Applications of CFD Simulations on Microfluidic Systems for Nanoparticle Synthesis

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APPLICATIONS OF CFD SIMULATIONS ON MICROFLUIDIC SYSTEMS
FOR NANOPARTICLE SYNTHESIS

A Thesis

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in pursuit of the degree of
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in

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by

Yuehao Li
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Abstract

Microfluidics has been extensively investigated as a unique platform to synthesize nanoparticles with desired properties, e.g., size and morphology. Compared to the conventional batch reactors, wet-chemical synthesis using continuous flow microfluidics provides better control over addition of reagents, heat and mass transfer, and reproducibility. Recently, millifluidics has emerged as an alternative since it offers similar control as microfluidics. With its dimensions scaled up to millimeter size, millifluidics saves fabrication efforts and potentially paves the way for industrial applications.

Good designs and manipulations of microfluidic and millifluidic devices rely on solid understanding of fluid dynamics. Fluid flow plays an important role in heat and mass transfer; thereby, it determines the quality of the synthesized nanoparticles. Computational fluid dynamics (CFD) simulations provide an effective approach to understand various effects on fluid flows without carrying out complicated experiments.

The goal of this project is to utilize CFD simulations to study flow behaviors inside microfluidic and millifluidic. Residence time distribution (RTD) analysis coupled with TEM characterization was applied to investigate the effect of reagent flow rates on particle sizes distribution. Droplet-based microfluidics, as a solution to intrinsic drawbacks associated with single-phase microfluidics, depends on proper manipulation of the flow to generate steady droplet flow. The droplet / slug formation process inside a millifluidic reactor was investigated by both experiments and numerical simulations to understand the hydrodynamics of slug breaking. Geometric optimization was carried out to analyze the dependency of slug sizes on geometric dimensions. Numerical simulations were also performed to quantify the mixing efficiency inside slugs.

This work provides insight to understand fluid flow inside microfluidic and millifluidic systems. It may benefit the design and operations of novel microfluidic and millifluidic systems.
Chapter 1 Introduction

1.1 Microfluidics and millifluidics

What is microfluidics? Prof. George Whiteside defines microfluidics as the science and technology of systems that process or manipulate small ($10^{-9}$ to $10^{-8}$ liters) amount of fluids, using channels with dimensions of tens to hundreds of micrometers\(^1\). After the first conceptual introduction by Manz et al. at the 5\(^{th}\) International Conference on Solid-State Sensors and Actuators\(^2\), microfluidics has been developed into a multidisciplinary field, attracting numerous interests from both scientific and commercial communities.

The realization of microfluidics depends on miniaturization that develops small-scale products, devices or components with similar performance or better functionality as their macroscopic components. The most successful example is the miniaturization of micro-electronics. Every year electronic industries bring in more efficient, reduced weight and cost-effective portable devices using sophisticated micro-fabrication techniques. Since two decades ago, the concept of miniaturization has been extended to chemical, biological and bio-medical applications. The micro-scale devices are integrated onto one chip, and the chip may perform same functions as what are originally conducted inside laboratories. These devices are termed as Lab-on-a-Chip (LOC).

LOC devices, also named as micro-total analysis systems (µ-TAS) because of their first applications on chemical analysis, are demonstrated to be capable of carrying out conventional analysis laboratory tests within a single chip\(^3\). As depicted in Figure 1.1, a typical LOC system usually contains various sub-components such as pumps, reactors, separation devices and waste treatment devices on micron size scale. Besides providing similar functions as their macroscopic counterparts, the small scale of the sub-components offers remarkable benefits in terms of reduced size, enhanced mobility, less sample / reagent consumption and shortened analysis time.
Microfluidics promises numerous opportunities for commercial successes. With the advantage of small scale, they can enable novel applications that conventional devices cannot achieve. Nowadays one typical commercial interest is the plastic fabrication for single-use disposable microfluidic devices. For example, the diabetes test strip, also called glucose test strip, is one kind of widely used plastic microfluidic chip. The fantastic attributes, such as fast and precise analysis, cost-effectiveness and etc., have ensured a huge market for glucose meter manufactures. In a similar way, microfluidics might also change the way instrument companies conduct business, which may initiate a revolution on chemical analysis. Instead of selling a few expensive analysis systems, companies may sell cheap, disposable microfluidic devices. Making analysis instruments, tailored drugs, and disposable drug dispensers available for everyone will secure a huge market similar to that of computers today.

![Figure 1.1: Schematic of typical Lab-on-a-Chip (LOC) device with various sub-components.](image)

As a response to the commercial potential, microfluidics has attracted research interests from academic communities. A variety of disciplines, such as chemistry, biology, medicine, material science and engineering (chemical, mechanical, electrical etc.), are applying microfluidic to their research; their contributions have developed microfluidics into a truly multidisciplinary field. One application in chemical engineering is the development of micro-devices for traditional chemical synthesis. Taking advantage of their intrinsic property of small length scale, microfluidic devices offer favorable heat and
mass transfer\textsuperscript{5}. Hassel et al. have utilized a micro-mixer within a microfluidic reactor for Phenyl Boronic Acid process and found 25 \% higher yield, higher selectivity and less energy consumption compared to stirred tank process\textsuperscript{6}. Although various researches have shown promising results, it is still impossible to scale up micro-reactors to a mass chemical production facility. Massive parallelization of miniaturized systems (numbering up) is suggested as a possibility but integration and assembly of such a system remains a challenge. If massive parallelization is achieved, it could possibly be the next milestone of chemical engineering for massive manufacturing of chemicals utilizing microfluidic devices.

Several disadvantages have been encountered when apply microfluidic technology to industry. One is the high cost for fabricating complicated microfluidic devices. They are usually fabricated by lithography or etching inside a clean room. Recently, researchers have turned to millifluidics which has presented considerable advantages. Millifluidics is referred to those microfluidic devices that are scaled up to millimeter size. Millifluidic fabrication usually proceeds following steps in normal conditions: using precise micromachining to fabricate metal mold inserts, injection molding for cost-effective chip replication, and lamination for adequate sealing of the devices/chips. Recently, Panizza and his co-workers have demonstrated their work to produce hierarchically organized larger emulsions by using combinations of modular millifluidic devices\textsuperscript{7}. Their setup included an assembly of capillaries or flexible tubes connected together with elementary home-made modules. The tubes and modules could be assembled and disassembled easily; therefore, modular set-ups could be designed on demand in a short time\textsuperscript{8}. This method promises a great versatility to set up new millifluidic systems for various applications. Tachibana et al. have adopted a millifluidic system to produce microporous silica ceramic particles\textsuperscript{9}. They claimed that utilization of multiple millifluidic reactors in parallel could pave the way to an industrial integrative formulation of dispersed materials with very large characteristic sizes ranging from typically 100 \(\mu\)m to several mm and new complex architectures. Since millifluidics is scaled up from microfluidics and the major difference between them is the dimensional scale only, microfluidics is used in general for the following sections that illustrate their applications in material synthesis.
1.2 Microfluidic reactors for controlled synthesis of nanomaterial

Nanoparticles exhibit a variety of size-, shape-, and crystal-structure-dependent physical and chemical properties; therefore, synthesis of nanoparticles requires superior controls over reactions, both kinetically and thermodynamically, so as to produce materials of required features and properties\textsuperscript{10}. Wet-chemical synthesis, involving liquid phase reactions in simple equipment, is a traditional but an effective approach to produce a large amount of nanoparticles coated with organic stabilizers to protect them from aggregation or oxidation\textsuperscript{11}. With proper controls over the process, wet-chemical synthesis can address several particular challenges in nanoparticle synthesis, for example, the uniformity in particle size distribution. In this study, metal salt reductions are adopted to synthesize metal nanoparticles.

Conventional wet-chemical syntheses are carried out in batch reactors such as stirred flasks. The turbulence created from the mechanical or magnetic agitators usually results in poor control over reaction conditions, producing nanoparticles with broad size distribution. In the past decade, there has been a strong shift towards the utilization of microfluidic devices to synthesize nanomaterial under continuous flows. Microfluidic reactors have several unique features for controlled synthesis of nanoparticles.

One is the thermal and chemical homogeneity pertained through the entire reaction volume inside microfluidic reactors. Microfluidic reactors are manipulated in laminar regime: the absence of turbulence enables a homogeneous environment for particle synthesis. Micromixers are usually integrated into the system to enhance mixing and thereby improve the yield. Edel et al. demonstrated the synthesis of CdS nanoparticles in a continuous-flow microfluidic reactor with a micromixer based on distributive mixing\textsuperscript{12}. In contrast to the nanoparticles synthesized in traditional flask reactors, nanoparticles synthesized in their microfluidic reactors showed a sharp decline in poly-dispersity tending toward mono-dispersity by manipulating the flow rates of the reagents. Song et al. also reported that Pd nanoparticles obtained from a polymer-based microfluidic reactor with mixing components had smaller particle diameters and narrower
size distribution than those obtained from batch process\textsuperscript{13}. Over all, downsizing the reactor from bulk to microfluidic reactor is sufficient to improve the mono-dispersity of the nanoparticles.

In addition to the homogeneous environment, microfluidic systems may also provide unique platforms for studying the fundamental reaction process through spatially resolved analysis of nanoparticle formation process within the micro-channels. Since the reaction time of chemical reactions inside batch reactor is fundamentally same as the residence time inside microfluidic reactor, implementing insitu analysis to microfluidic reactors may provide kinetic information of the reaction\textsuperscript{14}. Zinoveva et al. probed the cobalt nanoparticle formation utilizing synchrotron-radiation-based X-ray absorption spectroscopy at three different locations of a PMMA microfluidic reactor\textsuperscript{15}. The particle formation was depicted by the spectra recorded at these locations together with the reference spectra of the precursor and the final product collected at the outlet of the micro-reactor.

Another advantage of using microfluidic reactor is the ability of adding additional reagents downstream as required; therefore, pre and post treatment and multistep synthesis in a single microfluidic chip are achieved by such a unique feature. Shestopalov et al. carried out a multistep synthesis of Q dots at room temperature using the microfluidic droplet reactor shown in Figure 1.2\textsuperscript{16}. Two aqueous reagents R\textsubscript{1}, R\textsubscript{2} and a separation stream S were injected upstream to initiate reactor 1. Taking advantage of rapid mixing using wind channels, a homogeneous environment was attained inside droplets. The reaction time, same as the residence time, was controlled by manipulating the flow rate of oil. The second reaction was initiated when the third reagent R\textsubscript{3} was injected from another side channel and added to the aqueous droplets. Multiple purposes can be realized, such as quenching the reaction or withdrawing part of the product, through proper operations on the side channel. The core/shell nanoparticle synthesis using such microfluidic devices have been demonstrated to have the ability to control overcoat thickness, avoid secondary nucleation and aggregation, and maintain a narrow size distribution\textsuperscript{16-17}.
Microfluidic reactors have another potential advantage to control the properties of nanoparticles by controlling their formation. One possible way is to separate the nucleation and growth stage to obtain nanoparticles of desired size and size distribution. The generally accepted mechanism of particle formation in a wet-chemical synthesis process, as proposed by Lamer and Dinegar\textsuperscript{18}, consists of four distinct stages: supersaturated solute formation, nucleation, growth and aggregation. As the solute concentration formed by chemical reactions exceeds the super saturation limit and eventually reaches a critical concentration, numerous nuclei are generated in a short burst by nucleation. At growth stage, the solute deposits on particle, thus its concentration decreases to a value below critical concentration; therefore, the number of nuclei is haltered during growth stage. Particles continue to grow until all the
solutes have been consumed so as to lower the overall free energy of the system (particles and solutes). During this stage, aggregation might also occur since aggregation of individual particles also lowers the free energy of the system. The particles tend to coagulate and precipitate out of the solution\textsuperscript{18-19}. Nanoparticles of desired size and size distribution can be produced only if the amount of reagent is controlled so that the growth stage stops at the proper time, and suitable stabilizer is utilized to avoid aggregation. Investigations by Sounart et al. suggested the possibility to separate the nucleation and growth stage: the homogeneous reaction, solute formation and nucleation are diffusion limited and occur instantaneously; in contrast, the growth stage occurs on a longer time scale (seconds)\textsuperscript{20}. Similar observations were also demonstrated by Wager et al. in the case of gold nanoparticle synthesis\textsuperscript{21} and also by Khan et al. in the case of silica nanoparticle synthesis\textsuperscript{22}.

1.3 Droplet-based microfluidics

Conventional microfluidic devices are operated with continuous flow in laminar regime. They are associated with several inherent problems. One is the large residence time distribution (RTD) due to the velocity variance in cross section. In laminar regime, a parabolic profile is established along the cross section of the channel with high velocity in the center and no-slip assumption at wall. Since the fluid elements in the center region have large velocity, the residence time is small; in contrast, those fluid elements near wall have smaller velocity thus in turn longer residence time. The distribution in residence time leads to distribution in particle growth time and concomitantly poly-dispersity in particle size. Another disadvantage is the low yield resulted from poor mixing of the reagent: mixing in laminar regime without any mixer is based on molecular diffusion, which is much slower compared to convection. Additional external micromixer must be integrated into the system, but it in turn arguments the complexity for fabrication. Traditional single-phase microfluidic reactor suffers from fouling, i.e., the deposition of solid material on channel surface, eventually leading to the blockage of the channel\textsuperscript{23}. Surface treatment on channel walls is an effective approach to eliminate fouling. Wagner reported\textsuperscript{21c} that fouling was successfully prevented by carrying out reactions at elevated pH values and by making the
internal channel surface hydrophobic through silanization. However, this method may not be applicable for other material synthesis, and suitable treatment must be adopted based on particles being synthesized as well as channel material.

“Droplet-based microfluidics” has been firstly introduced in 2003 as an alternative method to address these problems simultaneously\textsuperscript{24}. One typical setup of the droplet-based microfluidic reactor is illustrated in Figure 1.2 and Figure 1.3. The aqueous reagents are encapsulated inside nanoliter-scale droplets and segmented by oil plugs. Two immiscible phases are involved: aqueous phase and oil phase (or carrier fluid). Since the aqueous droplets are segmented by oil plugs, the two phases are also termed as dispersed phase and continuous phase respectively. The setups illustrated in Figure 1.2 and 1.3 are typical microfluidic T-junction devices: aqueous reagents are injected from the side channel while oil is injected from another channel; discrete droplets are sequentially pinched off from the aqueous solution at the junction region. As depicted in Figure 1.3, droplet-based microfluidics has several advantages over single-phase microfluidic reactors: rapid mixing, no dispersion and minimized surface deposition.

![Figure 1.3 Advantages of using droplet-based microfluidic reactor. Reproduced from reference 24 with copyright 2003 from WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.](image-url)
The strong convection enables rapid mixing inside droplets without presence of eternal micro-mixers. Vorticity is generated inside droplets due to velocity distribution and immiscible condition: fluid elements in the center are moving faster than those near channel walls; circulating occurs since the fluid elements in the center are forced to move backward because they cannot penetrate the fluid interface. If a homogeneous environment is required within a short time, wind channels are integrated into the microfluidic system to further enhance mixing by taking advantage of chaotic advection.

Dispersion is eliminated as reagents are isolated within droplets. With the aid of rapid mixing, homogeneity in heat and mass is attained, thus each isolated droplet is served as an individual batch reactor. Since they travel with same speed, all droplets have same residence time; therefore, the reaction / growth time inside each “batch” reactor is same. Consequently, uniform residence time distribution leads to narrow size distribution of the synthesized nanoparticles.

Another advantage offered by microfluidics is the ability to prevent surface deposition because of a thin lubricate layer. If the reagents are in aqueous phase, the channel walls are accordingly fabricated by hydrophobic material, thus a thin layer of the continuous phase is developed between the translating droplets and the channel walls. This thin layer prevents deposition of nanoparticles on channel walls. The existence of the thin layer has been indicated through experiments, but a definitive optical evidence for the film thickness and its consequential effect on nanoparticle synthesis has not been reported yet.

Droplet-based microfluidics has gained much research interests from multi-disciplines due to its advantages and superior controls. Numerous publications demonstrating its applications on various research fields have been reported within these ten years. Particularly in nanoparticle synthesis, it has shown fantastic capability for synthesizing nanoparticles with mono-dispersity and controlled morphology. Duraiswamy and Khan have applied droplet-based microfluidics to synthesize anisotropic metal nano-rods with controlled aspect ratios as shown in Figure 1.4. Xu et al. has also reported their syntheses of polymer nanoparticles with controlled shapes and sizes as shown in Figure 1.5.
Figure 1.4 TEM images of rod-shaped nanoparticles with varying aspect ratios. The corresponding aspect ratios are: (a) 2.3±0.5 (b) 3.2±0.5 (c) 4±0.5 and (d) 2.7±0.3. Reprinted from reference 29 with copyright 2009 from Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

Figure 1.5 Monodispersed particles with controlled shape and sizes generated in droplets. (a) polymer microsphere (b) a crystal of polymer microspheres (c) polymer rods (d) polymer disks (e) polymer ellipsoids (f) agarose disks (g) bismuth alloy ellipsoids. Reprinted from reference 30 with copyright 2005 from WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.
Droplet-based microfluidics has encountered several disadvantages that limit its applications. One arises from the requirement to find a suitable choice of reaction fluid and carrier fluid, since they should be immiscible over all the range of experimental conditions (pressure, temperature, pH value, etc.). Another disadvantage is the further separation downstream to separate the product from oil, which has been conditionally addressed by adding an in-line phase separator. It is worthy to point out that liquid-liquid flows in microfluidic channels may exhibits other flow patterns rather than droplet flow; therefore, suitable operating conditions, i.e., flow rate, viscosity ratio, interfacial tension, must be selected to operate droplet-based microfluidic in droplet flow regime.

1.4 Apply numerical simulations to microfluidics

With the development of computational power and simulation techniques, numerical simulations have opened a new approach to investigate microfluidics. Since the flow characteristics inside microfluidic devices are important, computational fluid dynamics (CFD) simulations provides an easy way to study those flow behaviors that are difficult to observe through experiments.

Fluid flows are described by Navier–Stokes (N-S) equation, which is a set of partial differential equations with time and space dimensions. The idea of CFD simulations is to obtain the flow field inside those microfluidic devices by solving N-S equation through numerical methods. Typical numerical methods include finite difference method (FDM), finite volume method (FVM) and finite element method (FEM). Many commercial CFD software or packages are available now, i.e., ANSYS Fluent, ANSYS CFX and Comsol Multiphysics. There are also open source numerical solvers such as OpenFoam, Fluent and OpenFoam are based on FVM while Comsol and CFX adopt FEM methods.

CFD simulations have been adopted by researchers in microfluidic field in many respects. One is in the characterization of mixing performance in microfluidic devices. The experimental characterizations of mixing are often carried out by diluting dye or fluorescence with water. In numerical simulations, the mixing performance can be investigated by N-S equation coupled with transport equations. As fluid flow
inside microfluidic devices is laminar, the simplicity in flow patterns ensures a good agreement of the simulation results with the experimental observations. Many researchers have adopted numerical simulations to design novel microfluidic devices and test their mixing performances in order to save time and labor effort\textsuperscript{33}.

Another application of CFD simulation is to study the droplet formation process inside microfluidic devices which is critical for droplet-based microfluidics. Droplets in microfluidics are micrometer scale, and their formation process usually occurs within milli-seconds. Experimental investigations require sophisticated equipment such as microscope and high-speed cameras. Various factors affect the droplet formation process, increasing the complexity of investigation. Recently, CFD simulations are attracting many attentions as an alternative. Researchers have adopted various numerical methods, i.e, volume of fluid method (VOF), level-set method (LSM), lattice-Boltzmann method to study the multiphase problem\textsuperscript{34}. Numerical studies can help to understand the role of various effects and also save the efforts of fabricating chips and carrying out experiments.

1.5 Scope of this thesis

This project seeks to apply CFD simulations to understand the flow behavior inside microfluidic reactors so as to find suitable operating conditions and optimal designs for nanoparticle synthesis. The organization of this thesis is as follows: the second chapter discusses the spatial evolution of Au nanoparticle at various locations inside a millifluidic reactor. In the third chapter, numerical simulations were carried out to investigate the slug formation process inside a millifluidic flow-focusing reactor and analyze the effect of geometric dimensions on slug lengths. In the fourth chapter, mixing performances inside slugs were investigated under various operating conditions. The last chapter is the references been cited in this thesis.
Chapter 2 Size Evolution of Gold Nanoparticles in a Millifluidic Reactor*

2.1 Introduction

Microfluidic reactors have gained extensively research interests from multi-disciplines, especially for synthesis of novel nanomaterial.\textsuperscript{28b, 35} However, they usually rely on sophisticated fabrication techniques, for example, lithography or etching in a clean room, which increase their cost and hinder their applications. In addition, there remain a number of issues related to process scale-up in order to meet the requirements for industry-level applications.\textsuperscript{10a, 35b}

Millifluidics, referred to those devices which have a length-scale larger than 500 µm, has emerged as a bridge between microfluidics and bulk systems.\textsuperscript{8b} In contrast to expensive microfluidic fabrications, the large scale of the channel size makes millifludic devices relatively easy to fabricate and consequently low cost. Another potential advantage of millifluidic reactors is that the fluid volume is many folds higher than that of microfluidic reactors while offering similar controls. The larger channel size also provides better opportunity than microfluidics for in situ characterization of nanocluster with various spectroscopies, especially when carrying out time-resolved in situ analysis using synchrotron radiation-based X-ray absorption spectroscopy where larger probe dimensions provide better signal to noise ratio\textsuperscript{15}. Recently time resolution studies with microfluidic reactors have been carried out using a number of probes such as surface-enhanced resonance Raman spectroscopy (SERRS), Coherent Anti-Stokes Raman scattering microscopy, photoluminescence imaging and spectroscopy, and X-ray absorption spectroscopy probes.\textsuperscript{15, 36} Applying these spectroscopic probes to millifluidics is believed to provide better performances. These advantages have promised millifluidic reactors as an important alternative to microfluidic reactors. Surprisingly, they have not been investigated thoroughly for their utility in general\textsuperscript{37} and for nanomaterial synthesis in particular.\textsuperscript{38}

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In this work, a snake-shape millifluidic reactor is utilized as a platform to carry out spatial evolution analysis of Au nanoparticle formation inside millifluidic channel using Transmission Electron Microscopy (TEM) as a probe. Converting the spatial resolution information to time resolution, the size evolution of nanoparticle within the channel elucidates a general particle growth process. Numerical simulations are performed to compute corresponding residence time distribution (RTD) at different sampling locations under various flow rates. The correlation between RTD and particle size distribution (PSD) reveals the effect of flow rates on particle formation process.

2.2 Experimental method

![Figure 2.1: (a) Milli-fluidic chip (Left chip utilized for the synthesis) (b) schematic diagram of the milli-fluidic channel](image)

The Au nanoparticles were synthesized in both batch and continuous processes by modifying a previously reported procedure. The millifluidic reactor has a snake shape as shown in Figure 2.1 (purchased from Microplumbers) with channel dimensions of 2 millimeters width and 125 micrometers depth. Only the reaction channel on the right side of the chip was utilized in this work. The mixing length inside the channel is approximately 14 centimeters. The two reagents, DMSA (dimercaptosuccinic acid) and chloroauric acid (HAuCl₄) were injected into the millifluidic reactor with same flow rates from two inlets. The total injecting rate was set as 2mL/h, 6mL/h, 10 mL/h and 40 mL/h respectively through computer controlled syringe pumps (NE-500 OEM Syringe Pump from SyringePump.com; New Era
Pump systems Inc.). The chloroauric acid was prepared by dissolving 1.7 mg of Au (III) gold salt dissolved in 5 mL deionized water. DMSA solution, serving as both reducing agent and stabilizer, was prepared by dissolving 1.8 mL of DMSA in 5mL deionized water. The final solution was collected from desired sampling locations inside small glass bottles and used for various characterization purposes.

Mixing between the two reagents was studied by a dilution process of the fluorescent dye with deionized water. Photographs of the millifluidic channel were taken with a Leica DM RXA2 fluorescence microscope equipped with a 5x N.A. 0.15 objective, a Cooke SensiCam QE digital camera as well as a Xenon lamp. Images were acquired and processed using Slidebook version 4.0 (Intelligent Imaging Innovations, Denver, CO). After post-processing the images in Adobe Photoshop CS5, the intensity of the fluorescence was measured across the channel by Image J. A typical acquired image is shown in Figure 2.2. Since the camera used to take the photos was not capable to measure the intensity in the depth, the measurements of Image J was taken to be the average value on the depth.

![Figure 2.2](image_url)

Figure 2.2: A typical image of fluorescent mixing with water. The red line indicates where the intensity is measured by Image J after post processing the image with Photoshop.

The millifluidic chip was dissected at two required locations, location 1 and 2 as shown in Figure 2.1 (b) to collect the nanoparticle product. The spatial particle size distribution (PSD) was investigated by collecting a drop of product solution from the dissected locations as well as from the outlet onto a TEM
grid. After evaporating the solvent, TEM analysis of the samples was performed to provide information regarding on the size and size distribution evolution at these locations. This procedure was identical for all the samples collected at different locations and at different flow rates and therefore provided reliable information about relative growth of particles at different locations within the channels. It was also important to mention that the particle deposition on the channel wall was virtually eliminated as one chip was used only once to run the experiment at each flow rate in order to avoid particle deposition, if any, on channel walls. This was one of the advantages of using “use and throw” and inexpensive polymeric millifluidic chips. In order to compare PSD between millifluidic and batch products, samples were taken from batch reactors at specified time same as the residence time of those samples taken from millifluidic reactors. TEM images were recorded at University of Texas in Arlington (UTA) using Hitachi H-9500 High-resolution TEM. Particle size and size distribution were obtained by analyzing TEM images using Image J.

### 2.3 Numerical methods

Numerical simulations were adopted to study the mixing inside the millifluidic reactor and analyze the residence time distribution (RTD) at various flow rates. The accuracy of the numerical model was estimated by comparing the prediction of mixing between two reagents to the observation in fluorescent dilution. The mixing process is governed by three equations: continuity equation (Eq. 2.1), incompressible Navier-Stokes equation at steady state (Eq. 2.2) and steady-state species transport equation (Eq. 2.3).

\[
\nabla \cdot \vec{v} = 0 \quad (2.1)
\]

\[
\rho \vec{v} \cdot \nabla \vec{v} = -\nabla p + \mu \nabla^2 \vec{v} \quad (2.2)
\]

\[
\vec{v} \cdot \nabla c_i = D \nabla^2 c_i \quad (2.3)
\]

where \( p \) is pressure, \( \vec{v} \) is velocity vector, \( \rho \) is density, \( \mu \) is viscosity, \( D \) is diffusivity and \( c_i \) is a scalar representing the concentration of fluorescent.
The diffusivity of the fluorescent dye was set as $5 \times 10^{-10}$ m$^2$/s with constant diluting assumption. Density and viscosity were set to be same as the properties of water. Zero pressure condition was imposed on outlet while no-slip condition was applied for solid wall. Similarly, zero flux condition across channel walls and convection flux across the outlet were imposed on the species transport equation.

The RTD analysis was carried out by injecting an inert tracer at certain time $t=0$ and then measuring the tracer concentration $C$ at the sampling point as a function of time. It should be pointed out that the tracer should have physical properties similar to the reaction mixture and be completely soluble in the mixture; in addition, it should be non-reactive. Thus Au ion was selected as the tracer. Two most frequently used injecting methods are pulse input and step input. In pulse input, which was adopted in this work, an amount of tracer is suddenly injected by one shot into the reactor in as short a time as possible. The residence time distribution function $E(t)$, describing how much time difference fluid elements have spent in the reactor, is defined as $C(t)/\int_{0}^{\infty} C(t)dt$.

The flow field is governed by Eq. (2.1) and (2.2) while the transient mass transport of tracer is described by a dynamic species transport equation (Eq. 2.4). The value of diffusivity of tracer was set as $10^{-9}$ m$^2$/s in the model.\footnote{2.4}

$$\frac{\partial c_i}{\partial t} + \nabla \cdot \nabla c_i = D \nabla^2 c_i \quad (2.4)$$

where $t$ stands for time and $c_i$ is the concentration of tracer.

The mean residence time $t_{\text{m}}$, indicating the average time that species spend in the reactor, was calculated by Eq. (2.5). The width of the distribution\footnote{2.5} $\Delta t$ was employed to describe the spread of residence time. The width of the distribution was defined as the time required for fraction $\alpha$ of total injected volume of tracer to travel to the sampling point, and it could be determined by Eq. (2.6) and (2.7), where $t(\alpha)$ stands for the time that $\alpha$ fraction of elements emerge at the sampling point, and $t(\beta)$ stands for the time that the elements begin to appear at the sampling point. In this study, $\alpha$ is set as 0.99.
\[ t_m = \frac{\int_0^\infty tE(t)dt}{\int_0^\infty E(t)dt} \]  
(2.5)

\[ \alpha = \int_{t(\beta)}^{t(\alpha)} E(t) \, dt \]  
(2.6)

\[ \Delta t = t(\alpha) - t(\beta) \]  
(2.7)

All the numerical simulations were carried out in a two-dimensional domain. Comsol Multiphysics 3.5a was adopted as the numerical solver.

**2.4 Results and discussion**

Figure 2.3 : TEM results of Au nanoclusters obtained at (a) 10mL/h, location 1–B11 (b) 10mL/h, location 2–B12 (c) 10mL/h, outlet (d) 6mL/h, location 1–B21 (e) 6mL/h, location 2–B22 (f) 6mL/h, outlet (g) 2mL/h, location 1–B31 (h) 2mL/h, location 2–B21 (i) 2mL/h, outlet. (* Bar at the bottom of each picture is 5nm to scale except for d which is 2nm.)

Typical TEM images of the nanoparticles obtained from location 1, location 2 and the outlet at flow rates 2ml/hr, 6ml/hr and 10ml/hr are shown in Figure 2.2. The mean particle diameter and distribution are listed in Table 2.1. The histogram of the particle size distribution obtained at these locations at the corresponding flow rates are shown in Figure B1 on the Appendix. The results indicate
that for any particular flow rate, the average particle size increases due to surface growth as reagents flow through channels. The broadest size distribution was seen at the outlet, which was found to be the case for all the three different flow rates (2, 6, 10 mL/h). It is also to be noted that with the increase in particle size there is also tendency for particles to agglomerate leading to further increase in particle size distribution, which is believed to be the reason for large nanoparticles obtained from the outlet at 2 mL/h. One can see relatively better control over size and size distribution at a high flow rate of 10mL/h at location 1.

Table 2.1: Mean residence time, width of residence time distribution and particle size at different locations and at different flow rates.

<table>
<thead>
<tr>
<th>Flow rate, mL/h</th>
<th>Mean Residence Time, s and Particle size, nm</th>
<th>Width of distribution, s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Location 1 Location 2 Outlet</td>
<td>Location 1 Location 2 Outlet</td>
</tr>
<tr>
<td>2</td>
<td>48.88 ± 0.55 76.11 ± 0.61 121.73 ± 1.07</td>
<td>69 94 119</td>
</tr>
<tr>
<td>6</td>
<td>17.60 ± 0.64 26.88 ± 0.48 42.22 ± 0.91</td>
<td>37 49 63</td>
</tr>
<tr>
<td>10</td>
<td>11.04 ± 0.52 16.79 ± 0.69 26.24 ± 0.74</td>
<td>25 35 43</td>
</tr>
</tbody>
</table>

It is not difficult to understand the reason for increasing particle sizes as well as size distributions in the direction of the flow if one can understand the flow environment inside the millifluidic reactor. The fluorescent dilution process illustrated the particle formation process. As the two reagents are injected into the millifluidic reactor, they flow in parallel with same speed. Mixing between these two reagents are dominant by molecular diffusion, thus a mixing zone is formed across the interface. Supersaturated solute formation, nucleation and particle growth are all proceeding inside the mixing zone. The dilution experiments aims to visualize the spreading of fluorescence along the millifluidic channel using a microscope and a video camera. The normalized fluorescent intensity profiles were plotted across the cross section of the millifluidic channel at 2mL/h and 5 mL/h in Figure 2.4(A). This mixing process was
also modeled as mixing two streams (of concentration of 0 and 1) at steady state. The good agreements of simulation results with experimental observations validate the accuracy of the simulation model.

Figure 2.4 (A) Normalized dye intensity profile at location 1 from experimental and simulation studies. (B) RTD analysis of 10 mL/h at different locations. (C) RTD analysis of 2 mL/h, 6 mL/h and 10 mL/h at outlet. (D) Comparative analysis of residence time dependent particle size and size distribution of Au nanoparticles from batch and millifluidic reactors

The region where intensity/concentration increases from 0 to 1 indicates the mixing zone inside microfluidic channel. If compared two flow rates at same location, high flow rate leads to confined mixing zone due to less dispersion time. Since molecular diffusion is a random movement, larger mixing zone is expected to produce poly dispersed particles. At a flow rate of 10 mL/h, the mixing zone is confined so that the concentration change between the two fluids behaves almost as a step change, and more uniform particles are expected.
The disadvantage associated with single phase synthesis is the possibility for large residence time distributions (RTD) due to velocity distribution. From Figure B2 in the Appendix, we know that a parabolic velocity profile with maximum velocity in the center and zero velocity at the wall is established over the channel cross-sections under the hydrodynamic pressure driven conditions. This means that a reaction mixture sampled after the initiation of the mixing is formed from an ensemble of volume elements that have spent varying time inside the reactor. As shown in Figure 2.4(B) and (C), the residence time distribution of the reagents exhibits a non-Gaussian distribution. The motion inside the reactor is dominated by two effects: convection and diffusion. If the process is purely driven by diffusion, a Gaussian distribution is expected. On the other hand, if only convection occurs, the RTD curve behaves like a sharp pulse with long tails, which is similar as the E curve of 10 mL/h. From Figure 2.4(B) and (C), long tails in RTD curve are observed at high flow rate (6mL/h and 10mL/h), indicating a convection-dominant process. At 2 mL/h, the strong effect of diffusion leads to a shape of E-curve similar to Gaussian distribution. Table 2.1 lists the residence time and width of residence time distribution of different flow rates and locations.

RTD analysis can qualitatively predict the spread of particle size distribution (PSD) since the varying residence time determines the varying particle sizes. The data from the Table 2.1 indicates that the size and size distribution increase as the fluid moves from location 1 towards the outlet at the same flow rate, which is consistent with the residence time distribution. The size distribution in the outlet at 2 mL/h, 6 mL/h and 10 mL/h is also consistent with the residence time distribution. If one compares the particle size at different locations that have approximately same residence time, for example location 2 at 10 mL/h and location 1 at 6 mL/h (highlighted in blue) or outlet at 6 mL/h and location 1 at 2mL/h (highlighted in orange) or location 2 at 6mL/h and outlet at 10 mL/h (highlighted in green), one can see a good correlation of particle size and size distribution with the corresponding residence times. However, the correlation in the dispersion between the numerically obtained RTD and the experimentally obtained PSD is not one-to-one because of a number of reasons: (a) the numerically obtained RTD simulates only
the included growth time of the particles while the experimentally obtained PSD also includes the effects of nucleation and growth kinetics; (b) The experimental procedures, particularly nucleation, are subject to stochastic fluctuations and such features are not present in numerical simulations of the mixing process. While the measured sizes are consistent with the RTD, the dispersion in the measured sizes is subject to random variations. In addition, the variations in sampling time to arrest the reaction on the TEM grid could also cause variations in the dispersion of the sizes. One needs to notice that the particle size depends on two factors: growth time which is controlled by residence time and growth rate which is controlled by kinetics. The RTD analysis provides a key part of particle growth time, but actual capture of particle size needs kinetic information of particle growth rate. This is the long term goal since no kinetic data for this reaction has been revealed in literature.

Based on the results shown in Table 2.1, one may hypothesize that nanoparticles of smaller size and narrower size distribution may be produced if further increase the flow rate. Although no quantitative information on nucleation and reaction kinetics are available at this stage, the nucleation process is expected to be a rapid process indeed so that the particle size grows to 2 nm as soon as the two reagents are mixed. Therefore, additional experiments were conducted at a higher flow rate of 40 mL/h where the residence time on the outlet was calculated to be only 3.53 s. The average particle size obtained was 2.53 nm, which supports the expectation. The TEM images of sampling location 1, 2 and outlet are shown in Figure 2.5. Surprisingly, a fourfold increase in the flow rate did not result in either decrease in the particles size or narrowing in size distribution compared to the flow rate of 10 ml/hr. It appears that the nucleation time for the reaction under consideration is probably smaller than 3.53 s, which is the smallest possible residence time in location 1 at the total flow rate of 40 mL/h. Our arguments are strengthened by the recent insitu SAXS investigation of Ag nanoparticle formation where results show that silver nanoparticles are formed via three distinct periods within 6 ms. 44
In order to test if the millifluidic reactor provide better control over batch reactors, samples were taken from batch reactor at the time approximately similar to the investigated residence times within the millifluidic channels. Figure B3 in the Appendix shows the TEM images and the particle size histograms for the particles obtained at different time intervals. Clearly, the increasing particle size with time is seen in the case of the flask process as well. Additionally, the size distribution of the particles was also found to be broad.

Figure 2.4(D) compares the particle growth process of Au nanoparticles obtained from the batch and the millifluidic reactor. Clearly, the batch reactor results in larger size distributions than millifluidic reactor for the same reaction\growth time. One can also see that the size distribution of particles from the millifluidic process is tending narrower as the residence time decreases. In contrast, the size distribution continues to broaden with time in the flask reactor. It is also to be noted from the literature that similar situation is encountered even within a microfluidic reactor where when the residence times are adequately small, further increase in flow rates have smaller effects in reducing the particle size distribution.\cite{35a} The reason for this is that the particle size distribution depends on both the residence time effect as well as the growth dynamics of the particles. Krishnadasan\cite{13} revealed that the growth rate decreases with increase of particle size, and small particles catch up with large particles which results in narrowing the size distribution over time. What is also noticeable is that the particle size within the millifluidic reactor remains constant up to the residence time of about 40 sec and then there is a gradual increase in the size.
as well as size distribution. Combining this information with the fact that even at the smallest possible residence time (3.53 s) in location 1 at the total flow rate of 40 mL/h, we do not obtain either smaller or narrower size distribution compared to the flow rate of 10 ml/hr. It is, therefore, likely that the nucleation time for the particular gold reduction reaction we examined is smaller than 3.53 s. One can also conclude that there could be three different phases’ reduction & nucleation, coalescence of nuclei to form the particles and growth of the particles to the gold nanoparticle formation within the millifluidic channels; similar to the case of microfluidic channels. This conjecture is supported by recent observations based on in situ small X-ray scattering investigations on nucleation and growth of gold nanoparticles.44-45 In principle, one can take advantage of these differences to arrive at conditions for the preparation of monodisperse gold nanoparticles utilizing the millifluidic reactors.

2.5 Conclusion

In conclusion, we have developed a novel approach to study the time resolved growth of nanoparticles at different locations utilizing TEM of samples obtained through dissection of the millifluidic chip at specific locations. Taking advantage of the possibility to convert spatially resolved information from the millifluidic channel into time resolved information, we have been able to map the growth of gold nanoparticles within the channel. The time resolved formation of gold nanoparticles was also found to be dependent on the flow rates and therefore on the residence time. In addition to the residence time, kinetics of the reaction appears to be critical in controlling the size and size distribution of the particles. We have also demonstrated that numerical simulations can be used to predict the flow rate dependent properties of nanoparticles formed within millifluidic channels. While the experimental results obtained so far do not demonstrate formation of monodisperse gold nanoparticles, the approach presented here has a great potential to lead to identification of experimental conditions based on numerical simulations for such a result. Similar to the case of microchannels, our work demonstrate that there are potential opportunities for millifluidic reactors to separate nucleation and growth phases and in general, higher flow rates could result in smaller size distributions and normally smaller nanoparticles provided
kinetics of the reaction are appropriate. Although the surface area of the geometry (where the fluid is in contact with the solid) is vastly different in milli and microfluidic reactors, it is the interfacial area between the two reacting fluids that important in governing the initiation and propagation of the reactions. The reactions occur where the two reagents flow in parallel with an interface in the middle of the channel. Any nucleation that is triggered at the solid fluid interface must be small as it is only a line segment on the top and bottom of the channel. (The reaction interface is right in the middle of the channel intersection the top and bottom cover plates at a line). So we expect similar size and PSD in milli and micro systems, only the throughput will be higher in the milli system because of the larger interfacial area between the reactants.

We hope that the experimental results coupled with numerical simulation results reported here will form the basis for future studies towards optimization of millifluidic reactor systems with parameters such as shorter mixing times, narrower residence time distributions and smaller separation times in order to enable better control over nanoparticle size and size distribution. Our results also demonstrate that in addition to the residence times, reaction kinetics involved in nanoparticle formation need to be taken into consideration for developing the millifluidic synthesis process for nanoparticles.
Chapter 3 Geometric Optimization of Liquid–Liquid Slug Flow in a Flow-focusing Millifluidic Device for Synthesis of Nanomaterials†

3.1 Introduction

As seen in Chapter 2, traditional microfluidic/millifluidic reactors manipulated with single-phase flow are associated with large residence time distribution due to the intrinsic laminar flow behavior. Consequently, large residence time distribution results in nanomaterial with broad size distribution, leading trouble to the cases where size, size distribution and shape control is extremely important. Therefore, investigation of multiphase flows in microfluidic devices has been gaining much attention recently as a solution to improve the performances of single-phase flows.²⁸b, ²⁴⁷

Multiphase flow systems introduce a second immiscible flow to enhance mixing and transverse channel transport.²⁸a The resulting flows have various forms such as stratified flow, slug flow or jetting flows, depending on the interactions among surface tension force, inertia force and viscous forces.⁴⁸ Among these flow patterns, the slug flow takes advantage of the large interfacial area, fast heat and mass transfer and reduced axial dispersion; therefore, it has been used in various applications,⁴⁹ especially in chemical synthesis.²²a, ²⁹, ⁵⁰ Multiphase flows in microfluidics are generally carried out either by gas-liquid flow or liquid-liquid flow. Since we have been interested in utilizing multiphase flows for the controlled synthesis of nanomaterial, liquid–liquid flow is desirable as the thin film of carrier fluid, usually developed on the channel wall, prevents surface growth of the nanomaterial. As most of the microfluidic devices are fabricated using polymers, the weak sealing limits the flow to be manipulated at low Reynolds number (Re) and Capillary number (Ca) regimes. The flow pattern in this regime usually exhibits a slug flow.

Many designs on multiphase microfluidic devices have been reported to generate slug flows and these can be categorized into flow–focusing devices,⁵¹ co-flowing devices,⁵² T-junction devices.⁵³

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Uniform bubbles or slugs can be generated in these devices; however, the formation mechanics especially in liquid-liquid slug flows is still not well understood. Several researchers point out that the bubble size depends mainly on the ratio of the gas flow rate and liquid flow rate in flow-focusing devices,\textsuperscript{51b,54} and is independent of Ca for both low and high Re flows\textsuperscript{55}. For nanoparticle synthesis, liquid slugs usually serve as the batch reactors; Tice et al. points out that mixing efficiency inside slugs depends on the length of slugs,\textsuperscript{26a} thus designs producing uniformly small slugs are desired to produce nanoparticles with narrow size distribution.

Microfluidic devices in general and those for droplet based applications have certain disadvantages that hinder their applications. For example, their fabrication usually requires expensive and time-consuming techniques such as lithography and etching in a clean room. In addition, there remain a number of issues related to reaction control and process scale up in order to meet the requirements for practical applications.\textsuperscript{35b} Yet another drawback is the difficulty to withstand high pressures associated with high flow rates and small residence times, which is often required for controlled synthesis of uniform nanomaterial.\textsuperscript{56}

Scaling up of microfluidic devices into millifluidic ones presents some considerable advantages over microfluidics while retaining similar flow characteristics.\textsuperscript{8a} One is the low cost for fabrication of millifluidic devices. They can be produced by using precision micromachining to fabricate metal mold inserts, injection molding for cost-effective chip replication, and lamination for adequate sealing of the devices/chips. Since the connecting capillary tubes and the various modules of the system can assemble and disassemble easily, the modular setup can be designed on demand in a short time.\textsuperscript{8b} These advantages have attracted many research interests recently. Droplet – based microfluidics have been applied to investigate polymerization reactions\textsuperscript{57}, to microbiology analysis\textsuperscript{58} and screening.\textsuperscript{59} The use of millifluidic device has also been reported to offer the potential to produce multiple emulsions.\textsuperscript{9} We have recently demonstrated the utility of millifluidic reactors in single phase synthesis of ultrasmall nanoclusters\textsuperscript{60b} and also as a tool for probing the time resolved growth of nanoparticles.\textsuperscript{23a} To the best of
our knowledge a millifluidic device for segmented flow applications in general and for nanomaterials synthesis in particular has not been developed to date.

While several experimental investigations were carried out to study the effects of flow rates of multiphases, fluid properties (viscosity and surface tension), and channel geometry on liquid-liquid flow regimes within micro systems, a detailed understanding of the effects of operational and design parameters on the hydrodynamics within millifluidic systems has not been carried out. Recent development in computational fluid dynamics (CFD) modeling has provided a new approach to study slug flows. Several numerical methods, such as the volume of fluid method (VOF), level-set method, lattice-Boltzmann method and phase field method have been used to study the hydrodynamics of slug flow, and they are able to capture the slug formation hydrodynamics. Numerical simulation can provide insight in slug breaking mechanics that are difficult to observe in experiments. They are also relatively simple and time–saving to carry out so that intensive experimental studies may be avoided. Many researchers have utilized two dimensional (2D) numerical simulations to study droplet formation process. Compare to 3D simulations, it assumes that the channel is infinite long in the third dimension to reduce the computational effort; however, the third dimension plays an important role in droplet formation process especially when the aspect ratio (depth/width of the channel) is large. In this study, we adopted VOF method in a three-dimensional (3D) domain to study the slug formation process inside the flow-focusing millifluidic devices.

Our previous investigations were focused on a single phase snake mixer type millifluidic device, and here we report our studies on the slug flow of two immiscible fluids within a ‘hydrodynamic focused’ polymeric millifluidic reactor at the squeezing regime (Ca < 0.002) by varying a number of process parameters in order to control the generation of periodical, and uniform slugs. Based on the literature, prior investigations suggest that the slug length can be tuned by varying the flow rates of each phase inside microfluidic devices. Especially in squeezing regime, the slug lengths were found to depend only on the flow rate of the two phases. In order to investigate the possibility to create
controlled slugs within a flow focusing millifluidic chip, we carried out experiments under various flow rates. The chip showed the similar ability, as that of microfluidics, in controlling slug lengths except that the slug lengths were very long. Uniform copper nanoparticles are also obtained inside the millifluidic chip, indicating its similar capability in nanomaterial synthesis as microfluidic reactors.

Since the geometric dimensions in microfluidic flow focusing devices play important roles in droplet formation process, we hypothesized that the internal geometry of the focusing region also plays an important role on slug size other than the flow ratio; therefore, we investigated the evolution of the slug formation within two modified geometries. The results discussed below validate our hypothesis and lead us to propose alternate millifluidic designs to produce slugs with smaller sizes. In addition, we demonstrate for the first time that the slugs generated within the millifluidic reactors are suitable for controlled synthesis of copper nanoparticles.

3.2 Experiments

3.2.1 Chemicals and reagents

Methylene blue, rhodamine B, tetradecane (purity: 99.0%) and silicon oil (viscosity: 10 cSt) Copper(II) nitrate hydrate (99.999%), sodium borohydride ($\geq$ 98.0%), Sodium hydroxide pellets (99.998%) and O-[2-(3-Mercaptopropionylamino)ethyl]-O′-methylpolyethylene glycol (Mw 5000) [MPEG], Tetradecane were obtained from Sigma-Aldrich. All chemicals were used as received without further purification. Water was supplied by a Barnstead Water Purifier Nanopure water system (18.3 $\Omega$ cm).

3.2.2 Fabrication of flow focusing millifluidic chip

Polymethyl methacrylate (PMMA) based millifluidic chips (Figure 3.1(a) and (b)) were replicated from a micromachined brass mold insert using a HEX 2 hot embossing machine (Jenoptik, Jena, Germany). The brass insert (Figure 3.1(c)) contained the inverse fluidic chip design and was patterned at the KERN Micro CNC machining center (Kern, Eschenlohe, Germany) using cutting tools with 50$\mu$m
smallest diameter. The brass insert containing the chip design as well as the cover slide was precisely transferred into PMMA sheet material at elevated temperature (150-160°C). Subsequently, the chips were separated by sawing and thoroughly cleaned with IPA and DI water, and dehydrated at 60°C for 1hr in a convection oven. The unstructured PMMA cover slides of ~1mm thickness were thermally welded onto the fluidic chips using the fixture shown in Figure 3.1(d). Thermal welding was performed in a convection oven using spring clamp fixture and a total force of ~100KN for the 3”x1” chip area. The maximum temperature of ~110°C was kept for 1.5hrs followed by a slow cool down ramp of several hours to room temperature. In the final step, fly-cutting completed the fabrication process leading to the opening of the inlet and outlet holes (Figure 3.1(e)) that connect the millimeter fluidic channels to the manifold as shown in Figure 3.1(f).

![Image](image.png)

Figure 3.1 (a) Millfluidic chip and cover slide hot embossed into PMMA at 150-160°C. (b) Millifluidic chip and cover slide after separation and cleaning. (c) Mold insert made from brass with inverted pattern of the millifluidic chip. (d) Spring-loaded clamping fixture for thermal welding of cover slides onto millifluidic chips. (e) Sealed chip after fly-cutting ready for testing. (f) Microplumber manifolds with clamped millifluidic chip ready for experiments.
3.2.3 Slug formation and its control

The experimental set-up for the slug formation is shown in Figure 3.2. In this setup, the PMMA flow focusing chip was mounted on a manifold (Model: 6 way manifold, MicroPlumbers microsciences LLC). Silicon oil was used as continuous phase and was pumped through the two outermost channels. The aqueous solutions of 0.1 mM rhodamine B and 0.1 mM methylene blue were used as a dispersed phase and were pumped through the two middle channels. The flow rate of each channel was controlled by high precision syringe pumps (NEMESYS, Cetoni). The generated slugs were recorded by the use of a handheld digital camera (Model: 44302, Celestron) which took pictures at a frequency of 30 frames per second. When setting a new flow rate, the system was run for at least 2 minutes to reach a steady state prior to taking the images. The slug sizes were averaged by taking more than 20 observed stable slugs.

![Figure 3.2 Schematics of the experimental setup for plug formation](image)

3.3 Numerical simulations

The VOF method was used to investigate the hydrodynamics of liquid–liquid slug formation between the aqueous solution (dispersed phase) and silicone oil (continuous phase) inside the millifluidic channels. It can be used to model two or more immiscible fluids by solving a single set of continuity and momentum equations and tracking the volume fraction of each fluid inside the computational domain. It
is naturally conservative and relatively simple in tracking topological changes of the interface. In addition to fast convergence, the other advantages are reasonably accuracy, relative simplicity and the ability to solve complex free surface flows. Its extensive application in modeling multiphase flows, including gas-liquid and liquid-liquid slug flows in microchannels is well documented.

The flows were manipulated in typical laminar flow regime (Re<1) and both fluids were modeled as incompressible Newtonian fluids. The VOF solver in commercial CFD software ANSYS Flunet 12 was adopted in this study.

Only a single set of continuity [Eq.(3.1)] and momentum equation [Eq.(3.2)] were solved continuously throughout the computational domain.

\[
\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \vec{v}) = 0 \quad (3.1)
\]

\[
\frac{\partial (\rho \vec{v})}{\partial t} + \nabla \cdot (\rho \vec{v} \vec{v}) = -\nabla P + \nabla \cdot [\mu (\nabla \vec{v} + \nabla \vec{v}^T)] + \vec{F} \quad (3.2)
\]

of which \(\rho\) and \(\mu\) are the volume – averaged density and viscosity, which are defined as (3.3) and (3.4) respectively:

\[
\rho = \alpha_q \rho_q + (1 - \alpha_q)\rho_p \quad (3.3)
\]

\[
\mu = \alpha_q \mu_q + (1 - \alpha_q)\mu_p \quad (3.4)
\]

The VOF method used the geometric reconstruction scheme which based on piecewise linear interpolation led to reconstructed interfaces. The interface was tracked by solving an additional advection equation [Eq.(3.5)], which yielded the volume fraction \(\alpha_q\) of each fluid.

\[
\frac{\partial (\alpha_q \rho_q)}{\partial t} + \nabla \cdot (\alpha_q \rho_q \vec{v}_q) = 0 \quad (3.5)
\]

The body force term in Eq. (2) was computed using the continuum surface force (CSF) model as shown in Eq. (3.6).
\[ \vec{p} = \sigma \left[ \frac{\rho \kappa \hat{n}}{\frac{3}{2}(\rho_p + \rho_q)} \right] \]  

(3.6)

where \( \sigma \) was the surface tension coefficient, and \( \hat{n} \) was the unit surface normal vector, and \( \kappa \) was the local surface curvature, which are defined by Eq. (3.7) to Eq. (3.9).

\[ n = \nabla \cdot \hat{\alpha}_q \]  

(3.7)

\[ \hat{n} = \frac{n}{|n|} \]  

(3.8)

\[ \kappa = \nabla \cdot \hat{n} \]  

(3.9)

The wall adhesion force was also taken into account by specifying contact angle as a boundary condition. We assumed that the contact line maintained a constant value and was independent of the velocity and the direction of contact line, thus a constant contact angle \( \theta_w \) was used for all the operation conditions. The interface normal in the cells near the wall was calculated by Eq. (3.10):

\[ \hat{n} = \hat{n}_w \cos \theta_w + \hat{\ell}_w \sin \theta_w \]  

(3.10)

where \( \hat{n}_w \) and \( \hat{\ell}_w \) were the unit vectors normal and tangential to the wall. The calculated surface normal in one cell away from the wall was used to tune the local curvature \( \kappa \), and this curvature was used to calculate the body force term in Eq. (3.6).

For solution methods, a transient explicit solver was used along with the implicit body force formulation. The PISO (pressure-implicit with splitting of operators) scheme was used for pressure-velocity coupling of the momentum equation and continuity equation. For spatial discretization, Green-Gauss node-based method was used for gradients, the PRESTO! (pressure staggering options) scheme was used for pressure interpolation, and the second-order up-wind differencing scheme was used for the momentum equation.
Figure 3.3 (a) The internal structure of focusing region inside the millifluidic chip. The width of the straight channel is 0.5 mm. The chip has uniform depth of 1 mm. (b) Geometry of the flow focusing millifluidic chip used in three dimensional numerical simulations. The computational grids show one layer in z direction and focus on the flow focusing region. The computational domain consists of 180,400 hexahedral elements, of which the grids in the focusing region and in the straight channels are refined to capture the gradient in these regions. The four inlets and the outlet have the same dimensions as 1 mm depth and 0.5 mm in width.

The internal structure of the focusing region of the millifluidic chip is shown in Figure 3.3(a). As the corners inside the millifluidic channels were rounded during fabrication, the internal structure in the focusing region was read into Image J to measure and use it to mimic the shape for numerical simulations. The three-dimensional computational setup of the millifluidic chip, as shown in Figure 3.3(b), has four inlets and one outlet. Aqueous solution ($\rho_d = 1000 \text{ kg/m}^3, \mu_d = 0.001 \text{ Pa} \cdot \text{s}$) was injected into the chip from the central inlets (inlet B and C) while silicone oil ($\rho_c = 963 \text{ kg/m}^3, \mu_c = 0.0093 \text{ Pa} \cdot \text{s}$) was injected through the side inlets (inlet A and D). The interfacial tension ($\sigma$) between the two solutions was assumed to have a constant value of 0.0365 N/m.\(^{53a, 61b}\) The four inlets were all modeled as velocity inlets, and the outlet was modeled as outflow. No-slip boundary condition was imposed on the channel walls. Raj et al. have carried out similar numerical simulations of water-silicone oil slug flow in a T-junction.
microfluidic channel and found that the value of the contact angle was crucial in determining the flow pattern but only marginally affected the slug lengths. The suitable contact angle ($\theta_w$) was in the range of 120 to 180 degrees. Our preliminary simulations showed that stable slugs were obtained if the value of $\theta_w$ was larger than 120 degree, and slug lengths were insensitive to the value of contact angles. Therefore, in this study, $\theta_w$ was set as 120 degree. Same boundary conditions were also applied to the other designs.

The numerical simulations were carried out in a three-dimensional domain to quantitatively capture the slug formation process. The computational mesh was generated by ANSYS ICEM (ANSYS INc.). Hexahedral elements were generated with the mapped meshing scheme. The grids near the wall were refined to ensure good quality of gradient calculation. The lengths of the inlet channels were truncated so as to reduce the computational cost; however, the necessary length was chosen to ensure complete laminar flow development prior to the focusing region. The slug formation was studied at two sets of flow rates: for the first set, the flow rate of the aqueous solution ($Q_d$) in each inlet was varied from 50 µL/min, 25 µL/min and 10 µL/min while the flow rate of silicone oil ($Q_c$) remained at 50 µL/min. In the second set, the flow rate of the aqueous solution in each inlet was varied from 25 µL/min, 10 µL/min and 5 µL/min while the flow rate of silicone oil remained at 100 µL/min. The maximum Ca calculated from the total flow rate of continuous phase inside the straight channel ($Q_c = 200 \mu\text{L/min}$) was 0.0017.

Three meshes with different grid resolutions were prepared to investigate grid resolution on the slug lengths. The slug length to the corresponding coarse mesh (44,980 elements), medium mesh (180,400 elements) and finer mesh (588,039 elements) were 6.15 mm, 6.02 mm, and 5.98 mm respectively. Therefore, the slug lengths were found to be independent from grid resolution in medium mesh. Similar mesh method was also adopted in other geometries.

The time steps during the simulations were selected appropriately to keep the maximum Courant number (Cr) less than 0.25. The numerical runs were performed remotely with 8 processors on cluster Philip the HPC (High Performance HPC) facility located at Louisiana State University.
3.4 Copper nanoparticle synthesis using slugs generated within the millifluidic reactor

Copper nanoclusters were synthesized using the new PMMA based four channeled millifluidic reactors as described connected with pressure pumps (Mitos P-pumps, Dolomite). Each slug formed within the millifluidic reactor, by two immiscible fluidic flows (tetradecane and water), acted as a mini-reactor for reagent combination and reaction. Tetradecane was used as a non-solvent carrier fluid injected through two outer inlet channels of the millifluidic reactor. The two aqueous based reagent streams were delivered through the two center inlet channels under nitrogen at room temperature. One of the centered inlets contained solutions of copper nitrate and polymeric surfactant (MPEG) as stabilizer while the other contained the solution of sodium borohydride and sodium hydroxide in water. The concentration of each inlet solution is accurately prepared as described previously.\textsuperscript{23b} Copper nanoparticle formation took place within the individual fused slug as it traversed along the switchback channel. The copper nanoparticles were collected under nitrogen and characterized using Transmission Electron Microscopy (TEM).

3.5 Results and discussion

3.5.1 Slug formation process in fabricated flow-focusing millifluidic chip

The slug formation process in the fabricated millifluidic chip can be described to proceed through five different stages: (1) the two streams of dispersed phase (aqueous solution) penetrates the continuous phase into the focusing region [Figure 3.4 (a)]. (2) The two streams merge together; meanwhile, the dispersed phase grows and effectively blocks the focusing region [Figure 3.4 (b)]. During this stage, the dispersed phase expands with a parabolic shape before it reaches the edge of the straight channel. As the continuous phase flows faster inside the gap between the tip of the dispersed phase and the channel wall in order to maintain the flow rate, a high pressure drop is built from each inlet to the interface of two phases [Figure 3.4 (c)].
Figure 3.4 Left: Predicted slug formation process in the fabricated millifluidic chip from numerical simulation. Right: Observed slug formation process by experiments. The flow rate of the continuous phase in each inlet is 100 µL/min while the flow rate of the dispersed phase is 25 µL/min.

(3) Due to the shear force and the pressure exerted by the continuous phase, the continuous phase drives the thread in its axial direction, and a visible neck forms while the dispersed phase is squeezed into the straight channel [Figure 3.4 (d)]. (4) The neck of the dispersed phase breaks asymmetrically adjacent to
the channel wall in the junction region [Figure 3.4 (e)]. (5) Finally, a slug is continuous phase drives the thread in its axial direction, and a visible neck forms while the dispersed phase is squeezed into the straight channel [Figure 3.4 (d)]. (4) The neck of the dispersed phase breaks asymmetrically adjacent to the channel wall in the junction region [Figure 3.4 (e)]. (5) Finally, a slug is pinched off from the dispersed phase and pushed into the straight channel [Figure 3.4 (f)]. A good agreement of slug formation process between the experimental observation and numerical prediction indicates that our numerical model is able to capture the slug formation hydrodynamics.

3.5.2 Slug size as a function of flow ratio

Many reports show that the slug size obtained from liquid-liquid slug flow inside microfluidic chips can be easily tuned by adjusting the flow ratio of oil phase to water phase. The slug length was reported to increase with the volumetric ratio of water phase to oil phase based on both experimental observations\textsuperscript{26a, 53a, 72} and numerical simulations.\textsuperscript{53e, 61b} In this study, the effects of the flow rates ($Q_c$ and $Q_d$) on slug lengths were investigated using numerical simulations supported by experiments. The obtained slug lengths under explored flow rates are shown in Figure 3.5.

Due to the irregular motion of syringe pumps, pressure fluctuations were induced to $Q_c$ and $Q_d$; therefore, fluctuations in slug lengths were observed. The fluctuations of flow rates became especially noticeably when $Q_c$ and $Q_d$ varied significantly, which was also observed by Tice et al. during their investigation of liquid-liquid slug flow inside microfluidic channels.\textsuperscript{26a} The slug flow could be considered as nearly monodispersed as the maximum fluctuation of slug lengths was found to be less than 20%. The predicted slug lengths from numerical simulations agreed fairly well with the observed average slug lengths from the experiment. They both indicated that the slug lengths decreased with the flow ratio of the continuous phase to dispersed phase ($Q_c/Q_d$), suggesting that in this millifluidic channel the slug lengths can be tuned by adjusting the flow ratio.
Figure 3.5 Observed and predicted slug length under various flow ratios. The flow rates of the continuous phases are set as 50 µL/min and 100 µL/min respectively. The curves are the fitting results of the scaling law $\frac{L}{W_c} = \varepsilon + \omega \frac{Q_d}{Q_c}$. The spread of the slug lengths in experiments is shown by the error bar.

In the squeezing region, the slug length was reported previously as a function of the ratio of the flow rate of the two phases. Garstecki et al.\textsuperscript{11} proposed, based on their observations of slug flow inside a T-junction microfluidic device, a linear scaling law in squeezing region as shown in Eq. (3.11).

$$\frac{L}{W_c} = 1 + \omega \frac{Q_d}{Q_c} \tag{3.11}$$

where $L$ is the slug length, $W_c$ is the inlet width of the continuous phase, $\omega$ is the fitting constant related to the thinning width, and $Q_d/Q_c$ is the flow ratio of dispersed phase to continuous phase which is inverse to the x axis of Figure 3.5. The scaling law showed that the slug lengths in squeezing regime was independent of Ca and viscosities and depended only on the flow ratio. Their experimental results agreed well with the scaling law when $\omega$ was unity. Xu et al.\textsuperscript{75} compared their work with other experimental data
and modified the linear scaling law to Eq. (3.12), suggesting that the channel geometry also played a role in controlling the slug lengths

\[
\frac{L}{W_c} = \epsilon + \omega Q
\]  

(3.12)

where \(W_c\) is the width of inlet channel of continuous phase, \(\epsilon\) and \(\omega\) are two fitting constants depending on the channel geometry.

In this study, the linear scaling law shown in Eq. (3.12) was adopted to show the effect of geometric dimensions on slug lengths, and \(W_c\) is selected as 0.5 mm. The obtained slug lengths from both experiments and numerical simulations can be fitted well. The linear relationship confirmed that the millifluidic reactor may provide similar control as microfluidic reactors, and the slug sizes can be manipulated inside this millifluidic chip easily by adjusting the flow ratios.

3.5.3 Synthesis of copper nanoparticles using the slugs generated within the millifluidic reactor

In order to test the capability of this millifluidic reactor, we carried out copper nanoparticle synthesis at two different flow ratios: a lower flow ratio (\(Q_c:Q_d = 1:1\), slug length = 7.13 mm) and a higher flow ratio (\(Q_c:Q_d = 4:1\), slug length = 4.35 mm). Each slug formed within the millifluidic reactor by the two immiscible fluidic flows (tetradecane and water) acted as a mini-reactor for reagent combination and reaction. Tetradecane was used as a non-solvent carrier fluid injected through two outer inlet channels of the millifluidic reactor. The two aqueous based reagent streams were delivered through the two center inlet channels under nitrogen at room temperature. One of the centered inlets contained solution of copper nitrate and polymeric surfactant, \(O-[2-(3-Mercaptopropionylamino)ethyl]-O^\prime\)-methylpolyethylene glycol (Mw 5000) [MPEG], while the other contained the solution of sodium borohydride and sodium hydroxide in water. We have previously demonstrated the utility of MPEG in a single phase millifluidic synthesis to provide stable metal cluster colloids due to better coordination with metals, steric stabilization and superior colloidal stability.\(^{23b}\) In the current situation where copper nanoparticle formation took place within a slug, the surfactant was able to provide similar advantages due to better
chelation with copper surface through bi-dentate ligands present at the terminal. Copper nanoparticle formation took place as each individual fused slug traversed the long switchback channel. The copper nanoparticles formed were collected under inert atmospheric conditions (nitrogen flow) at two different flow rates. As seen from the Transmission Electron Microscopy (TEM) images in Figure 3.6, lower flow ratio led to the formation of bigger (14.09 nm $\sigma = 3.41$) but less uniform particles compared to those (5.99 nm $\sigma = 1.14$) formed at a higher flow rate. In comparison with copper nanoparticles formed within the slug versus a single phase in a millifluidic reactor one could delineate some distinct differences on the characteristics of the copper nanoparticles formed. Both the snake mixer type millifluidic device previously used for single phase synthesis $^{23b}$ as well as the current segmented flow focused millifluidic devices provided size controlled copper nanoparticles while retaining the spherical shape of the particles. At lower flow rate in the segmented flow millifluidic device yielded much bigger sized nanoparticle (14.09 nm $\sigma = 3.41$) while the single phase flow synthesis at a comparable flow rate of 6.8 ml/h flow rate resulted in obtaining copper nanoparticles of average diameter 3 nm with broader size distribution. $^{23b}$ At a higher flow rate (850 $\mu$L/min ~ 51 ml/h) both types of millifluidic devices yielded very small copper nanoparticles of comparable size (2-3 nm).

The results indicate that the shorter slugs yield more uniform nanoparticles. This is likely to be due to better mixing and reduced axial dispersion inside the shorter slugs. Tice et al., have studied the mixing performances of aqueous slugs inside a T-junction microfluidic device, and they concluded that the shorter slugs have better mixing due the relatively small amount of fluid. However, in our case where millifluidic channels have been used, the larger dimensions resulted in longer slugs. This could be one of the reasons for the inability to produce uniform nanoparticles under the selected flow conditions. Therefore, both geometry as well as flow conditions need to be further optimized in order to arrive at optimum millifluidic design necessary to produce more uniform nanoparticles.
Figure 3.6 Copper nanoparticles synthesized at two different flow rates (a) 50 mbar pressure (150 µL/min) and (b) 200 mbar (850 µL/min)

3.5.4 Geometric optimization through CFD simulations

3.5.4.1 The effect of flow rate on slug size

A good understanding of how the geometry and operating conditions affect the slug length is necessary before starting geometric optimization. Based on the previous discussion on droplet formation, the volume of the slug can therefore be divided into two parts: the blockage volume ($V_{\text{block}}$) and the squeezing volume ($V_{\text{squeeze}}$). $V_{\text{squeeze}}$ may be expressed as the volume of aqueous solution squeezed into
the straight channel during the squeezing stage (stage (4)); therefore, it is proportional to \( Q_d \) and the time that the continuous phase takes to squeeze the dispersed phase (\( V_{\text{squeeze}} \propto Q_d \cdot \tau_{\text{squeeze}} \)). However, \( V_{\text{block}} \) is fairly complicated to express as a function of \( Q_d \); nevertheless, it may be considered as the accumulated volume of the aqueous solution inside the focusing region during the expanding stage (stage (2) ~ stage (3)).

In order to qualitatively understand the effect of \( Q_c \) and \( Q_d \) on slug breaking, the evolution of the neck width (\( W_n \)) was plotted as shown in Figure 3.7(b). As illustrated in Figure 3.7(a), \( W_n \) was measured at the center line connecting the two inlets of the continuous phase. The \( t=0 \) was selected at the point when the dispersed phase first emerged at the line. \( W_n \) first increased as the dispersed phase expanded in the junction region. When the dispersed phase reached the straight channel, \( W_n \) grew to its maximum value; when squeezing occurs, \( W_n \) started to decrease until one neck broke in the junction region. Due to the asymmetric breaking, \( W_n \) maintained constant value till the second neck broke. As the slug separated from the dispersed phase, its tail slug formed a large sphere inside the junction region due to the surface tension force. As shown in Figure 3.7(c), this phenomenon was referred as “tailing”; which was not observed experimentally due to the fast process. When the tail passed through the center line, \( W_n \) first increased and then decreased. The evolution ended when the tail of the slug left the center line.

From Figure 3.7(b), one can find that maximum \( W_n \) remained approximately constant (\( W_n \approx 1.4 \) mm) under all the three flow rates. This suggested that the flow rates of the two phases (\( Q_c \) and \( Q_d \)) had marginal effect on \( V_{\text{block}} \); \( V_{\text{block}} \) depends only on the geometry of the focusing region. As seen in Eq. (12), the slug lengths were determined by a geometry-controlled parameter \( \varepsilon \), which was controlled by \( V_{\text{block}} \). On the other hand, if \( Q_c \) was fixed (\( Q_c = 50 \) µL/min while \( Q_d = 50 \) and 25 µL/min respectively), the squeezing rate or the squeezing time was almost the same (as we can see from the slope in the squeezing stage). This indicated that \( \tau_{\text{squeeze}} \) was a function of \( Q_c \) only, and high \( Q_d \) resulted in large slug size.
Figure 3.7 (a) The scheme of the flow–focusing region and the liquid–liquid interface. For the analysis of the breakup, we track the width of neck of the dispersed phase (W_n) at the center line. (b) The predicted evolution of the neck width of the dispersed phase (W_n) from numerical simulation under various flow rates. The time t=0 is selected when the dispersed phase approached the line connecting the center of the two inlets of continuous phase. (c) The “tailing” phenomenon observed in numerical simulation.

As Q_c increased (Q_d=25 µL/min while Q_c=50 and 100 µL/min respectively), \(\tau_{\text{squeeze}}\) decreased dramatically; this meant that increasing Q_c can reduce \(V_{\text{squeeze}}\) so as to reduce the total volume of the slug. However, Q_c was usually limited by the material and sealing of the chip during fabrication; the high pressure drop resulting from the high flow rate might cause leaking or damage. Another way to reduce the slug length, as an alternate to increasing the flow ratio, is to reduce \(V_{\text{block}}\) by optimizing the geometry.

3.5.4.2 The effect of channel depth

The internal structural mainly affects \(V_{\text{block}}\); which can be defined as the fluid volume enclosed by the parabolic surface in 3D as shown in Figure 3.7(a). \(V_{\text{block}}\) is influenced by two parameters: the depth of
the channel h and the width of the shoulder in the focusing regime W_J. For the fabricated millifluidic channel, W_J is approximately 2 mm and h is 1 mm.

Gupta and Kumar have studied the effect of h on slug length within a T-junction and Liu et al. have also studied the effect of geometry on slug lengths in a cross-junction through numerical simulation. They both indicated that reducing the channel depth may shorten slug lengths.

In order to investigate the influence of channel height on slug lengths within this millifluidic reactor, two channels of same planner geometry but different depths (h = 0.5 mm and 0.25 mm respectively) are simulated at various flow ratios. Although reducing channel width lead to an increase in Ca, the influence is insignificant and the slug formation processes were still dominated by squeezing mechanism.

From the Figure 3.8 one can see that by reducing the channel height one may obtain smaller slugs to an extent. The corresponding ε values for h = 1 mm, 0.5 mm and 0.25 mm are 6.98, 5.89 and 4.84 respectively, which indicated that reducing channel height lead to a decrease in V_block. One can also conclude that by further reduction in channel height leads to a very small aspect ratio (channel depth / channel width). This may lead to even smaller slug formation albeit may not be practical from the standpoint of view of fabrication as it may lead to collapse of the channel walls during fabrication.

3.5.4.3 The effect of W_J

In order to study the effect of W_J, we proposed two extra designs with optimized focusing region as shown in Figure 3.9. Compared to the fabricated chip, the optimized design 1 (Figure 3.9(a)) shrank the focusing region by directly connecting the four channels without rounded transitional channels; the width of the shoulder (W_J) was 1 mm. The optimized design 2 (Figure 3.9(b)) further reduced the W_J to 0.5 mm. The depth of both channels was 1 mm.
Figure 3.8 Predicted slug lengths of the millifluidic reactor under various channel height, h. The flow rates of the continuous phases are set as the same as the explored flow ratios. The curves are the fitting results of the scaling law $L = \varepsilon + \omega \frac{Q_d}{Q_c}$.

Figure 3.9 Geometry and computational grid of two optimized millifluidic chip. (a) Optimized design 1 with 121,600 hexahedral elements in the computational domain. (b) Optimized design 2 with 90,000 hexahedral elements in the computational domain. The four inlets and the outlet of both designs have the same dimensions as 1 mm depth and 0.5 mm in width. The grids in the focusing region and near channel walls are refined to capture the gradient in these regions.
In the optimized design 1, the slug formation process also underwent expansion (Figure 3.10 (b)–(c)) and squeezing (Figure 3.10 (d)–(e)) stages. The evolutions of \( W_n \) at three flow rates were plotted in Figure 3.11, and they exhibited similar shapes as in the fabricated chip. In this design, the breaking points were inside the focusing region adjacent to the inlets of dispersed phase; therefore, “tailing” phenomenon was also observed for all the explored flow rates. Due to the reduced shoulder (\( W_j \)), the maximum neck width at the expanding stage decreased to approximately 0.95 mm. Therefore, \( V_{\text{block}} \) was significantly reduced, as one can also see from the significant reduction in \( \varepsilon \) (\( \varepsilon = 3.07 \) for this design compared to \( \varepsilon = 6.98 \) for the fabricated chip). Meanwhile, \( \tau_{\text{squeeze}} \) was also shortened because of the smaller neck width. As seen from Figure 3.12, much smaller slugs were obtained in all the explored flow rates in comparison with those in the fabricated chip.

Different from the fabricated millifluidic chip and optimized design 1, the optimized design 2 showed different breaking mechanism. The slug formation process shown in Figure 3.13 proceeded thorough expanding ((a)–(c)), squeezing with oscillations ((d)–(f)) and pinch-off stages ((g)–(i)). The breaking point moved downstream to the vicinity of the center line connecting the two continuous phase inlets. As we had carried out mesh dependence studies with two grid resolutions (mesh 1 had 63,000 elements and mesh 2 had 90,000 elements), same oscillations were observed in both meshes; therefore, the numerical errors were likely eliminated. We concluded that the flow region had moved away from the squeezing regime described previously; it was in the transition from squeezing to dripping regime. Although the inlet flow rates were maintained same as in previous chips, the local Ca was increased due to the smaller focusing region; therefore, the viscous force played more effect in this design. De Menech et al. mentioned that in this flow regime, the use of only Ca calculated for continuous phase to describe the dynamics of break up is not sufficient; one needs to take account an effective Ca calculated on the basis of both phases. Since our goal here is to obtain small slugs through optimizing geometries, we did not focus on the flow behaviors of the dripping regime in detail.
Figure 3.10 The Predicted slug formation process from numerical simulation in optimized design 1. The formation process is shown at $Q_c = 100 \mu$L/min and $Q_d = 25 \mu$L/min

Figure 3.11 The predicted evolution of the dispersed phase neck width. The time starts when the dispersed phase first approached the line connecting the center of the two inlets of continuous phase.
Figure 3.12 Predicted slug lengths of the two optimized designs under various flow ratios. The flow rates of the continuous phases are set as 50 µL/min and 100 µL/min respectively. The curves are the fitting results of the scaling law \( \frac{L}{w_c} = \varepsilon + wQ \).

Figure 3.13 Predicted slug formation process from numerical simulation in optimized design 2. The formation process is shown at \( Q_c = 100 \mu\text{L/min} \) and \( Q_d = 25 \mu\text{L/min} \).
The maximum neck width at the expanding stage for design 2 was reduced to approximately 0.63 mm, leading to a significant reduced $V_{\text{block}}$. Therefore, smaller slugs were observed for all the explored flow ratios than design 1, as seen from Figure 3.12. Compared to the other geometries, changing the flow ratio inside the optimized design 2 did not lead to noticeable differences in slug length, which gives us another support that the slug breaking mechanism is in the transition from squeezing to dripping regime.

Since the breaking points propagated downstream in optimized design 2, the internal structure above the breaking points had less effect on $V_{\text{block}}$ compared to the other two geometries; therefore, we may expect that further reducing $W_J$ could not lead to a noticeable reduction in slug sizes. Other approaches that may produce smaller slugs in dripping regime should be adopted.

### 3.6 Conclusions

We have carried out experiments and numerical simulations of volume of fluid (VOF) method to investigate the liquid-liquid slug flows in a fabricated flow-focusing millifluidic device. The millifluidic device showed similar controllability on producing monodispersed slug lengths and also on nanoparticle synthesis as in the case of microfluidic devices. The slug formation process was found to experience expanding and squeezing stages; therefore, the slug volume was expressed as the volume accumulated during these two stages. Through numerical simulation, we found that while manipulating flow rates can control the slug volume during squeezing stage, the blockage volume accumulated during the expanding stage depended only on the internal structure of the focusing region. Reducing the channel height does not significantly shorten the slug lengths. Further optimization of the geometry suggested two designs with better focusing region to reduce blockage volume; which produced slugs with smaller sizes. When the focusing region was reduced to certain value (as seen in the case of optimized design 2), the flow pattern shifted to the dripping region where the effect of the continuous phase was not significant. Although further reduction of the focusing region could reduce the blockage volume, the effect of reducing the slug lengths would be marginal. Preliminary investigations confirm the utility of slugs generated within the
millifluidics for flow controlled synthesis of copper nanoparticles and the possibility to produce smaller sizes of particles at high flow rates. With recent advances reported in the synthesis of complex materials using segmented flow based microfluidics, our investigations reported here are anticipated to catalyze the development of future of lab-on-a-chip devices based on millifluidics.

3.7 Notations

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
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<tbody>
<tr>
<td>A</td>
<td>cross sectional area (m²)</td>
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<tr>
<td>Q</td>
<td>volumetric flow rate (µL/min)</td>
</tr>
<tr>
<td>F</td>
<td>body force</td>
</tr>
<tr>
<td>W</td>
<td>neck width of the dispersed phase or the width of channel (mm)</td>
</tr>
<tr>
<td>n</td>
<td>normal of the two fluid interface</td>
</tr>
<tr>
<td>h</td>
<td>channel height (m)</td>
</tr>
<tr>
<td>t</td>
<td>time (ms)</td>
</tr>
<tr>
<td>U</td>
<td>superficial velocity (=Q/A, m/s)</td>
</tr>
<tr>
<td>D</td>
<td>hydraulic diameter (m)</td>
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Greek letters

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
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<tbody>
<tr>
<td>α</td>
<td>volume fraction in each computational cell</td>
</tr>
<tr>
<td>ρ</td>
<td>density (kg/m³)</td>
</tr>
<tr>
<td>µ</td>
<td>dynamic viscosity (Pa*s)</td>
</tr>
<tr>
<td>υ</td>
<td>velocity (m/s)</td>
</tr>
<tr>
<td>θ</td>
<td>contact angle (degree)</td>
</tr>
<tr>
<td>κ</td>
<td>curvature of the two fluid interface</td>
</tr>
<tr>
<td>σ</td>
<td>liquid – liquid interface tension (N/m)</td>
</tr>
<tr>
<td>ω</td>
<td>geometric fitting coefficient of flow ratio</td>
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<tr>
<td>ε</td>
<td>geometric fitting coefficient</td>
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Subscript

<table>
<thead>
<tr>
<th>Symbol</th>
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<tbody>
<tr>
<td>c</td>
<td>continuous phase</td>
</tr>
<tr>
<td>d</td>
<td>dispersed phase</td>
</tr>
<tr>
<td>n</td>
<td>neck of the dispersed phase</td>
</tr>
</tbody>
</table>
w  wall

Re  =  \frac{\rho U_{l}D}{\mu} \quad \text{Reynolds number (inertial forces vs. viscous forces)}

Ca  =  \frac{\mu_{e}U_{e}}{\sigma} \quad \text{Capillary number (viscous force vs. interfacial forces)}

Dimensionless numbers
Chapter 4 Numerical Investigations of Mixing Performances Inside Slugs

4.1 Introduction

The previous chapter has discussed the slug formation process inside a flow-focusing millifluidic reactor where long slugs were observed due to the large internal area in the focusing region. The synthesized Cu nanoparticles did not show a significant improvement over those from single phase millifluidic reactors as expected. We attributed the reason to the poor mixing inside long slugs. In this chapter, numerical simulations are adopted to study mixing performances inside slugs at various operating conditions.

One advantage associated with slug flows is the rapid mixing inside slugs\textsuperscript{24} driven by the strong convection. When slugs are travelling inside channels, the shear force exerted from the channel wall creates vorticity: the fluid elements in the center have large velocity while those near wall have small velocity; the center fluid elements are forced to circulate along the wall as they cannot penetrate the two-phase interface, creating two parallel layers of vorticity. Based on their experimental observations, Tice et al.\textsuperscript{26a} reported that mixing efficiency inside slugs is critically determined by the initial distribution of the reagents. Ideally, there are two types of initial distribution: axial and radial distribution as shown in Figure 4.1(a). Axial distribution leads to rapid mixing because the strong convection of the vortex can efficiently mix the reagents. In contrast, if the reagents are initially distributed in radial direction, mixing is dominated by molecular diffusion between these two layers, resulting in a slow mixing process. The initial distribution in reality is complicated because “twirling” effect redistributes the reagent into different part of the slugs. As the dispersed phase is injected into the immiscible continuous phase, the shear force between the two phases creates an eddy, which is referred as “twirling effect” by Tice et al.\textsuperscript{26a} as shown in Figure 4.1(b). Twirling effect not only accelerates mixing before the slugs are separated from the dispersed phase but also distributes the reagents in axially direction. After slugs are separated, the recirculation mixes the reagents efficiently as they are on the path of the vortex.
Experimental studies can give qualitative information about mixing, but the quantitative information is limited due to the complexity in measuring mixing efficiency. CFD simulations can provide the insightful knowledge without conducting experiments. In this work, CFD simulations are carried out to study the slug formation process and mixing performance inside slugs in a T-junction microfluidic reactor. The accuracy of the model is verified by comparing the data of slug formation dynamics with the experimental from Tice et al.\textsuperscript{26a} The work provides insights in mixing performances in various operation conditions.

4.2 Numerical model

VOF method, as discussed in section 2.5, is applied to study the slug formation process. In the dispersed phase, two aqueous streams are injected into the system. Dye solution is modeled with concentration of 1 while water solution has concentration of 0. The species transport equation is used to study the transport of dye into water solution as shown in Eq. (4.1):

\[
\frac{\partial C_i}{\partial t} + \nabla \cdot \nabla C_i = D \nabla^2 C_i
\]  

(4.1)
of which $C_i$ is defined as the concentration of dye solution, $\vec{v}$ is the velocity field that solved by Eq. (3.1) and Eq. (3.2), and $D$ is the diffusion coefficient of dye in water. Assuming constant dilution approximation, the diffusivity of dye is set as $10^{-11} \text{m}^2/\text{s}$. In this work, mixing occurs only inside slugs, and the reagent does not transport to the continuous phase.

The mixing efficiency index $\eta$ is employed to quantify the mixing performance as shown in Eq. (4.2), which evaluates the deviation from perfectly mixed state.

$$\eta = \left[1 - \frac{\sqrt{\frac{1}{N} \sum_{i=1}^{N} (\bar{C}_s - \bar{C}_s^0)^2}}{\sqrt{\frac{1}{N} \sum_{i=1}^{N} (\bar{C}_s^0 - \bar{C}_s^0)^2}}\right]$$

(4.2)

In this equation, $N$ is the total number of cells inside the slugs used for estimation of the mixing index. The variable $\bar{C}_s$ represents the scaled concentration value in each cell, while $\bar{C}_s^0$ and $\bar{C}_s^*$ are the scaled concentration values if the solutions are unmixed or perfectly mixed respectively. It should be noted that $\bar{C}_s^0$ has a value either 0 or 1. Based on Eq. (4.2), the theoretical limit for $\eta$ is between 0 and 1. A user defined function is used to exact the position, the phase value and concentration data out from the computation domain. The perfect mixing condition is calculated by Eq. (4.3)

$$\bar{C}_s^* = \frac{\sum_{i=1}^{N} \alpha_i V \bar{C}_s}{\sum_{i=1}^{N} \alpha_i V}$$

(4.3)

where $V$ is the volume of the computational cell, and $\alpha_i$ is the volume fraction of aqueous phase.

The commercial CFD solver ANSYS Fluent 12.1 (ANSYS Inc., USA) is adopted for the numerical simulations. A transient explicit solver is used along with the implicit body force formulation and the PISO (pressure – implicit with splitting of operators) scheme is used for pressure – velocity coupling of the momentum equation and continuity equation. For spatial discretization, Green – Gauss node – based method is used for gradients, the PRESTO! (pressure staggering options) scheme is used for
pressure interpolation, and the second – order up – wind differencing scheme is used for the momentum equation.

Figure 4.2 Geometric dimensions of the microfluidic T-junction

The computational domain consists of uniform hexahedral elements, which are generated with the mapped meshing scheme in ICEM CFD software (ANSYS Inc., USA). The geometric setup of the microfluidic T-junction is shown in Figure 4.2. The width and depth of the entire channel is 50 μm, and the length of the channel after junction region is set as 1000 μm which ensures to hold at least two slugs. The lengths of the inlet channels are reduced so as to reduce the computational cost; however, proper values are assigned to ensure that fully laminar flows are developed prior to the junction. Velocity inlets are specified for these two inlets, and the outlet is modeled as outflow. No-slip boundary condition is imposed on the channel walls associated with constant contact angles. The time step is selected appropriately to keep the maximum Courant number (Cr) under 0.25. Numerical runs are performed
remotely with 8 processors on cluster Philip – the HPC (High Performance HPC) facility located at Louisiana State University.

The properties of the fluids in this work follows the experimental values of Tice et al.\textsuperscript{26a}: the PFD solution is a 10:1 mixture of perfluorodecalin (PFD) and 1H, 1H, 2H, 2H – perfluoroocatanol. The density and viscosity are 1893 and 5.1 cp respectively. The aqueous phase contains dye and transparent water solution. The properties of these two solutions are close to water solution: the densities of both solutions are 1000 kg/m\textsuperscript{3} while the viscosities are set as 1.08 and 1.05 cp respectively. The interfacial tension between two phases has a constant value of 14 mN/m\textsuperscript{26a}.

4.3 Results and discussion

In the present study, the slug formation dynamics are validated with the experimental observations by two factors: slug length and slug frequency. Since the slug formation process is fast, Tice et al.\textsuperscript{26a} adopted a length variable- “period” to avoid measuring the short slug formation time directly. Period is defined as the center-to-center distance between two adjacent slugs. The operating conditions are controlled by two parameters: water fraction (wf, the ratio of volumetric flow rate of aqueous phase to total flow rate) and total velocity (U\textsubscript{total}). The effects of these two parameters on slug formations are investigated through numerical simulations.

4.3.1 Mesh dependence study

In order to eliminate the effect of grid resolution on simulation results, mesh dependence study is carried out at U\textsubscript{total} =50 mm/s and wf = 0.40. The simulations are performed at three structured grids with different resolutions: a coarse grid (edge length=5 µm), a medium grid (edge length =2 µm) and a fine grid (edge length =1 µm). The averaged slug length and period predicted from these grids are shown in Table 4.1. The slug length and period are believed to be converged with medium and fine grid resolution.
Table 4.1 Dependence of slug formation dynamics on grid resolution

<table>
<thead>
<tr>
<th>Slug formation dynamics</th>
<th>Grid resolution</th>
<th>Experimental observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coarse</td>
<td>Medium</td>
</tr>
<tr>
<td>Slug length (µm)</td>
<td>100</td>
<td>114</td>
</tr>
<tr>
<td>Period (µm)</td>
<td>241</td>
<td>230</td>
</tr>
</tbody>
</table>

At high flow rates, the interface of the two phases propagates fast downstream; since VOF method uses geometric reconstruction to capture the two-phase interfaces inside each computational cell, low grid resolution might lose accuracy in capturing the interfaces at high moving velocity. The capability of the medium and fine grid resolutions to handle high flow rates ($U_{\text{total}} = 150 \text{ mm/s}$) is studied at $\omega f = 0.52$. The corresponding slug lengths for medium and fine grid resolutions are 102 and 100 µm while the periods are 144 µm and 142 µm respectively. Since the predicted slug lengths and periods may be regarded to be independent from the grid resolutions, the medium mesh is believed to be capable to handle the highest flow velocity in this study. Therefore, the medium grid resolution is used for the following numerical simulations.

4.3.2 Four steps of slug formation process

Garstecki et al. postulated that the dynamics of slug break-up is dominated by the balance of pressures in the continuous phase and dispersed phase at the junction\textsuperscript{53a, 53e}. Three types of forces are exerted at the tip of dispersed phase during breakup: surface tension force, shear stress force and the force arising from the increased velocity of continuous phase around the tip (take as resistance force for short). The surface tension force stabilizes the interface while the other two forces act as destabilizing forces. The interaction of the three forces changes the pressure between two phases at the junction region and
breaks the slugs from dispersed phase. The slug formation process may be disrobed as four steps as shown Figure 4.3:

(A) The tip of dispersed phase (water) penetrates into continues phase (oil phase), and the slug begins to grow in the junction region. (B) As the tip of the dispersed phase grows downstream, it blocks the cross-section of the channel. The velocity of the oil phase is accelerated; the high velocity builds up a pressure drop from the inlet of oil phase. The shear stress force and resistance force squeeze the neck that connects the slug to the dispersed phase. (C) As the aqueous phase elongates and grows downstream, and the neck is further squeezed and pushed towards the upper corner in the junction. (D) Finally, the neck breaks, and the slug with well-defined shape separates from the dispersed phase and travels downstream.

Garstecki et al. have provided detail information on the relative magnitude of the three forces during break-up process$^{53a,53e}$. As it is not the key point in this study, we do not discuss them in detail here.

4.3.3 The effect of water fraction on slug formation

The effect of water fraction on slug length and period is studied by varying $w_f$ while $U_{\text{total}}$ remains constant at 50 mm/s. Tice et al.$^{26a}$ reported that short slugs formed when the flow rate of the aqueous stream was lower than that of the PFD stream, and long slugs formed when the flow rate of the
aqueous stream was high than that of the PFD stream. Similar phenomena were also observed in silicone-water\textsuperscript{53a}, and kerosene-water\textsuperscript{72} systems, which suggest that the slug length could be easily controlled by varying the relative ratio of aqueous phase to carrier fluid\textsuperscript{26a}.

Numerical simulations were performed to study the effect of water fraction at $U_{\text{total}} = 50$ mm/s while $w_f$ varies from 0.14 to 0.84. The contact angle is set as $140^\circ$. A comparison of predicted slug lengths and periods from simulations and measured from experiments are shown in Figure 4.4 (a). The predicted slug lengths and periods agree quantitatively with the experimental values except at $w_f=0.84$. If the contact angle is set as $150^\circ$, the predicted slug length and period agrees with the experimental results better. The sensitivity of slug lengths and periods on contact angle is discussed in section 4.3.6.

Clearly from Fig. 4.4(a), the curve of slug length consists of two regimes. At low $w_f$ region ($w_f = 0.14 - 0.40$), the slug lengths increase slowly with $w_f$; however, at $w_f = 0.60 - 0.84$, the slug lengths increase faster. As mentioned before, slug breaking process is the interaction of shear stress force, resistance force and surface tension force. Garstecki postulated that the viscous force plays an important role in slug formation dynamics if Ca of the continuous phase is above an approximate critical value of 0.01\textsuperscript{53a, 53e}. At low $w_f$ ($w_f=0.14-0.40$), the breaking mechanism is governed by dripping that shear force dominates the breaking process. As shown in Fig. 4.4(b), slugs are separated from the dispersed phase quickly as before the dispersed phase effectively blocks the entire width of the channel, thus short slugs are obtained. At high $w_f$ region ($w_f=0.60-0.84$), the shear stress force is not significant; resistance force takes major effect in slug breaking. The slugs do not separate in the junction region immediately after the dispersed phase blocks the entire channel; instead, it propagates downstream and forms a segment before slugs separate from the dispersed phase. As a result, long slugs are produced, and the slug lengths are linearly proportional to water fraction.
Figure 4.4 (a) The slug length and period as a function of various water fraction. The experimental values are obtained from Tice et al., 2003. (b) Contour of slug formation at various wfs. The contact angle is set as 140° for \( wf = 0.14 \sim 0.73 \) while for \( wf = 0.84 \) the contact angle is 150°.

4.3.4 Effect of total velocity on slug formation

Numerical simulations are also performed to investigate the effect of \( U_{\text{total}} \) (\( U_{\text{total}} = 20\), 50, 100 and 150 mm/s) on slug formation dynamics. The simulations are carried out at constant \( wf \) (\( wf = 0.52 \)) and contact angle of 140°.

Tice et al. has reported that the total flow velocity and water fraction are the two important parameters that decide the flow patterns. Under low Ca numbers, the usual flow patterns are slug and stratified flow. If Ca increases to certain threshold, the dispersed phase forms a short segment and the separation point is beyond the junction. At high Ca, the flow shifts to jetting regime. The segment propagates further downstream and its length fluctuates. The slug sizes also decrease noticeably.

At the explored velocities in the experimental work, the flow patterns were reported to belong to slug flow regime, and the slug length and period were reported to be virtually dependent of the total flow rate. The simulations agree well with experimental observations at 20 mm/s and 50 mm/s as shown in
Fig. 4.5 (a) and (b). Slugs separate from dispersed phase inside the junction region, and the lengths of slugs and periods are marginally changed by flow velocities.

(a) Comparison of slug length and period length at various velocities. The experimental values are obtained from Tice et al., 2003. (b) Contours of slug formation at various velocities.

However, the predictions of high total velocities deviate from the experimental observations. As $U_{\text{total}}$ increases to 100 mm/s, the flow pattern shifts to jetting regime. A segment forms near the junction region and the slug length and period decrease noticeably. Further increase of velocity to 150 mm/s leads to a longer laminar segment; meanwhile, the period decreases significantly while the slug length is marginally influenced. One possible reason for the deviation might be due to failure modeling of wall adhesion force at high velocities. In this study, constant static contact angle is specified; in reality, dynamic contact angles are formed when the flows are moving along the wall. At low flow velocities, the difference between static contact angle and dynamic contact angle might be ignored; however, at high velocities, the difference between them might be significant. The sensitivity of slug formation dynamics is discussed in the following section.
4.3.5 Sensitivity of contact angle

The effect of wall adhesion on slug formation is taken into account by specifying a constant contact angle near wall. Other researchers have reported that the contact angle has a significant effect on determining the flow patterns (stratified flow or slug flow) while the slug lengths are marginally influenced by contact angle\textsuperscript{61b, 72, 78}. In reality, because a thin film of oil phase is developed on the wall (wetting by oil phase), other researchers suggested to use a quasi-non-wetting condition that set the contact angle of dispersed phase as $180^\circ$.\textsuperscript{79} However, due to the poor near-wall grid resolution, the thin film cannot be observed\textsuperscript{71b}; therefore, a small contact angle is assigned to tune the slug size.

The slug formation at various $\text{wf}$ ($\text{wf} = 0.14 \sim 0.84$) are investigated $U_{\text{total}} = 50 \text{ mm/s}$ with two different contact angles ($140^\circ$ and $180^\circ$). As shown in Fig. 4.6, the different of predicted slug length and period is small at low $\text{wf}$ ($\text{wf}=0.14\sim0.40$); however, at high $\text{wf}$ ($\text{wf}=0.60\sim0.84$), they start to differ from each other significantly. The large deviation is due to the different wall adhesion force resulting from the contact angle that exerted on the dispersed phase before slug separation. At low $\text{wf}$, because the slug are separated before the dispersed phase block the channel, the difference of adhesion force that exerted on the dispersed phase is small; therefore, the slug length and period have approximate same value. At high $\text{wf}$, the dispersed phase forms a long segment before separation; thus different contact angle leads to large difference in wall adhesion force, thus in turn different slug length. Longer segment gives larger difference; thus a significant difference in slug length is observed at $\text{wf}=0.84$. Among the explored contact angles, the slug length predicted by contact angle of $150^\circ$ matches the experimental results best; thus in the following study, the contact angle is set as $150^\circ$ for $\text{wf}=0.84$. As discussed in section 4.3.5, the predicted slug formation dynamics at high velocities deviate from experimental observations. The reason might be the dynamic contact angles are different from the statistic contact angle at high velocities. Therefore, the contact angles are varied to see if the slug formation dynamics at high velocities can be predicted. As shown in Figure 4.6(b), increasing contact angle marginally affects the slug length and
period. The observed slug formation dynamics at high velocities (100 mm/s and 150 mm/s) cannot be observed at the explored contact angles.

Figure 4.6 (a) Comparison of slug length and period at various wfs if the contact angles are set as 140° and 180° (b) Slug lengths and periods at different contact angles

In a short conclusion, the VOF model with static contact angle can predicate the slug formation dynamics well at low flow velocities (20 mm/s and 50 mm/s). At high velocities, it fails to capture the breaking mechanisms and dynamic contact angle model is needed. Thus the following studies about mixing inside slugs are carried out at low flow velocities.

4.3.6 Mixing efficiency as a function of water fraction

Tice et al. reported that mixing efficiency is virtually dependent on slug length, and mixing inside long slugs is not as good as inside short slugs. However, quantitative comparison of mixing efficiency inside slugs is more difficult to obtain from experiments than numerical simulation. In this section, numerical simulations on mixing inside slugs are carried out at $U_{\text{total}} = 50$ mm/s while $w_f$ varies from 0.14 to 0.84. The predicted mixing performances as shown in Figure 4.7(b) agree well with the experimental observations in Figure 4.7 (a).

A qualitative conclusion can be made from Figure 4.7 that mixing inside short slugs is better than it in long slugs. Two factors mainly influence mixing inside slugs: twirling effect and slug size. When the
dispersed phase penetrates the carrier fluid, the shear force between the immiscible phases creates an eddy that mixes dye and water before the separation of slug as well as redistributes these two reagents into axial direction of the slugs. As indicated from both experiments and simulations, twirling occurs before the tip of the dispersed phase made contact with the low channel wall. Two effects may influence twirling: twirling time and twirling strength. Twirling time is controlled by the flow rate of the dispersed phase: the smaller the flow rate is, the longer time twirling has to redistribute the reagents. Tice et al. argued that twirling strength is the amount of carrier fluid (oil phase) that flows past the tip of dispersed phase; in other words, twirling length can be regarded as the shear force between two phases. However, direct evidences were not provided in their experiments.

Figure 4.7 (A) Experimental observation of mixing at different water fraction reported by Tice et al. (B) Contour of dye centration

Slug size plays an important role in mixing for two aspects. Long slugs have large amounts of dye to be twirled to axial direction; therefore, twirling effect on long slugs is not as significant as in short slugs in distributing the initial reagents in axial direction when the twirling time is same. The other aspect is that long slugs have long circulation path, thus the recirculation period is longer.
In order to qualitatively understand the relatively importance of these factors on mixing, the mixing efficiency indices of slugs obtained under various $wf$ are plotted with residence time as shown in Figure 4.8. The starting time ($t=0$) is adopted as the moment as the second slug is separated from the dispersed phase. The residence time ends at the time this slug approaches near the outlet of the channel. Clearly there are two regimes: convection dominated and diffusion dominated regime. In the convection dominated regime, the mixing efficiency increases rapidly with residence time; recirculation mixes the reagents inside the two parts efficiently as dye is distributed in axial direction; after the concentrations of the two layers become uniform, mixing is controlled by diffusion between these two layers. The lines in diffusion dominated regime have approximately same slopes, indicating that the difference of the circulation length marginally affected mixing in this regime. As soon as the reagents diffuse to the other part (dye or water intensive zone), they are mixed by recirculation effectively.

With the increase of $wf$, the mixing efficiency is noticeably dampened in the convection dominated regime. The initial mixing resulting from twirling effect drops down dramatically because of the large amount of reagents to be twirled. There are three possible reasons: first one is with the $wf$ increases, the velocity of dispersed increase, thus the reagents have less twirling time. The other reason is
that as the \( \text{wf} \) increase, the slug length increase, thus the amounts of reagents inside the slugs are large, thus twirling effect is not significant to redistribute such large amounts of dye. The third reason is that with \( \text{wf} \) increases, the flow rate of the continuous phase decreases; therefore, twirling strength is decreased. In this stage, one can know that which reason is dominant. The question is answered by varying \( U_{\text{total}} \).

4.3.7 The effect of total velocity on mixing

Additional simulations are carried out at \( U_{\text{total}} = 20 \) and 50 mm/s with \( \text{wf} \) of 0.20 and 0.52 respectfully. From previous discussion, one knows that the sizes of the slugs are independent of total velocities. Thus the amount of reagents inside slugs is same for a particular \( \text{wf} \). The mixing efficiencies inside slugs are plotted as a function of residence time in Figure 4.9.

![Figure 4.9](image)

(a) Contour of dye concentration at different total velocities (b) mixing efficiency with residence time at different total velocity

While remaining \( \text{wf} \), increasing total velocity increases twirling strength as the shear force augments with the flow rate of the continuous phase. As shown in Figure 4.9(b), although the twirling time increases approximately 2.5 times if the total flow rate increases from 20 mm/s to 50 mm/s, the mixing efficiency is marginally affected by the increase of twirling time. Therefore, the twirling strength
is not the dominant reason. Similarly, increasing the total velocity simultaneously increases the velocity of the dispersed phase, thus twirling time is reduced. Thus, one can argue that twirling time is not the dominant effect either.

Similar mixing performances for identical slug lengths indicate that slug length is the dominant effect: long slugs have large amount of fluid to be redistributed thus lead to poor mixing performances.

4.4 Conclusion

We have adopted VOF method coupled with species transport equation to simulate mixing performances inside slugs. The simulation results agree with the experimental results well, and it provides useful information on mixing. The conclusion of the present work can be summarized as follows:

1) Slug length increases with water fraction and marginally affected by total flow rate.

2) The current VOF model captures slug formation dynamics well at low flow velocities; at high flow velocities, dynamic contact angle model is needed.

3) The flow field is well captured by VOF method. Vortex is formed in the upper and lower part of the slug.

4) Twirling effect occurs during slug formation process and improves mixing. It improves mixing in slugs of medium size but have little effect on long slugs. At very short slugs, over – twirling occurs thus mixing is undermined.

5) Slug depends mainly on slug length. At certain water fraction, decrease total velocity does not accelerate mixing significantly.

The results provide insights to understand mixing process inside slugs and may benefit future designs of novel droplet-based microfluidics and manipulations on the operating conditions to achieve desired mixing performances.
References


Appendix A Letters of Permission


Figure A1: The approval letter of rewriting Chapter 2 by a published research paper in ChemPhysChem.
The Chapter 3 is reproduced with permission from the research paper published on Chemical Engineering Journal: Li, Y.; Yamane, D. G.; Li, S.; Biswas, S.; Reddy, R. K.; Goettert, J. S.; Nandakumar, K.; Kumar, C. S. S. R., Geometric optimization of liquid-liquid slug flow in a flow-focusing millifluidic device for synthesis of nanomaterials. *Chem. Eng. J.* 2012, accepted. The licensed copyright belongs to Elsevier. The approval letter is shown as Figure A2:

Figure A2: The approval letter of rewriting Chapter 3 by a published research paper in *Chemical Engineering Journal*. 
Figure B1: Histograms of size distribution of Au nanoparticles obtained in milli-fluidic reactor at different flow rates and different locations. The first index (1, 2 and 3) represents the flow rate of 10, 6, and 2 respectively while the second index (1 and 2) represents the sampling location marked in Figure S1(b).
Figure B2: Velocity profile across the width of the channel

T10 (Scale: 20 nm)  

T20 (Scale: 20 nm)

T75 (Scale: 100 nm)  

T90 (Scale: 100 nm)

Figure B3: TEM images and histograms of size distribution of Au nanoparticles obtained at different times during the flask reaction. T10, T20, T75 and T90 stand for the sampling time at 10 s, 20 s, 75 s, and 90 s respectively.
Vita

Yuehao Li was born in 1985 in Huai’an, Jiangsu Province, China. He completed his high school in Jiangsu Huai’an High School in 2005 and at the same year joined East China University of Science and Technology (ECUST). From August, 2008 to May, 2009, he spent one year in Lamar University, Beaumont, Texas as an exchange student between ECUST and Lamar University. He received his Bachelor’s degree in Chemical Engineering from ECUST in July 2009. This thesis completes his requirement to receive a Master of Science in Chemical Engineering in Louisiana State University.