid properties lead to much differences in term of the emulsion productions thus far in all engineering approaches. Conventionally, emulsion is prepared using high-pressure homogenizers and colloid m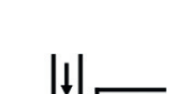ill. These devices apply high mechanical shear force to break up the large emulsion into smaller ones that are subsequently stabilized by the use of emulsifier [2]. However, such method contributed to large size distribution of emulsions formed [3], leading to material loss as well as emulsion function efficiency issue. This dispersity issued was then resolved by integration of microfluidic technology that was firstly developed in 1950s [4]. Microfluidic technology is defined as a branch of fluid mechanics that focuses on the understanding, designing, fabrications and operations of system that convey liquids inside channels with two of the three geometry length scales in the order of microns [5]. Furthermore, with the length scale associated within the microchannel, the flow regime formed in a microfluidic channel will not develop into turbulent flow, enables fluid to be manipulated that will form emulsion with high monodispersity. The wide range of technology options from decades of microfluidic multiphase system developments has allowed emulsion to be generated and manipulated.

In this chapter, we aim to summarize the main technologies for emulsion formation non-Newtonian microfluidic multiphase system using Newtonian fluid as a comparison. The chapter will start with the review of fundamental two-phase flow in microfluidic followed by discussion of the fundamental flow physics of microdroplets translocation and breakup phenomena in microfluidics. The detailed differences between Newtonian and non-Newtonian flow system will be illustrated and compared. Emphasis will be placed on the advancement of emulsions formed, i.e. encapsulation and fission from single emulsion. Finally, we conclude with an outlook to the future of the field. This chapter is meant to familiarize readers who may be new to the field of microdroplets formation in Newtonian and non-Newtonian fluid systems, as well as those readers who are new to the field of microdroplets formation via encapsulation and fission approaches, and eventually bridge the knowledge gap between the two correlations, disciplinary fields.

2. Two-phase flow in microchannels

In two-phase flow microfluidics, dispersed and continuous phase fluids generally were dispensed separately into the microfluidic device. The continuous and dispersed phase channels typically meet at a junction, depending on the specific geometry of a microfluidic device. Each shape of the junction helps to define the local flow fields that deform the interface between the two immiscible fluids [6, 7]. These configurations are also shown schematically in **Table 1**. When the instabilities of free surface between phases are sufficiently large, drops in microscale emerge and eventually pinch-off from the dispersed phase. There are many controlling parameters that will affect the microdroplet generation regime such as, interfacial tension [8, 9], surface

Approaches	Breakup regimes	Flow regime description	Diagrams
Co-flowing streams	Dripping	Droplet forms at the exit of the capillary tube tip and propagates downstream with the flow.	
	Jetting	Droplets pinch off from an extended thread downstream of the capillary tube tip.	
Cross-flowing streams	Squeezing	Dispersed threads block the outlet channel leads to dramatic increase in the dynamic pressure upstream of the droplet, thus forcing the interface to neck and pinch off into a droplet.	
	Dripping	Dispersed thread does not touch the wall of the channel in the entire droplet formation process.	
	Jetting	Droplet breakup point moves progressively downstream of the outlet channel.	
Elongational strained flows	Squeezing	The tip of the droplet phase effectively blocks the cross-section of the orifice.	
	Dripping	Droplets are periodically formed in the orifice.	
	Jetting	The tip of the droplet phase extends downstream of the orifice and small droplets are formed at its terminus.	
	Threading	Each droplet is formed a long and thin thread of the inner liquid is dragged behind the droplet. This thread subsequently breaks up into a group of tiny secondary droplets	

Reproduced from Ref. [7, 15–17] with permission from the Physics of Fluids, Physical Review Letter and Lab on Chip.

Table 1. Main approaches for droplet breakup in microchannel.

wettability or wall adhesion [10], the volumetric flow rate [11, 12], viscosities of both immiscible fluids [9, 11, 13] and channel geometry [14].

For microdroplet formation to be made possible in microfluidics, a defined flow conditions must be fulfilled in order to achieve the dripping regime [16, 18–20]. In the case of Newtonian fluids, the dripping regime occurs when the Weber number (We) of the dispersed phase and the Capillary number (Ca) of the continuous phase are less than one. Under these conditions, droplets formed are highly uniform and their uniformity is unaffected over a wide range of flow rates. However, non-Newtonian fluids rarely fulfill these conditions and pose a challenge in achieving monodispersed microdroplets due to their complex rheological characteristics. As general thumb rule, non-Newtonian fluids can be further classified intro three groups, i.e. purely viscous fluids, time-dependent fluids, and viscoelastic fluids. Each fluid group possess distinct characteristic respectively; however, there is no single constitutive equation that has been established to describe the rheogram for these fluids. For instance, the extensional viscosity of the fluid can resist the pinching at the tip of the capillary that is required for a microdroplet to form. This results in a long cylinder of fluid forming from the capillary tip to a distance downstream from the tip before breaking into non-uniform sized or polydispersed microdroplets formation due to the Rayleigh-Plateau instability [21]. Non-Newtonian fluids also exhibit a variety of behaviors that are unique to their chemical compositions, mixture combinations and many physical conditions that include flow rate, temperature, etc. Such complexities in the characteristics of non-Newtonian fluids prevent a thorough understanding of the dispersion stability and break-up of individual emulsions in microfluidics. Moreover, it is also known that an emulsifying non-Newtonian solutions in microfluidics in a controllable manner is a persistent problem [21] that prevents these techniques from being suitable for industrial applications. Understanding the dynamical mechanisms of microdroplets formation of non-Newtonian fluids in microfluidic channels is essential to ensure microdroplets can be created based on the droplet size, patterns, and productivity.

In microfluidic systems, the length scales demands that all flow to be laminar. Based on the Newtonian and non-Newtonian flow through the microchannel with rectangular cross-section, the axial velocity in the fully developed region is a function of two independent variables and the study of the hydrodynamic behavior in a rectangular microchannel requires a two-dimensional or three-dimensional analyses. The non-linear partial differential momentum Navier-Stokes equation with the associated boundary condition of zero velocity at the wall for a pressure-driven, steady-state, incompressible, constant viscosity, known as Newtonian fluid and the flow without body forces in microchannel is being presented as follows:

$$0 = -\frac{\partial P}{\partial x} + \eta \left(\frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2} \right) \text{ for } -\frac{w}{2} < y < \frac{w}{2} \text{ and } 0 < z < h \tag{1}$$

where u is average velocity characteristic of the flow, dynamic viscosity is η, and P is the pressure, x is the coordinate axes along the channel length, y is the coordinate axes along the channel width, z is the coordinate axes along the channel height, w is the channel width, and h is the channel height, respectively. With no-slip boundary condition, the geometry of the cross-section of the rectangular is fixed and an analytical solution solutions is possible [22, 23].

In applying the Navier-Stokes equation, the analytical solutions of the Poiseuille flow for rectangular cross-section are shown as follows:

$$u_x(y,z) = \frac{4h^2 \Delta P}{\eta \pi^3 l} \sum_{k=1,3,5...}^{\infty} \frac{1}{k^3} \left[1 - \frac{\cosh\left(k\pi \frac{y}{h}\right)}{\cosh\left(k\pi \frac{w}{2h}\right)} \right] sin\left(k\pi \frac{z}{h}\right) \tag{2}$$

where l, w and h are the length, width and height of the channel, respectively, ΔP is the driven pressure drop, η is the viscosity of liquid. Most real fluids exhibit non-Newtonian behavior, which means that the flow curve presents a nonlinear relationship between shear stress and shear rate or does not pass through the origin. The laminar velocity profile of a power-law fluid flowing through a rectangular duct to the governing equation is shown as below [24]:

$$\frac{u(y,z)}{U} = \sum_{i=1}^{6} A_i sin\left[\alpha_i \pi \frac{(z/h)}{2} + 1\right] sin\left[\beta_i \frac{(y/w + 1)}{2}\right] \tag{3}$$

where constant α_i and β_i and A_i is the constants selected to minimize an integral. Six constants which are to be computed by the Ritz-Galerkin method are identical to the corresponding Fourier coefficient and tabulated as a function of aspect ratio and fluid-behavior index (**Figure 1**).

2.1. Microdroplets translocation and breakup phenomena in microfluidics

An emulsion contains a mixture of two immiscible liquids as one phase being dispersed throughout the other phase in small droplets. Most common emulsions include oil-in-water, or direct emulsions, and water-in-oil, or inverted emulsions [19]. The characteristics of emulsion products, foremost the droplet size distribution is the most important parameters that affect the stability, rheology, chemical reactivity, and physiological efficiency of any emulsion
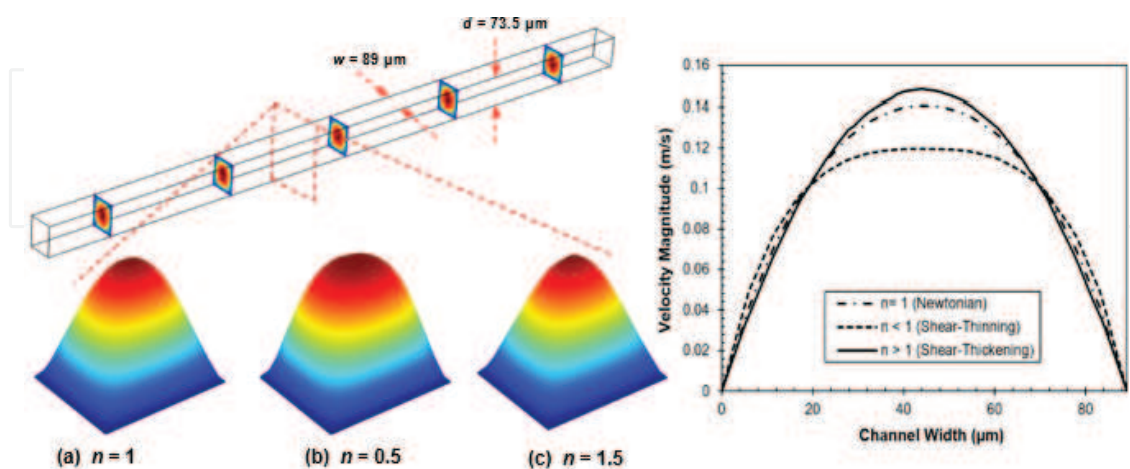
Figure 1. Velocity profile for laminar (a) Newtonian (n = 1) and (b) non-Newtonian shear-thinning (n < 1) and (c) shear-thickening flow (n > 1): Two-dimensional (2D) plot with velocity height expression and one-dimensional (1D) plot with parabolic velocity profile in rectangular microchannel at different power-law index n. w denotes the channel width and d denotes the depth of the microchannel.

[25–27]. For most microfluidic applications, the Reynolds number is much smaller than 1, indicating the effects of volume-based inertia and gravity are not as significant as that in macroscale. The surface-based interfacial tension, flow rates, surface chemistry, and the viscosity become more significant and play in controlling flow behavior of multiphase flow in microscale. Moreover, the degree of confinement, channel aspect ratio, and geometrical structure also significantly induce the impact on capillary pressure, which promote the destabilization of the interface and the drop formations.

2.1.1. Newtonian flow systems

Under this system, interfacial tension between two liquid phases becomes dominant above all physical forces such as gravitational forces, viscous forces and inertia forces as the interest of dimension gets smaller due to the existence of a high surface-to-volume ratio within a microscale device. With that, an approximation of the magnitude of surface tension force, which has the stabilizing effect on the emerging tip [13], arising from

$$\Delta P_L = \sigma \left(\frac{1}{r_\alpha} + \frac{1}{r_\gamma} \right) \tag{4}$$

where r_a and r_r are the radii of axial and radial curvature across the interface in a squeezing regime.

Much studies were conducted in particular on the predominance of interfacial tension on characters of microfluidic Newtonian droplet formations [8, 9, 28, 29] and its changes in presence of surfactants in microfluidic systems [30, 31]. Surface flows of surfactant can induce variations in surface tension, i.e. Marangoni effect, which can substantially alter the interfacial morphology and resulting droplets size [32]. Apart from the presence of surfactant, depending on the fluid viscosity or concentration [12, 33], temperature [34] and the presence of micro- or nanoparticles in the fluid [34, 35] can modify considerably the value of surface tension of the fluid in nature and thus tailor the two-phase flow behavior within the microfluidic system. The effect of aforementioned is summarized in **Figure 2**.

The interaction between the solid surface and fluid in a microchannel has also been a major research focal point as the interaction impacts the dynamics of the droplet formation process. **Figure 2** (V) illustrates the flow patterns for different wetting conditions in a T-shaped microchannel. Most studies of droplet generation in microfluidic devices involve the numerical studies of the contact angle effect on the shape, size, the distance between two neighboring droplets, detachment point and the generation frequency of droplets in microfluidic system [12, 29], in which the channel wall surface plays significant role in generating larger droplets with smaller contact angle provide longer contact time with the surface, especially for small values of capillary number, in consistent with the numerical results.

The flows in a microscale or nanoscale device naturally emphasize phenomena associated with interfacial tension and wetting properties. In addition, inertial and viscosity effects are two important parameters in characterizing the role of the shear-stress exerted from the continuous phase acts to deform the interface during the microdroplet breakup process, i.e. **Figure 2** (I)
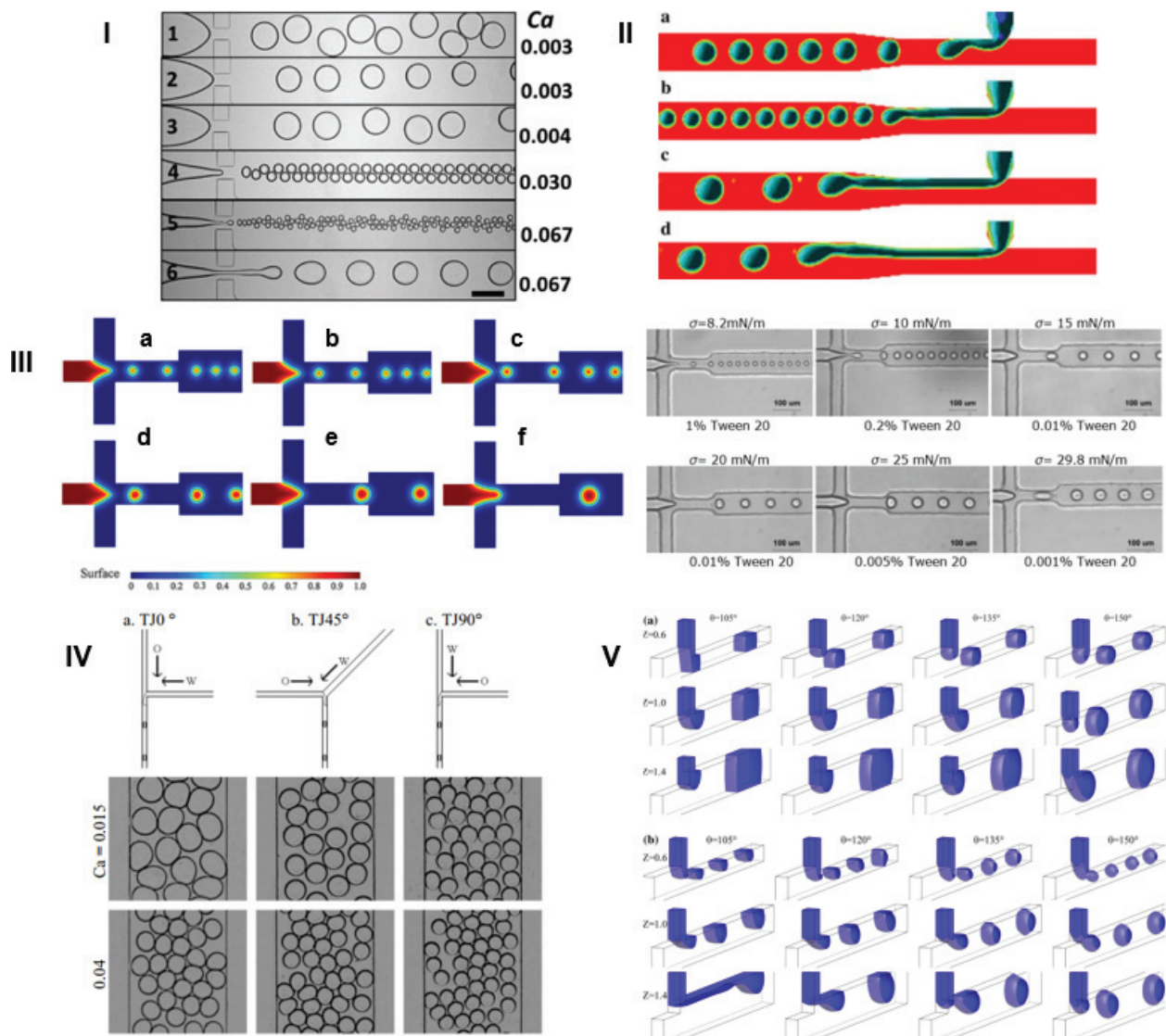
Figure 2. Passive Newtonian droplet generation with microfluidics. (**I**). Oleic acid droplet production at aqueous glycerol solution with varying flow rate ratios: (1) 0.16, (2) 0.8, (3) 0.667, (4) 0.11, (5) 0.1 (6) 0.2. (**II**) Drop images at different values of continuous phase viscosity in Newtonian System. The images a–d are μ_{CP} = 0.00332, 0.008, 0.01 and 0.018 Pa.s, respectively. (**III**) The effect of interfacial tension on droplet breakup dynamics with experimental and numerical justification: (a) 8.2 mN/m, (b) 10 mN/m, (c) 15 mN/m, (d) 20 mN/m, (e) 25 mN/m and (f) 29.8 mN/m. (**IV**) The impact of different inlet channel geometries and angle on microfluidic drop formation. (**V**) Droplet formation mode under various contact angles. **I** is reproduced with permission from [36], Copyright 2015, Royal Society of Chemistry. **II** is reproduced with permission from [37], Copyright 2009, Springer. **III** is reproduced with permission from [31], Copyright 2011, Springer. **IV** is reproduced with permission from [21], Copyright 2009, American Physical Society. **V** is reproduced with permission from [38], Copyright 2015, Elsevier.

and (II). The influence of two phase flow rates and viscosities on the size of water-in-oil emulsion study at a T-shape microfluidics concluded that the relationship between shear stress and flow rate of continuous phase, thus quantifies the magnitude of shear stress ($\tau \propto \eta_c Q_{oil}$, where η_c is the viscosity of continuous phase) acting on the interface [13]. As Q_{water}, the volumetric flow rate of dispersed phase increases, the shear stress exerted on the droplet is increased due to the difference of the flow rate of the two fluids decreases with increasing

Q_{water}. These numerical and experimental results imply that the flow rate of the both phases considerably alter the microdroplet formation mechanisms under laminar flow in different microfluidic configurations. Apart from the effect of two phase flow rates or flow rate ratio, $Q = Q_d/Q_c$, the length of the microdroplet formed is also depending on the viscosity ratio ($\lambda = \eta_d/\eta_c$). Previous investigations reported that an increase of the viscosity of continuous phase gives rise to the viscous stress added on the dispersed phase, and thus decreasing the microdroplet size and alter the flow pattern [11, 20, 39]. This was further validated by a numerical study on the microdroplet detachment mechanism for Newtonian fluids that subjected to cross-flow drag, continuous phase inertia, interfacial tensions, and viscosity ratio, which are shown by the following equations

$$\text{Interfacial tension force, } F_\sigma = \frac{\pi\sigma w_d{}^2}{d} \tag{5}$$

$$\text{Cross} - \text{Flow drag force, } F_D = 3\pi\eta_c(v^* - v_d)df(\lambda_\eta) \tag{6}$$

where d is the droplet diameter, v^* is the continuous phase velocity at the height of the microdroplet center, v_d is the microdroplet velocity, $\lambda_{\eta = }\eta_d/\eta_c$ is the viscosity ratio and $f(\lambda_\eta) = \left(\frac{2}{3} + \lambda_\eta\right)/(1 + \lambda_\eta)$ captures the effect of the disperse phase viscosity on the microdroplet drag. When $\lambda_\eta \gg 1$, the disperse phase viscosity is sufficiently high that the microdroplet is solid-like and the interfacial tension force reduces to the drag from Stokes flow around a solid sphere. On the contrary, internal flow within the microdroplet becomes possible and this acts to reduce the drag on the microdroplet from the continuous phase for smaller values of λ_η [40]. Meanwhile, a detailed studies of droplet microfluidics performance as function of flow conditions as it is crucial when designing the geometry of the microchannel, particularly is one of the major parameter which can be very sensitive to flow conditions and drop properties [41]. Specifically, the cross-sectional area of the main channel can influence the volume of microdroplets detached significantly in both the squeezing regime as well as in the dripping regime as presented here.

2.1.2. Non-Newtonian flow systems

Although there are many methods of producing monodispersed microdroplets, controlling the size of the droplets within the range of 1–100 μm remains to be a challenge that has yet to be fully resolved. Non-Newtonian fluids have far more complex rheological properties that are normally physical and chemical conditions dependent. It also exhibits more complex behaviors in terms of its dynamics in comparison to its Newtonian counterpart, particularly in the field of microfluidics [17]. This is due to the non-linear relationship between the shear rate of the fluid and its viscosity as compared to Newtonian fluids, whose viscosities remain constant regardless of the shear rate. Generally, non-Newtonian fluid can be classified into three general groups in shear flow, which are shown in **Table 2**.

In an attempt to develop an efficient and reliable drug delivery system, researches have been carried out using various types of non-Newtonian fluids in order to determine which materials would yield the most desirable results. Of all, shear thinning fluids are the most commonly encountered fluids in our everyday lives, many existing as ordinary fluids such

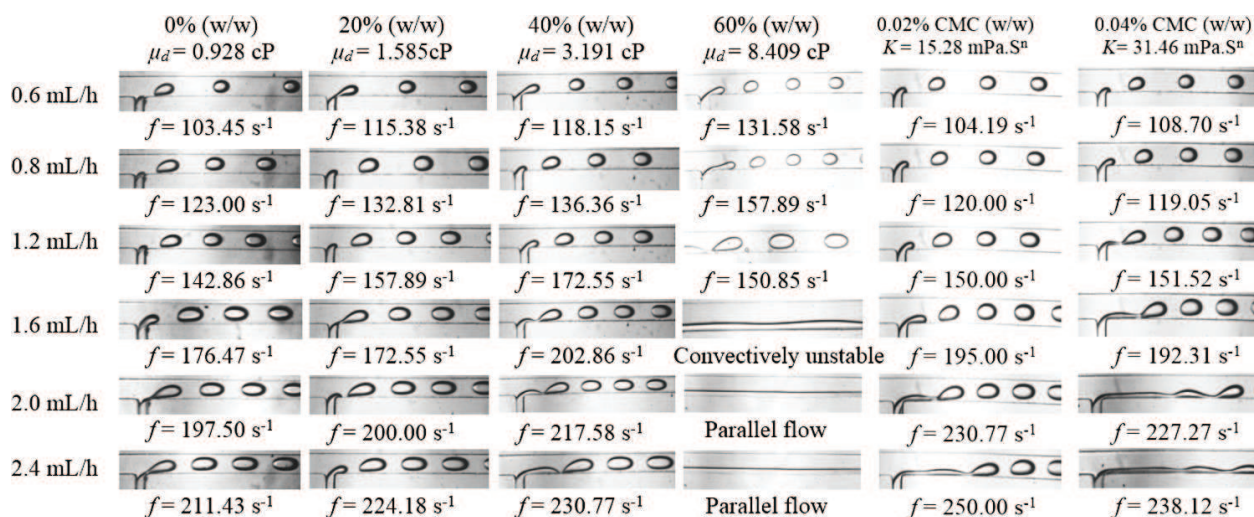| Fluids	Description	Fluid type	Model	Constitutive equations
Purely viscous/Time-Independent	The rate of shear at any point is determined only by the value of the shear stress at that point at that instant; can be known as time-independent fluids/ generalized Newtonian fluids (GNF).	Dilatant (*Shear-Thickening*)	Ostwald Waele	$\mu = m\,(\dot{\gamma})^{n-1}$
			Carreau-Yasuda	$\frac{\mu - \mu_\infty}{\mu_o - \mu_\infty} = \left\{ \left(1 + (\lambda\dot{\gamma})^2\right) \right\}^{(n-1)/2}$
		Pseudoplastics (*Shear-Thinning*)	Cross	$\frac{\mu - \mu_\infty}{\mu_o - \mu_\infty} = \frac{1}{1 + k(\dot{\gamma})^n}$
			Ellis	$\mu = \frac{\mu_o}{1 + \left(\tau/\tau_{1/2}\right)^{\alpha-1}}$
		Viscoplastics	Bingham Plastics	$\tau = \tau^B + \mu(\dot{\gamma}) \text{ for } |\tau| > |\tau^B|$ $\dot{\gamma} = 0 \qquad \text{ for } |\tau| < |\tau^B|$
			Herschel-Bulkley	$\tau = \tau^H + m(\dot{\gamma})^n \text{ for } |\tau| > |\tau^H|$ $\dot{\gamma} = 0 \qquad \text{ for } |\tau| < |\tau^H|$
			Casson	$(|\tau|)^{1/2} = (|\tau_o{}^c|)^{1/2} + \left(\mu|\dot{\gamma}|\right)^{1/2} \text{ for } |\tau| > |\tau^c|$ $\dot{\gamma} = 0 \qquad\qquad\quad \text{ for } |\tau| < |\tau^c|$
Time-dependent	The relation between shear stress and shear rate further dependence on the duration of shearing and their kinematic history.	Thixotropy Rheopexy	Generalized Herschel-Bulkley	$\tau = (\tau_o + \tau_1) + (m_o + \xi m_1)(\dot{\gamma})^n$
Viscoelastic[*]	Substances exhibit characteristics of both viscous fluids and elastic solids and showing partial elastic recovery after deformation.	Viscoelastic	Oldroyd-B	$\tau_1 + \lambda_1 \overset{\triangledown}{\tau}_1 - 2\mu_1\left(D - \lambda_2 \overset{\triangledown}{D}\right) = 0$
			Giesekus-Leonov	$\tau_p + \lambda_1 \tau_p - \frac{\alpha\lambda_1}{\mu}\tau_p{}^2 + \mu\dot{\gamma} = 0$
			Phan-Thien-Tanner	$\overset{\triangledown}{\tau} + \xi\left(D\cdot\tau - \tau\cdot D^T\right) + \frac{Y}{\lambda}\cdot\tau = 2GD$ $\tau = \tau_1 + \tau_2$ $\tau_2 = 2\mu_2 D$
			White-Metzner	$\tau_1 + \lambda(\gamma)\overset{\triangledown}{\tau} = 2\mu(\gamma)D$
			K-BKZ	$\tau_f = \mu(\gamma)\frac{nL^3}{24\ln\left(\frac{2h}{d}\right)}u_{1,2}S_{12}S_{ij}$ $\tau_p = \int\limits_{-\infty}^{t} \sum\limits_{k=1}^{N} \frac{G_k}{\lambda_k}\exp\left(-\frac{t-t'}{\lambda_k}\right)H(I_{c-1}, II_{c-1})C_t^{-1}(t')dt'$
			Upper-Convected Maxwell	$\tau + \lambda_1 \overset{\triangledown}{\tau} = 2\mu D$ $D = \frac{1}{2}\left[(\nabla u) + (\nabla u)^T\right]$

*Note: Most common models for viscoelastic fluids. μ denotes the shear viscosity; γ denotes the shear rate; f denotes the fiber volume fraction; d and L are the diameter and fiber length; n is the number of the suspension; h is the average distance from a given fiber to its nearest neighbor; τ_p denotes the shear stress for the polymer; λ denotes relaxation times and G_k denotes relaxation moduli; N denotes the number of relation modes; C_t^{-1} denotes finger strain tensor; I_{c-1} and II_{c-2} denotes first and second invariants; H is the strain memory function; $\overset{\triangledown}{\tau}$ denotes upper convected time derivative of the stress tensor; D denotes the strain rate tensor; ξ denotes the adjustable parameters of the model.

Table 2. Comparison of non-Newtonian power-law model fluid behavior [18, 24, 42, 43].

as paints and blood. Due to the rheological property of the latter, the common rule of thumb in designing and developing drug delivery system usually consider shear thinning approach as working mechanism. A mathematical model to simulate the deformation of droplets

through an axisymmetric contraction using shear thinning fluids. When the dispersed phase was a shear thinning fluid and the continuous phase was a Newtonian fluid, the local viscosity of the microdroplet decreased upon entering the contraction, remained at a low viscosity within the contraction and increased upon exiting, resulting in a compact bullet-shaped microdroplet at the exit. In contrast, when the continuous phase was shear thinning and the dispersed phase was Newtonian, the microdroplet exited the contraction with a very irregular shape [44, 45].

The influence of the dispersed phase viscosity between Newtonian and shear-thinning fluid on generated droplet size in microfluidic T-junctions are illustrated in **Figure 3**. The experimental results indicate that the larger viscosity of dispersed phase fluid brings the significant effect on reducing the size of generated microdroplet at each constant value of Q_d. Also, when the concentration of dispersed fluid is increasing from 0 to 60 wt% at constant value of Q_d of 0.6 mL/h; there will be a reduction in microdroplet size formed due to the change in the viscosity from 0.928 to 8.406 cP. Nevertheless, the similar phenomenon is not found when Q_d exceeds 1.2 mL/h in the condition of 60 wt%, viscosity of 8.406 cP for dispersed fluid. At Q_d of 1.2 mL/h, for the lower dispersed fluid viscosity ranging from 0.928 to 3.191 cP, the microdroplet volume is decreased. However, it is increased for the higher viscosity dispersed fluid (8.406 cP) due to a convectively unstable jetting regime that took place in which microdroplet formation lacks both periodicity and size uniformity therefore highly polydispersed in size were produced. When Q_d is further increased to a high relatively flow rate, a transition between convectively unstable flow and droplet breakup begins to prevail. This can be explained by the instabilities of microdroplets due to the inertia effects at the T-junction, begin to dominate in the dispersed phase and then evolve in the microchannel which is characterized by long instability wavelengths [46]. The behavior of the perturbations propagates in the direction of the flow and the dispersed phase does not break into microdroplet which is also defined as convective instability or unstable stratified flow. In contrast, reduction in carboxymethylcellulose (CMC) microdroplet size relative to drop volume was observed in larger power-law index; however, the size of droplet shrinks

	0% (w/w) μ_d = 0.928 cP	20% (w/w) μ_d = 1.585 cP	40% (w/w) μ_d = 3.191 cP	60% (w/w) μ_d = 8.409 cP	0.02% CMC (w/w) K = 15.28 mPa.S^n	0.04% CMC (w/w) K = 31.46 mPa.S^n
0.6 mL/h	f = 103.45 s^{-1}	f = 115.38 s^{-1}	f = 118.15 s^{-1}	f = 131.58 s^{-1}	f = 104.19 s^{-1}	f = 108.70 s^{-1}
0.8 mL/h	f = 123.00 s^{-1}	f = 132.81 s^{-1}	f = 136.36 s^{-1}	f = 157.89 s^{-1}	f = 120.00 s^{-1}	f = 119.05 s^{-1}
1.2 mL/h	f = 142.86 s^{-1}	f = 157.89 s^{-1}	f = 172.55 s^{-1}	f = 150.85 s^{-1}	f = 150.00 s^{-1}	f = 151.52 s^{-1}
1.6 mL/h	f = 176.47 s^{-1}	f = 172.55 s^{-1}	f = 202.86 s^{-1}	Convectively unstable	f = 195.00 s^{-1}	f = 192.31 s^{-1}
2.0 mL/h	f = 197.50 s^{-1}	f = 200.00 s^{-1}	f = 217.58 s^{-1}	Parallel flow	f = 230.77 s^{-1}	f = 227.27 s^{-1}
2.4 mL/h	f = 211.43 s^{-1}	f = 224.18 s^{-1}	f = 230.77 s^{-1}	Parallel flow	f = 250.00 s^{-1}	f = 238.12 s^{-1}

Figure 3. Representative outcomes for the effect of Newtonian (water-glycerol) and non-Newtonian CMC dispersed phase viscosity on droplet generation frequency in microfluidics T-junction.

when the viscosity of the power law fluid is increased with lower behavior index. In the case of CMC, the frequency of microdroplet formation increased when viscosity of dispersed phase is increased (0.02 wt% (w/w)) at each constant rate of Q_d; however, the reduction in frequency of droplet formation was observed when the viscosity of CMC polymer fluid is further increased to 0.04% (w/w) where power-law index (n) is smaller than unity contributes to significant effect of shear thinning behavior. This was explained by the other non-Newtonian fluid when the fluid elasticity also plays a key role in resisting the drop pinch off contributes an increase in droplet breakup time.

While shear thinning fluids are described as the most commonly encountered non-Newtonian fluid, viscoelastic fluids take the center stage in the synthesis of microdroplets. Such microdroplets are often produced using polymer solutions, such as alginate compounds [47] and polyethylene glycol [48], which have viscoelastic characteristics. This phenomenon was clearly observed in the multiple beads-on-a-string formation. It is determined that for polymer solutions that have high elasticity and extensibility, an extensional response was obtained, even at very low viscosities [49]. An observation on viscoelastic polymers that have larger molecular weight result in a higher elasticity number, El, which consequently increases the pinch-off times of the microdroplets. It was found that the size of the aperture affects the pinch-off times, whereby increasing the size of the apertures increases the pinch-off times [50]. This was validated by a demonstration on the production of monodisperse double emulsion microparticles from various non-Newtonian polymer solutions, one of which exhibited viscoelastic characteristics [21]. It was determined that when the viscoelastic solution was used as the inner fluid, the viscoelasticity of the fluid prevented microdroplets from pinching off from the orifice. This resulted in oscillations that are brought downstream by the continuous phase, which consequently brought about the beads-on-a-string phenomenon [49].

3. Microdroplets formation

3.1. Microdroplets encapsulation

The development of emulsification via microfluidic in the past decades is embodied in various fields. In the aspect of system design and fabrication, continuous reports with regards to new material development coupled with creative, novel fabrication techniques, enable evolutional microfluidic system from conventional two-dimensional (2D) straight microchannel to multifunctional three-dimensional (3D) systems [51]. In the aspect of theory and applications, in-depth understanding of the flow dynamic as mentioned in the previous section leads to much unique systems design for generation and manipulation of droplets with diverse behaviors and surface morphologies in various applications being reported [52–54]. Although the encapsulation process may seem straightforward, there are few considerations need to be noted. One common technique used is the addition of surface active agent to either continuous or dispersed phase. Such addition can create distinctive microdroplets formation, but not always an ideal solution to the development of more complex microfluidic systems with

multi-inputs. Various innovative proposals have been attempted to resolve this issue, both for passive and active emulsion encapsulation system. An active encapsulation involves usage of external forces such as electricity to encapsulate emulsion, which is not favorable when it is deployed in biology-related application. While passive emulsion encapsulation method more often carries low throughput as its main shortcoming, the simplicity in encapsulation mechanism makes it a popular choice for microdroplet encapsulation.

There have been much microdroplet encapsulation attempts done in both Newtonian and non-Newtonian fluids system. In recent years, focus on microdroplets encapsulation had been given to non-Newtonian fluids especially in the medical field and in drug synthesis and released related work. In the case of non-Newtonian fluid systems, an integrated comprehensive droplet digital detection (IC 3D) was used to encapsulate bacteria such as E.coli in the blood content for detection purpose [55]. The device is able to encapsulate bacterial into microdroplets that will allow real time disease detection with high result accuracy. Such approach has shorten the conventional detection method that requires longer time. Much of other developments on microdroplet encapsulation can be found in various literatures.

3.2. Microdroplets fission

Generally, microdroplet splitting can be divided into two main approaches, i.e. active fission and passive fission, while the latter one is more widely accepted due to advantages including ease of implementation and low cost. Passive fission mainly depends on the fluid flow resistance and geometries in respective channels of the microfluidic system. A variety of geometries have been demonstrated in passive fission where microdroplet is split as it flows past T-junction [56], arbitrary angle [57], obstacle [58] or through a narrow constriction [59]. It was found that the microdroplet fission occurs at bifurcation if length of the droplet in the microchannel is greater than the circumference on the edge of the microdroplet. The microdroplet splits evenly if the resistances of the two daughter channels have the same fluidic resistance downstream of the bifurcation. Since fluidic resistance is proportional to microchannel length, changing the length of one of the two daughter channels allows microdroplets to split unevenly. In this way, the volume ratio of the daughter droplets produced by the fission can be changed. A large post can be employed near the middle of a microchannel to induce microdroplet fission, the ratio of sizes of daughter droplets can be changed by adjusting the position of the post in the microchannel [60]. A repeating bifurcation structure can be used to split a single parent droplet into 8 or 16 daughter droplets of nanoliter volumes. Droplet breakup occurs because of a high surface tension pressure relative to the pressure drop in the microchannel [61]. Multiple monodisperse droplets can be generated using a side-branch structure with varied resistance in the microchannel; the size of the daughter droplets was controlled by the size of the original liquid plugs, thus providing a wide tuning range of droplet size [62]. A hydrophobic valve was used to arrest the flow of fluid into each daughter channel, while placed a waste channel at downstream of the daughter channels to drain excess fluid. The series of daughter channels can split a single liquid sample plug into multiple smaller plugs effectively [63]. This technology can allow for simultaneous screening for multiple viruses [64].

Despite of these latest advances, the relevant techniques to manipulate droplet fission by constriction are commonly performed in a 2D single planar microchannel. For instance, Rosenfeld et al. investigated splitting and deformations of a large number of drops in a concentrated emulsion when it flows through a narrow constriction in 2D monolayer Poly (dimethylsiloxane) (PDMS) microchannel [59]. There is no design employing 3D bilayer microchannel consisting of constriction formed by bifurcated junction. Bifurcated junction work should be focused because the flow of emulsions through porous media is important in many industrial processes, while the porous media normally have small constrictions with bifurcated junction [65]. For example, natural porous media such as oil reservoir features with complex interior structure formed by a number of constrictions or pores with heterogeneity of physiochemical characteristics. Industrial processes such as mobility control in enhanced oil recovery requires prediction of the evolution of the microstructure of the injected fluids in microstructure and their bulk rheological properties. However, there is still a lack of complete understanding towards the stability and break-up of individual emulsions as they flow through simple constrictions or pores, especially when the interactions among the emulsions are important. Moreover, in some biomedical applications such as drug delivery, the encapsulated drugs must go through media with complex 3D constrictions, such as blood capillaries or the porous material of a tissue structure in the human body. These constrictions normally feature with bifurcated junction. In some cases, these constrictions are the locations for drug release, thus the emulsion droplets must burst to release its contents. In other cases, the emulsion droplets must be transported through the constrictions to reach the targeted release locations, thus breakup must not occur in the constrictions. Therefore, it demands a thorough understanding of the physics of emulsion flow through constrictions to predict and manipulate the release of active ingredients from such emulsions (**Figure 4**).
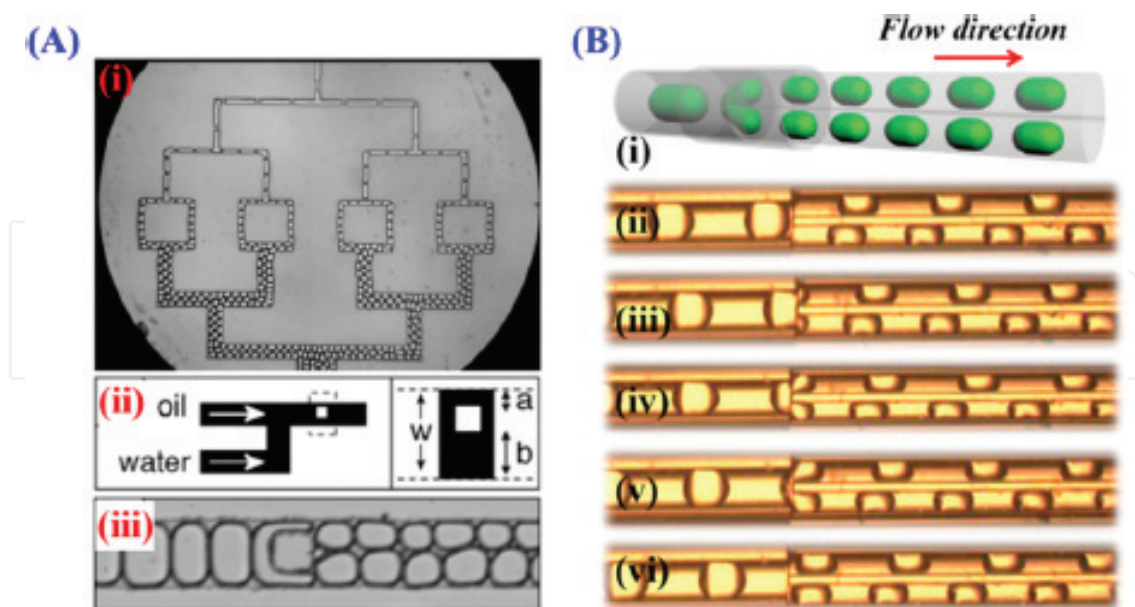
Figure 4. Droplet splitting in a microfluidic device. (A) 2D splitting: (i) droplets split repeatedly through Y-shaped junctions; (ii, iii) scheme illustration and microscopic image of droplet splitting mediated by a square obstruction. (B) 3D splitting: (i) scheme of the splitting process; (ii − vi) microscopic images showing droplets entering the junction and split into two daughter droplets. Reproduced with permission from [51]. Copyright 2017 American Chemistry Society.

4. Outlook

Emulsions, such as microcapsules and colloids, are crucial in daily life as well as playing vital role in different industrial applications such as pharmaceutical and food industry. Therefore, it is of important to understand the fundamental concept of Newtonian and non-Newtonian fluid behavior in the aspect of emulsification using microfluidic approach. Such understanding will bridge the practical application of the approach which aimed to control structure and monodispersed size in multiphase microsystem using emulsion as template. The two-phase flow understanding will stir the continuous development of emulsion to other applications such as microbeads for carbon capture and storage, wastewater treatment in environmental application as well as pharmaceutical drugs control. In this chapter, we have reviewed the fundamental two-phase multiphase model in emulsification process using microfluidic approach by outlining the main difference between Newtonian and non-Newtonian fluids and its corresponding pros and cons of each system. More effort should be given to non-Newtonian multiphase system research as non-Newtonian has more impact in daily life such as drug release kinetics in human blood, etc. Furthermore, more focus should also be given in the advancement of droplet size distribution control when both Newtonian and non-Newtonian fluids are used in a microfluidic multiphase system. This will eventually help to achieve applications such as advanced drug control and release as well as development of new food product that has better nutrient control.

Acknowledgements

Author details

Kai Seng Koh[1]*, Voon Loong Wong[1] and Yong Ren[2]

*Address all correspondence to: k.koh@hw.ac.uk

1 School of Engineering and Physical Sciences, Heriot-Watt University Malaysia, Putrajaya, Malaysia

2 Department of Mechanical, Materials and Manufacturing Engineering, The University of Nottingham Ningbo China, China

References

[1] Schramm LL. Emulsions, Foams, and Suspensions: Fundamentals and Applications. Germany: Wiley-VCH; 2005

[2] Sami S, Olesya B, Ana RC, Karin S. Microfluidic EDGE emulsification: the importance of interface interactions on droplet formation and pressure stability. Scientific Reports. 2016; **6**:26407. DOI: 10.1038/srep26407

[3] Ajay M, Abhijit S, Achinta B, Keka O. Characterization of oil−water emulsion and its use in enhanced oil recovery. Industrial and Engineering Chemistry Research. 2010;**49**(24): 12756-12761. DOI: 10.1021/ie101589x

[4] Mark D, Haeberle S, Roth G, von Steffen F, Zengerle R. Microfluidic lab-on-chip platforms: requirements, characteristics, and applications. Chemical Society Reviews. 2010; **39**:1153-1182. DOI: 10.1039/B820557B

[5] Garstecki P. Formation of droplets and bubbles in microfluidic systems. Bulletin of the Polish Academy Sciences. 2005;**53**(4)

[6] Gu H, MHG D, Mugele F. Droplet formation and merging in two-phase flow microfluidic. International Journal of Molecular Sciences. 2011;**12**(4):2572-2597. DOI: 10.3390/ ijms12042572

[7] Nunes JK, Tsai SSH, Wan J, Stone HA. Dripping and jetting in microfluidic multiphase flows applied to particle and fibre synthesis. Journal of Physics D: Applied Physics. 2013; **46**(11):23626378. DOI: 10.1088/0022-3727/46/11/114002

[8] Glawdel T, Elbuken C, Ren CL. Droplet formation in microfluidic T-junction generators operating in the transitional regime. II. Modeling. Physical Review E. 2012;**85**:016322. DOI: 10.1103/PhysRevE.85.016323

[9] Wehking JD, Gabany M, Chew L, Kumar R. Effects of viscosity, interfacial tension, and flow geometry on droplet formation in a microfluidic T-junction. Microfluidics and Nanofluidics. 2014;**16**(3):441. DOI: 10.1007/s10404-013-1239-0

[10] Raj R, Mathur N, Buwa VV. Numerical simulations of liquid-liquid flows in microchannels. Industrial & Engineering Chemistry Research. 2010;**49**(21):10606-10614. DOI: 10.1021/ie100626a

[11] DeMenech M, Garstecki P, Jousse F, Stone HA. Transition from squeezing to dripping in a microfluidic T-shaped junction. Journal of Fluid Mechanics. 208;**595**:141-161. DOI: 10.10 17/S002211200700910X

[12] Liu H, Zhang Y. Droplet formation in a T-shaped microfluidic junction. Journal of Applied Physics. 2009;**106**:034906. DOI: 10.1063/1.3187831

[13] Garstecki P, Fuerstman MJ, Stone HA, Whitesides GM. Formation of droplets and bubbles in a microfluidic T-junction-scaling and mechanism of breakup. Lab on Chip. 2006; **6**(3):437-446. DOI: 10.1039/b510841a

[14] Gupta A, Kumar R. Flow regime transition at high capillary numbers in a microfluidic T-junction: Viscosity contrast and geometry effect. Physics of Fluids. 2010;**22**:1-11. DOI: 10.1063/1.3523483

[15] Anna SL, Mayer HC. Microscale tipstreaming in a microfluidic flow focusing device. Physics of Fluids. 2006;**18**:121512. DOI: 10.1063/1.2397023

[16] Utada AS, Fernandez-Nieves A, Stone HA, Weitz DA. Dripping to jetting transitions in coflowing liquid streams. Physical Review Letter. 2007;**99**:094502. DOI: 10.1103/PhysRevLett.99.094502

[17] Baroud CN, Gallaire F, Dangla R. Dynamics of microfluidic droplets. Lab on Chip. 2010; **10**(16):2032-2045. DOI: 10.1039/c001191f

[18] Chhabra RP, Richardson JF. Non-Newtonian Flow and Applied Rheology. 2nd ed. Elsevier: Butterworth-Heinemann; 2008. 536 p. DOI: 10.1016/B978-0-7506-8532-0.00013-5

[19] Umbanhowar PB, Prasad V, Weitz DA. Monodisperse emulsion generation via drop break off in a coflowing stream. Langmuir. 2000;**16**(2):347-351. DOI: 10.1021/la990101e

[20] Cramer C, Fischer P, Windhab EJ. Drop formation in a co-flowing ambient fluid. Chemical Engineering Science. 2004;**59**(15):3045-3058. DOI: 10.1016/j.ces.2004.04.006

[21] Abate RA, Weitz DA. Faster multiple emulsification with drop splitting. Lab on Chip. 2011;**11**:1911-1915. DOI: 10.1039/C0LC00706D

[22] Nguyen NT, Wereley ST. Fundamentals and Applications of Microfluidics. 2nd ed. Artech House: Boston; 2002. p. 497

[23] Tanyeri M, Ranka M, Sittipolhul N, Schroeder CM. A microfluidic-based hydrodynamic trap: Design and implementation. Lab on Chip. 2011;**11**(10):1786-1794. DOI: 10.1039/c0lc00709a

[24] Cho YL, Hartnett JP. Non-Newtonian fluids. In: Cho YL, Hartnett JP, editors. Handbook of Heat Transfer Applications. 3rd ed. New York: McGraw-Hill; 1998. pp. 732-784

[25] Xu JH, Luo GS, Li SW, Chen GG. Shear force induced monodisperse droplet formation in a microfluidic device by controlling wetting properties. Lab on Chip. 2006;**6**(1):131-136. DOI: 10.1039/B509939K

[26] Xu JH, Li SW, Tan J, Wang YJ, Luo GS. Preparation of highly monodisperse droplet in a T-junction microfluidic device. American Institute of Chemical Engineers Journal. 2008; **52**(9):3005-3010. DOI: 10.1002/aic.10924

[27] Qiu D, Silva L, Tonkovich AL, Arora R. Micro-droplet formation in non-Newtonian fluid in a microchannel. Microfluidics and Nanofluidics. 2010;**8**(4):531-548. DOI: 10.1007/s10404-009-0487-5

[28] Wang K, Lu YC, Luo GS. Determination of dynamic interfacial tension and its effect on droplet formation in the T-shaped microdispersion process. Langmuir. 2009;**25**(4):2153-2158. DOI: 10.1021/la803049s

[29] Bashir S, Rees JM, Zimmerman WB. Simulations of microfluidics droplet formation using the two-phase level set method. Chemical Engineering Science. 2011;**66**(20):4733-4741. DOI: 10.1016/j.ces.2011.06.034

[30] Shui LL, Berg AVD, Eijkel JCT. Interfacial tension controlled W/O and O/W 2-phase flows in microchannel. Lab on Chip. 2009;**9**:795-801. DOI: 10.1039/B813724B

[31] Peng L, Yang M, Guo SS, Liu W, Zhao XZ. The effect of interfacial tension on droplet formation in flow-focusing microfluidic device. Biomedical Microdevices. 2011;**13**(3):559-564. DOI: 10.1007/s10544-011-9526-6

[32] Cubaud T, Mason TG. Capillary threads and viscous droplets in square microchannels. Physics of Fluids. 2008;**20**(5):053302. DOI: 10.1063/1.2911716

[33] Gu ZP, Liow JL.Microdroplet formation in a T-junction with xanthan gum solutions. In: Chemeca 2011: Engineering a Better World; 18-21 September; Sydney Hilton Hotel, NSW. Australia: Engineers Australia; 2011. pp. 1442-1451

[34] Murshed SMS, Tan SH, Nguyen NT. Temperature dependence of interfacial properties and viscosity of nanofluids for droplet-based microfluidics. Journal of Physics D: Applied Physics. 2008;**41**(8):085502. DOI: 10.1088/0022-3727/41/8/085502

[35] Wang RJ. Nanoparticles influence droplet formation in a T-shaped microfluidic. Journal of Nanoparticle Research. 2013;**15**:2128. DOI: 10.1007/s11051-013-2128-x

[36] Fang C, Lee D, Stober B, Fuller GG, Shen AQ. Integrated microfluidic platform for instantaneous flow and localized temperature control. RSC Advances. 2015;**5**(104):85620-85629. DOI: 10.1039/C5RA19944A

[37] Sang L, Hong Y, Wang F. Investigation of viscosity effect on droplet formation in T-shaped microchannels by numerical and analytical methods. Microfluidics and Nanofluidics. 2009;**6**(5):621-635. DOI: 10.1007/s10404-008-0329-x

[38] Ba Y, Liu H, Sun J, Zheng R. Three dimensional simulations of droplet formation in symmetric and asymmetric T-junctions using the color-gradient lattice Boltzmann model. International Journal of Heat Transfer. 2015;**90**:931-947. DOI: 10.1016/j.ijheatmasstransfer.2015.07.023

[39] Husny J, Cooper-White JJ. The effect of elasticity on drop creation in T-shaped microchannels. Journals of Non-Newtonian Fluid Mechanics. 2006;**137**(1–3):121-136. DOI: 10.1016/j.jnnfm.2006.03.007

[40] Wong VL, Loizou K, Lau PL, Graham RS, Hewakandamby BN. Numerical studies of shear-thinning droplet formation in a microfluidic T-junction using two-phase level-set method. Chemical Engineering Science. 2017;**174**:157-173. DOI: 10.1016/j.ces.2017.08.027

[41]   Abate AR, Poitzsch A, Hwang Y, Lee J, Czerwinska J, Weitz DA. Impact of inlet channel geometry on microfluidic drop formation. Physical Review E. 2009;**80**(2). DOI: 026310, 10.1103/PhysRevE.80.026310

[42]   Cherizol R, Sain M, Tjong J. Review of non-Newtonian mathematical models for rheological characteristics of viscoelastic composites. Green and Sustainable Chemistry. 2015;**5**(1): 6-14. DOI: 10.4236/gsc.2015.51002

[43]   Kostic M. Influence of viscosity function simplification on non-Newtonian velocity and shear rate profiles in rectangular ducts. International Communications in Heat and Mass Transfer. 1993;**20**(4):515-525. DOI: 10.1016/0735-1933(93)90063-2

[44]   Harvie DJE, Davidson MR, Cooper-White JJ, Rudman M. A parametric study of droplet deformation through a microfluidic contraction: Low viscosity Newtonian droplets. Chemical Engineering Science. 2006;**61**(15):5149-5158. DOI: 10.1016/j.ces.2006.03.011

[45]   Fu TT, Ma YG, Li HZ. Breakup dynamics of slender droplet formation in shear-thinning fluids in flow-focusing devices. Chemical Engineering Science. 2016;**144**:75-86. DOI: 10.1016/j.ces.2015.12.031

[46]   Mbanjwa MB, Land KJ, Jewell L, Moss EA, Gledhill IMA. Experimental observation of capillary instabilities of two phase flow in a microfluidic T-junction. In: Seventh South African Conference on Computational and Applied Mechanics (SACAM10); 10-13 January; Pretoria. Republic of South Africa:2010

[47]   KhosraviZanjani MA, Tarzi BG, Sharifan A, Mohammadi N. Microencapsulation of probiotics by calcium alginate-gelatinized starch with chitosan coating and evaluation of survival in simulated human gastro-intestinal condition. Iranian Journal of Pharmaceutical Research. 2014;**13**(3):843-852

[48]   Villa C, Manzoli V, Abreu MM, Verheyen CA, Seskin M, Najjar M, Molano RD, Torrente Y, Ricordi C, Tomei AA. Effects of composition of alginate-polyethylene glycol microcapsules and transplant site on encapsulated islet graft outcomes in mice. Transplantation. 2017;**101**(5):1025-1035. DOI: 10.1097/TP.0000000000001454

[49]   Oliveira MS, McKinley GH. Iterated stretching and multiple beads-on-a-string phenomena in dilute solutions of highly-extensible flexible polymers. Physics of fluids. 2005;**17**: 071705. DOI: 10.1063/1.1949197

[50]   Steinhaus B, Shen AQ. Dynamics of viscoelastic fluid filaments in microfluidic devices. Physics of Fluids. 2007;**18**:073103. DOI: 10.1063/1.2747660

[51]   Shang LR, Cheng Y, Zhao YJ. Emerging droplet microfluidics. Chemical Reviews. 2017; **117**(12):7964-8040. DOI: 10.1021/acs.chemrev.6b00848

[52]   Zhu PG, Wang LQ. Passive and active droplet generation with microfluidics:A review. Lab on Chip. 2017;**17**:34-75. DOI: 10.1039/C6LC01018K

[53]   Takeuchi S, Garstecki P, Weibel DB, Whitesides GM. An axisymmetric flow-focusing microfluidic device. Advanced Materials. 2005;**17**(8):1067-1072. DOI: 10.1002/adma.20 0401738

[54] Sun JS, Xianyu YL, Jiang XY. Point-of-care biochemical assays using gold nanoparticle-implemented microfluidics. Chemical Society Reviews. 2014;**43**:6239-6253. DOI: 10.1039/C4CS00125G

[55] Kang DK, Ali MM, Zhang KX, Huang SS, Peterson E, Digman AM, Gratton E, Zhao WA. Rapid detection of single bacteria in unprocessed blood using integrated comprehensive droplet digital detection. Nature Communications. 2014;**5**:5427. DOI: 10.1038/ncomms6427

[56] Samie M, Salari A, Shafii B. Breakup of microdroplets in asymmetric T junctions. Physical Review E. 2013;**87**:053003. DOI: 10.1103/PhysRevE.87.053003

[57] Menetrier-Deremble L, Tabeling P. Droplet breakup in microfluidic junctions of arbitrary angles. Physical Review E. 2006;**74**:035303. DOI: 10.1103/PhysRevE.74.035303

[58] Protiere S, Bazant MZ, Weitz DA, Stone HA. Droplet breakup in flow past an obstacle: A capillary instability due to permeability variations. EPL (Europhysics Letters). 2010;**92**(5): 54002. DOI: 10.1209/0295-5075/92/54002

[59] Rosenfeld L, Fan L, Swoboda R, Tang SKY. Break-up of droplets in a concentrated emulsion flowing through a narrow constriction. Soft Matter. 2014;**10**:421-430. DOI: 10.1039/C3SM 51843D

[60] Link DR, Anna SL, Weitz DA, Stone HA. Geometrically mediated breakup of drops in microfluidic devices. Physical Review Letters. 2004;**92**:054503. DOI: 10.1103/PhysRev Lett.92.054503

[61] Adamson DN, Mustafi D, Zhang JXJ, Zheng B, Ismagilov RF. Production of arrays of chemically distinct nanolitre plugs via repeated splitting in microfluidic. Lab on Chip. 2006;**6**:1178-1186. DOI: 10.1039/B604993A

[62] Xiong S, Chin LK, Yu YF, Yu JQ, Chen Y, Zhang GJ, Lo GQ, Kwong DL, Liu AQ. Multi-size droplets generation via side-branch microfluidic channels. In: Verpoorte S, editors. 14th International Conference on Miniaturized Systems for Chemistry; 3–7 October; Groningen, The Netherlands. 2010

[63] Mielnik M, Voitel J, Solli L, Furuberg L. Sample metering and parallel liquid plug actuation for multiple biochemical assays. In: 11th International Conference on Miniaturized Systems for Chemistry and Life; Paris, France. p. 1513-1515

[64] Furuberg L, Mielnik M, Gulliksen A, Solli L, Johansen IR, Voitel J, Baier T, Riegger L. RNA amplification chip with parallel microchannels and droplet positioning using capillary valves. Microsystem Technologies. 2008;**14**(4–5):673-681. DOI: 10.1007/s00542-007-0515-x

[65] vanDinther AMC, Schroën CGPH, Boom RM. Separation process for very concentrated emulsions. Innovative Food Science & Emerging Technologies. 2013;**18**:177-182. DOI: 10.1016/j.ifset.2012.12.007