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A Novel Microchemical System for Rapid Liquid-Liquid Chemistry

by

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Submitted to the Department of Chemical Engineering In Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in Chemical Engineering

at the

Massachusetts Institute of Technology

February, 2002

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Microchemical systems are sub-milliliter systems for chemical processes. They are constructed using microfabrication techniques originally developed for the fabrication of microelectronic circuits. The reduction in size, as compared to conventional systems, offers several advantages in improvement of heat and mass transfer and control of flow fields. In addition, microchemical systems are smaller, therefore inherently safer and capable of shorter thermal response times.

The focus of this work has been a microchemical system with a multi-inlet contactor for liquid-liquid processes. The systems are fabricated using, primarily, silicon and glass in which feature sizes range from approximately 10 to 500 μm. The multi-inlet contactor consists of 10 alternating inlets for two components. Fluids continuously enter the contactor, are focused by a converging channel, mix and react in a 50 μm channel. The contactor is the central element in the microchemical system that also includes a parallel plate heat exchanger, infrared transmission detection capabilities and thin film metal temperature sensors. Quantitative data are obtained using on-chip optical detection methods, integrated thin film sensors, and off-chip pressure sensors.

For microchemical systems, the length scales are short. Consequently, Reynolds numbers are small and the flow is laminar. When two or more streams are contacted in a homogeneous system, the flow is stable. The short length scales of the resulting lamellar stream enable rapid diffusion mixing for applications, such as kinetics studies or reaction-rate-limited operation of fast reactions. The mixing characteristics in the multi-inlet contactor are investigated through experiments and simulations. Without optimization, sub-second mixing times are achieved. By using experiments and simulations to gain a better understanding of diffusion mixing in the system, 99% mixing is achieved in less than 25 ms. Characterization of the microchemical system also includes determining the overall heat transfer coefficient for the parallel plate heat exchanger and demonstrating on-chip infrared transmission detection from 4000-1000 cm⁻¹. Thus, these devices combine all the features necessary for kinetic studies, specifically control of residence time, control and monitoring of temperature, and concentration measurement by infrared spectroscopy.

As a demonstration of microchemical systems as tools for kinetics studies, the microchemical mixer was used with in situ Fourier Transform infrared spectroscopy to monitor the alkaline hydrolysis of methyl formate. This reaction follows second order kinetics and is fast with a half life of 70 ms for the conditions used in this study. The rate constant that was extracted was in good agreement with the literature value. Moreover,
in contrast to a previous study, no sample post processing was needed and the half-life of the reaction was reduced by an order of magnitude.

Microchemical systems can also be useful tools in achieving and understanding heterogeneous fluid contacting. When an aqueous phase and organic phase are contacted in a 1:1 volumetric ratio, flow segregation can occur. For the segregated flow profile, the droplet size exhibits an inverse dependence on flow rate so that at higher flow rates, smaller droplets are formed. Using the multi-inlet configuration, contacting an aqueous phase and an immiscible organic phase in a 10:1 volumetric ratio forms dispersions. Reaction of a dispersion of isocyanate droplets in water with amine produces poly-urea encapsulated droplets. The resulting capsules exhibit lognormal size distributions with average capsule sizes ranging from 6.5 μm to 22.9 μm based on processing conditions. It is further demonstrated that the technique can be used to encapsulate quantum dots with a bright, homogeneous emission of green light. Based on results from quantum dots studies, this encapsulation procedure shows promise for other materials such as titanium dioxide as well as biological systems.

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Acknowledgements

The following are gratefully acknowledged for their contributions to this work: Professors Klavs Jensen and Martin Schmidt for supervising this thesis; the Jensen and Schmidt groups for all the little things; my thesis committee for its input; Joan Chisholm for taking care of the Jensen group; Dr. Rebecca Jackman and Dr. Aleks Franz for general consultation and guidance; David Quiram for helping me to get started in the field of microreactors; Dr. Ravi Srinivasan and Dr. I-Ming Hsing for their input during the early stages of the project; Dr. Samara Firebaugh for getting me started with the mixer fabrication; Dr. Matthew Losey for his contributions to the mixing studies; Dr. Kathleen Vaeth for her assistance with early IR work; Jinwook Lee, for an enjoyable collaboration on the microencapsulation work; Dr. Jean Condon for our collaborations on crystallization which motivated me to fabricate the co-axial contactor; David Fox for photographs; Jeremy Chou, my UROP who assisted with pressure drop measurements; Amy Chou, my UROP who cheerfully and diligently assisted with the study of contacting immiscible fluids; Hang Lu for volunteering to read portions of this thesis; and Andrea Zanzotto for her support during the later stages of this work. Every contribution to this work is appreciated.
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Chapter One

1 Introduction and Motivation

The chemical process industry (CPI) is one of the largest and most dynamic sectors of the US economy. It spans areas including industrial chemicals, plastics, drugs, cleaners, paints, allied products, and agricultural products [1]. The CPI actively responds to internal innovations. Consequently, there are numerous examples of previously important chemical techniques and processes within the CPI that were displaced by emerging technologies. Microchemical systems represent one of the emerging technologies in the CPI that can revolutionize research and development as well as the way that commercial chemicals are produced [2-3].

1.1 Advantages of Microchemical Systems

Microsystems have advantages over macro-scale systems. They are smaller and inherently safer. They require less space and can have both shorter response times and more efficiently use energy because of their small mass. The sizes of microchemical systems are not small enough for direct interaction with the molecules that are processed and the mean free path of molecules is short compared to the channel dimensions. Consequently, the chemistries don’t change and continuum equations apply. However, the reduction in size alone offers several advantages related to improvement of heat and mass transfer and control of flow fields [3]. For example, decreasing the linear dimensions of a system can increase the respective gradients for parameters such as temperature, concentration, density, or pressure. Consequently, heat transfer and mass transfer can increase with microreactors. Other advantages include larger surface-to-volume ratios and potentially improved selectivities due to shorter residence times.

1.2 Microchemical Systems as an Alternative to Batch Vessels

Microchemical systems are presumed to rival batch vessels. Batch vessels are used throughout the chemical industry for various small-scale operations, such as obtaining kinetic data, testing developmental processes, processing high value products, and for processes that are difficult to run continuously [4-5]. Whether used for chemical or
physical transformations, the batch vessel is charged with compounds, which are processed under controlled conditions [6]. For example, the batch vessel may be placed on a hot plate or in a thermostatted bath for isothermal operation [5], and the vessel contents are stirred to maintain a uniform concentration during the reaction [6].

Clearly, small-scale operations are important for chemical applications, but conventional systems such as batch vessels have limitations. For example, it is difficult to find a suitable method of analyzing the composition of the reactor versus time [5]. Also, confirming and maintaining thermal and concentration uniformity is an issue. Therefore, engineering further miniaturization of chemical systems while eliminating the limitations exhibited by conventional systems (such as batch vessels) can improve, enable and potentially revolutionize chemical systems [2,7-8]. These are systems that require precious materials, research and development systems, and in some cases production systems. The area of biological applications has benefited from microfluidics. This work addresses chemical applications, specifically liquid-liquid applications such as kinetics studies and materials processing.

1.3 Miniaturization for Liquid-Liquid Applications

One of the early examples of miniaturization for liquid systems was by Ramshaw for process intensification [9]. Ramshaw defined process intensification as “the increasing of processing rate in a given volume of chemical plant by at least one order of magnitude” and as “a philosophy of plant design and construction whereby a given performance is achieved in very much smaller equipment—typically with a volume reduction of two or three orders of magnitude [10].”

Consistent with the definition of process intensification, Ramshaw developed the Higee rotating mass transfer unit, which separates fluids at a rate 500 times higher than a standard distillation column by operating at high g generated by rotation—hence the name “Higee.” In addition to better performance, the low volume in the system suggests that process equilibrium should be rapidly established. Also, the reduced size of the vessel as compared to distillation columns corresponds to a reduction in the cost of the materials of construction, and the inventory of hazardous process fluids can be reduced. Ramshaw outlined a number of ideas for process intensification including, but not limited
to, the following: heat transfer without phase change using a microstructure, rapid reactions and crystallizations, and continuous processing of fine chemicals [11].

Ehrfeld and colleagues, proponents of microsystems especially for chemical applications, reported the development of tools for fabricating microstructures [12-14]. The primary tool was the x-ray synchrotron for realizing high aspect ratio polymer molds, which were subsequently used to produce microstructures by electroforming, the so-called LIGA (Lithogaphie, Galvaniformung, Abformung) process. Injection molding would be done with this metal part. Ehrfeld suggested a plethora of applications for high aspect ratio microstructures such as sensors, integrated optical devices, electronic packaging, ink jet printers, micro-channel plates, catalyst carriers, and nozzles for uranium enrichment—the original application that the group targeted.

Manz and Harrison, initially motivated by chemical applications, were advocates of microdevices for biological applications [15-21]. They looked at both chromatography systems and capillary electrophoresis. The team also coined the term μTAS or Miniaturized Total Analysis Systems [17], which is still used today. Manz proposed that “[If a system] performs all sample handling steps extremely close to the place of measurement, [it should] be called a ‘Miniaturized Total Chemical Analysis System.’” Bergveld [22-26] and Ramsey [27] were also notable pioneers in the field of biological liquid phase microsystems. The area of biological applications has subsequently exploded with activity.

More recently, Ehrfeld suggested several applications, fabrication concepts and components for microchemical systems [28]. Potential applications identified include phase transfer catalysis, parameter testing of bio probes, and on demand production of chemicals. Fabrication methods discussed included the LIGA technique, laser LIGA and structuring of photosensitive glass. A mixer, reaction channels, and a micro optical cuvette were among key microreactor components identified.

1.4 Materials of Construction for Liquid Microchemical Systems

There are a number of materials available for microfabrication of liquid-liquid microchemical systems including, but not limited to, the following: metals, ceramics, polymers, glass and silicon [29]. The materials of fabrication for chemical processes are
typically chosen based on several considerations such as chemical compatibility with fluids used in the system, thermal properties and optical properties. The systems described in this work are fabricated in silicon for the following reasons: silicon is chemically inert for many substances and can be oxidized to form a glass-lined reactor as needed; silicon has a high thermal conductivity for ease of thermal management; silicon is infrared transparent for infrared detection; silicon is amenable to circuit integration; and the infrastructure for silicon processing is available.

1.5 Microfabrication Techniques for Silicon Microfluidic Systems

Transporting fluids through small channels (<1 μm) would require very high pressures and good sealing techniques to prevent leaks at system interfaces. Thus, it was clear at the onset of work in microfluidics that length scales larger than those typically used for integrated circuit applications were required. A related, emerging field, microelectromechanical systems (MEMS), developed a set of fabrication techniques known as bulk micromachining [29-30]. Bulk micromachining produces larger length scales as compared to silicon processing techniques used for integrated circuits.

Bulk micromachining consists of both wet etches and dry etches. When choosing an appropriate etch method, at least three issues are of concern for fabricating systems for liquid-liquid microfluidic applications: etch speed, ability to fabricate complex geometries, and the ability to fabricate vertical sidewalls so that 2-D designs can be extruded through a wafer’s depth.

Deep reactive ion etching (DRIE) was developed for the purpose of fabricating deep channels with vertical sidewalls. The technique uses a high density (inductively coupled) plasma source. It consists of a series of alternating SF₆ etches and C₄F₈ polymer depositions to passivate sidewall etching to create vertical sidewalls. The primary disadvantage of the technique is that it requires specialized equipment. DRIE was the fabrication method of choice for the silicon liquid-liquid microchemical systems discussed throughout this work because of the large aspect ratio channels enabled by this technique [31-32].
1.6 Potential of a Silicon Liquid-Liquid DRIE Microchemical System

Silicon liquid-liquid DRIE microchemical systems have the potential to enhance and enable a number of areas, two of which will be discussed: kinetics studies and materials processing. Rapid diffusion mixing can be achieved in these systems due to the small characteristic lengths \( t_{\text{mix}} \sim L^2/D \). Thermal management and fast response times are realized because of the high thermal conductivity of Si, the integration of thin film temperature sensors, the small mass of the systems and the incorporation of various thermally insulating layers where appropriate. Integration of optical detection ranging from UV-IR creates a completely integrated system. Thus, these systems have the potential to mix rapidly, manage heat effectively, and provide real-time feedback for any chemical system. In comparison to batch vessels, these systems yield comparable results with lower power requirements, reduction in sample volume, improved thermal uniformity and no sample post-processing.

1.7 Thesis Outline

Chapter Two focuses on a multi-layer mixer, the central element in the microchemical system that was developed. The mixer consists of 10 inlet channels designed for alternating streams of two components. Experiments and Computational Fluid Dynamics (CFD) simulations predicted the mixing behavior. In addition, insight about the theoretical limits of the design was gained.

Chapter Three describes the monolithic integration of the mixer with thermal control and chemical analysis capabilities. The mixer was initially expanded to include a parallel plate heat exchanger and thin film, silicon temperature sensors. This design was demonstrated. On-chip infrared, transmission detection was explored. Materials issues and fabrication issues were revealed and resolved using a simple T contactor design. The final system design includes the mixer, a parallel plate heat exchanger, an area for infrared detection probing, as well as platinum temperature sensors.

Demonstration of the fully integrated design for the kinetics studies of a rapid, homogeneous liquid-liquid reaction is presented in Chapter 4. For this application, the alkaline hydrolysis of methyl formate was considered. This is a homogeneous application whereas Chapter 5 describes a heterogeneous contacting application, the
encapsulation of quantum dots. Conclusions and recommendations for future work in the field of liquid-liquid microchemical systems are presented in Chapter 6.
Chapter Two

2 Deep Reactive Ion Etched Mixer

Significant advances in characterization and understanding of microfluidic systems are required for the technology to gain widespread utility. One such area for advancement is in the prediction of mixing in these systems. Studying chemical reactions without confounding effects of mixing time scales requires that mixing be fast relative to the chemical reaction. Turbulent jets, mechanical stirrers and inline static mixers have been used to achieve rapid mixing. These methods rely on quickly reducing large characteristic lengths so that molecular diffusion mixing can occur on a shorter time scale. Moreover, these methods are energy intensive and may require turbulence, which is difficult to achieve in microsystems [33]. Alternatively, the small features that can be fabricated in microsystems can be used to realize rapid mixing via micronozzle injectors [34] or channels that intersect to produce a lamellar or multi-layer configuration [28,35-46]. The mixer described in this work uses intersecting channels, which produce a lamellar configuration, to achieve rapid mixing. A converging channel focuses the layers to further reduce the characteristic mixing lengths.

The method of rapid mixing by diffusion in microfabricated systems is widely accepted. Nevertheless, very little work has been done to investigate and demonstrate the effects of operating conditions on the extent of mixing (EOM) that can be achieved. Previous studies have often used stagnant layer diffusion to obtain an approximate mixing time \( (L^2/D) \). However, for multi-layer continuous flow mixing, the mixing problem is complicated by the presence of several mixing pairs and three-dimensional spatial gradients. Based on simulations, Branjeberg recognized that outer layer widths should be approximately \( 1/2 \) the inner layer width for optimal mixing in a five-channel or four-pair mixer [35]. Ismagilov recently reported a scaling law based on edge effects for a "T" contactor [47].

The present work uses a specific case to develop a general approach to predicting and improving the EOM in microfluidic systems. Experiments reveal the mixing times that can be achieved for a ten-layer lamination in a channel converging to a 50 \( \mu \text{m} \) width.
Two-dimensional (2D) and three-dimensional (3D) computational fluid dynamics (CFD) simulations predict the velocity and concentration profiles in the mixer. Both the mixing sensitivity to the outer channel width and dispersion effects, caused by the 3D velocity profile, are investigated along with edge and focusing phenomena. The value of analytical solutions for predicting the velocity, concentration profiles, and power requirements in terms of pressure drop within the multi-layer mixer is also evaluated.

2.1 Experimental Study

2.1.1 Mixer Design

Figure 2.1-1 shows a schematic of the multi-layer mixer. The materials of construction are silicon and glass. Microfabrication permits the formation of structures with high dimensional tolerances, typically better than 1 μm. The fluids move through the channels defined in silicon, and glass caps the mixer. The channels are an extrusion of the 2D schematics shown. Either an additional silicon layer with holes etched or a drilled glass wafer provides fluid access to the channels.

During operation, two components enter alternating inlet channels and contact at the intersection of the inlet channels. After contact, the converging channel focuses the streams to reduce the diffusion mixing length. The mixing/reaction channel was chosen to be 50 μm at the narrowest location. In principle, narrower channels could be fabricated at the expense of very large pressure drops (see below). The silicon wafer thickness, approximately 400 μm, determined the channel depth. An approximate operating flow rate of 1 ml/min was anticipated, and previous work suggested an approximate, suitable die size [48]. The selection of the number of inlet channels (10) was based on the maximum feasible within space constraints on each die and can be varied according to the application. The inlet channel widths, which were 40-50 μm at the intersections points, were consistent with the mixing/reaction channel dimension. The channel widths at the intersection varied from 40-50 μm to control the mass flow rates and eliminate distribution effects originating from the manifold. Component 1 inlet channels started at 120 μm and tapered to 40-50 μm to equalize the pressure drop with component 2 inlets. The constraint that the residence time should be greater than or equal to the mixing time for the lamellar configuration determined the minimum
mixing/reaction channel length. Alignment tolerances for connections to the two external component reservoirs established the lengths of the inlet channels.

Figure 2.1-1: Top View (x-y) of the Mixer: (a) The mixer consists of two sets of inlet ports—one for each component—and a common outlet. After the solutions contact, they are focused by the converging channel to reduce the characteristic mixing length. The solutions mix and react in the long, narrow channel. The mixer is capped by glass. (b) Close-up of the focusing region (c) Cross section of the outlet port illustrating the inlet port/channel interface.

2.1.2 Mixer Fabrication

Figure 2.1-2 illustrates the fabrication sequences for the two methods used to fabricate the mixers: 1) silicon-on-insulator (SOI) substrate, and 2) silicon substrate. For method 1 (Figure 2.1-2(a)), the fabrication begins with an SOI wafer with a one micron thick silicon dioxide layer “sandwiched” between two (360 μm and 40μm thick) silicon layers. The sandwiched oxide serves as an etch stop to achieve uniform channel depths.
The pattern from Mask 1 is transferred to the thin-film silicon (40 μm), using photolithography to define inlet ports and shutters for optical transmission probing. Deep Reactive Ion Etching (DRIE) transfers the pattern to the silicon (Figure 2.1-2(b)). Wet etching of silicon dioxide, using a buffered silicon dioxide etch comprised of hydrofluoric acid and ammonium fluoride buffer, opens the inlet ports for the mixer. Figure 2.1-2(c) shows the structure after photolithography and DRIE transfer of the channel pattern from Mask 2 to the backside of the wafer. Finally, anodic bonding fuses the capping glass layer to the silicon layer (Figure 2.1-2(d)), and dicing the wafer releases individual mixers. Each 4" diameter silicon wafer can produce 8 mixers (2.9 cm x 2.2 cm). Alternatively, channels can be defined in a silicon wafer using Mask 2 (Figure 2.1-2(f)). Holes drilled in Pyrex wafer allow fluid access and a blank Pyrex wafer caps the mixer, as illustrated in Method 2. Mixers produced by method 1 allow integration of temperature sensors in the thin silicon layer. This added functionality is useful in monitoring chemical reactions. However, both types of mixers display the same fluidic characteristics, and no distinction is made between the two in the following results sections.

2.1.3 Test Station

The test station for the mixer (Figure 2.1-3(a)) consists of a syringe pump, pressure sensors upstream of the feed manifold, a poly-methyl-methacrylate (PMMA) feed manifold, a poly-dimethyl siloxane (PDMS) gasket, a charge coupled device (CCD) camera, a long working distance lens, tubing, a light source, light fibers, and a spectrometer.

A syringe pump delivers reagents to the mixer at a controlled rate. Poly-ether-ether-ketone (PEEK) tubing connects the syringes to the pressure sensors and the pressure sensors to the fluid manifold. Compressive force applied to the gasket with holes defined for fluidic access seals the mixer to the feed manifold. A CCD camera with a long-working distance lens facilitates visual observation of the mixer. Either a tungsten halogen light source or a deuterium light source provides light in the visible range for an absorbance measurement to determine the extent of mixing (EOM). A light fiber guides the light to the fluid manifold, where it passes through the optically transparent manifold.
and PDMS gasket to reach the reaction channel. A second optical fiber collects the light and guides it to the spectrometer.

Figure 2.1-2: Mixer Fabrication (A radial cross section (x-z), AA’, of the contacting region of 1 of 8 dice/per wafer is illustrated): (a) SOI wafer starting wafer (b) Inlet ports and optical shutters were defined using photolithography and the pattern (Mask 1) was transferred to silicon using DRIE. (c) Channels are defined (Mask 2) similarly on the backside of the wafer. (d) Anodically bonding to pyrex caps the mixer and completes fabrication. (e)-(g) Alternatively, etching through a silicon wafer defines the channels (Mask 2). A blank Pyrex wafer caps the mixer, and a drilled Pyrex wafer provides fluid access.
Alternatively, bonding tubing directly to each inlet and outlet allows individual access to the channels and thus, operation without a fluid manifold. For this type of arrangement, (shown in Figure 2.1-3(b)), the mixer, rather than the chuck, functions as the optical fiber mount.

2.1.4 Methods

Changing the total flow rates, rather than measuring the absorbance at different points in the channel varied the residence time. This test method allowed the measurement point to be fixed. The flow rates for this work ranged from 4.0 ml/min to 0.001 ml/min, corresponding to residence times of 3.18 ms and 12,700 ms, respectively. Absorbance measurements were collected 8 mm down the 13 mm mixing/reaction channel. For every measurement, the spectrometer collected at least 30 data points at steady state for integration times of 1-2 s. The data points for each residence time were averaged. Error bars reported in the following sections correspond to ± 2σ where σ is the standard deviation. The measured extents of mixing (EOM’s) for the experimental conditions were greater than 80%. To observe lower EOM’s (8 mm down the mixing/reaction channel), larger back pressures than feasible with the experimental set-up would need to be generated. Alternatively, the probe point could be moved upstream.

2.1.5 Extent of Mixing Definition

The acid-base reaction of two phosphate buffer solutions is one method for determining the EOM [49]. Each buffer solution has a 1 mM concentration of phenol red, a color indicator. Solution 1 (S1) has a pH of 6.4 and is yellow. Solution 2 (S2) has a pH of 8.0 and is red. Figure 2.1-4 shows an experimentally determined plot of the absorbance vs. pH for premixed solutions of S1 and S2 at 560 nm, the maximum absorbance for the indicator. The plot is generated by measuring the fully-mixed absorbance of volumetric ratios of the two solutions ranging from 0 to 1. These calibration solutions are prepared by mixing the two solutions externally and delivering them to the mixer pre-mixed. The straight line joining the ends of the pH calibration curve represents the absorbance obtained based on the average of the absorbances of the two solutions side-by-side at various ratios without mixing. The largest mixing window, and therefore, the highest sensitivity is obtained for the 50:50 ratio. Consequently, it forms the basis for this study. The maximum and minimum experimental absorbances for
the 50:50 ratio from the calibration curve are 0.81 and 0.33, respectively, expressed in arbitrary units (AU).

![Diagram with labels: Camera, Light Source, Syringe Pump, Pressure Sensors, microreactor, gasket, Disposal, Spectrometer.]

Figure 2.1-3: Test Station: (a) Side view of the test station consisting of a syringe pump, in-line pressure sensors, a CCD camera with a long working distance lens, optical fibers, a PMMA fluid manifold, a gasket for sealing to the fluid manifold, a light source and a spectrometer (b) Micromixer with integrated SMA optical fibers connected and direct feed/exit lines.
If the absorbance measured during an experiment is 0.33 AU, equal to the absorbance of the premixed solution, the solutions are 100% mixed. Similarly, if the absorbance is 0.81 AU, indicated on the linear portion of the calibration curve in Figure 2.1-4, the solutions are completely separated, i.e. not mixed. Linear interpolation was used to determine intermediate EOM values.

2.2 Simulation of Fluid Mixing

The small dimensions of microfluidic systems imply that the Reynolds numbers are low (<200) and flows are laminar. The equations of conservation of mass, momentum and species for the homogeneous mixing system then take the standard form where \( \vec{v} \) = velocity, \( t \) = time, \( \rho \) = density, \( \mu \) = viscosity, \( p \) = pressure, \( g \) = gravitational force constant, \( D \) = scalar species diffusivity, and \( C \) = concentration:

\[
\nabla \cdot \vec{v} = 0 \quad (2.2-1)
\]

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

\[
D \nabla^2 C + \vec{v} \cdot \nabla C = 0 \quad (2.2-3)
\]

These equations were solved for 2D and 3D mixer geometries by using the finite volume method [50] as implemented in the CFD-ACE\textsuperscript{TM} software (CFDRC Corp., Huntsville, AL). The model is restricted to diffusion mixing and does not consider a reaction. \( 3 \times 10^5 \) volume elements were used in the solutions of the 3D Navier Stokes equations (Equations 2.2-1-2.2-2). The resulting velocity field was subsequently used in predicting the species concentrations (Equation (2.2-3)).

An upwind differencing scheme for the continuity and momentum equations and a second order differencing scheme for the species equation were chosen. The conjugate gradient solver (CGS) solved the continuity, momentum and species equations, whereas an Algebraic Multi-Grid (AMG) solver determined the pressure correction. The solver imposed a constant plug-flow velocity profile and constant concentration boundary conditions at the inlet of each of the ten channels. Since the inlet channels are \( \geq 500 \mu m \)
in length and long compared to the channel widths (40-50 μm), the velocity profile developed fully prior to contacting, which reproduced experimental conditions.

Because of the large aspect ratio, the size of the grid in the z-direction (the depth of the channel) was an issue in going from 2-D (x-y) to fully 3-D grids. A grid dependence study minimized computational error and showed convergence for 8 nodes or more in the z-direction.

2.3 Results and Discussion

Figure 2.3-1(a) shows the contacting and hydrodynamic focusing of 10 streams of alternating acid solution (yellow) (S1) and base solution (orange) (S2) captured during a visualization experiment. Under the influence of laminar flow (Re approximately 10), the fluid streams laminate and the converging channel focuses them. The clarity of the visualization suggests that there are not any abnormalities disturbing the flow. Furthermore, the visual confirmation of the behavior supports the assumed lamellar configuration for the mixing determination.

Figure 2.3-1(b) shows a color-coded prediction of the mixing, where the light and dark fluids in the inlet channels correspond to the inlet conditions, and the intermediate shades indicate the extent of mixing. The simulation confirms the experimental observations that the fluids are lamellar, and back diffusion in the contacting region is minimal. The Peclet number for mass transfer at the outlet of the feed channels ranges from approximately 50 to 10⁵ for the range of flow speeds tested, so negligible back diffusion would be expected.

2.3.1 Velocity Profiles

Figure 2.3-2(a) shows predicted velocity contours for a top view, center slice of the micromixer. For plane poiseuille flow, which applies to the micromixer, a parabolic velocity profile results. For a flow rate of 1.0 ml/min, the maximum velocity is approximately 1.4 m/s.

Assuming that the channel is deep enough so that only the nearest channel edge influences the flow, the normalized velocity, \( \Theta \), may be expressed as Equation 2.3-1 [51] where \( \Theta = \text{dimensionless velocity} \), Z=dimensionless z axis position, X=dimensionless x axis position, \( \lambda = \text{eigenvalue} \).
Figure 2.3-1: Experimental and CFD Flow Visualizations: (a) Phenol red solutions at pH = 6.4 (yellow) and pH = 8.0 (red-orange) are contacted. (b) Predictions of concentration, color-coded for consistency with experimental data.

\[ \Theta(X, Z) = \frac{3}{2} (1 - X^2) - 6 \sum_{n=0}^{\infty} \frac{(-1)^n}{\lambda_n^3} e^{-\lambda_n Z} \cos \lambda_n X \]  
(2.3-1)

According to this equation, the velocity field depends on \( Z \) for about two channel widths. The channel depth is 360 \( \mu m \) and the channel width is 50 \( \mu m \). Thus, edge effects are expected to be significant for approximately \( \frac{1}{2} \) of the channel depth. Figure 2.3-2(b) is a contour plot of the cross section of the channel for a total flow rate of 1 ml/min. The velocity profile is fully developed, and edge effects are significant over a \( \sim 90 \mu m \) region at both ends of the channel. This observation agrees well with the prediction based on Equation 2.3-1.

Figure 2.3-2(c) is a plot of the velocity as a function of the channel position for several channel depths. 175 \( \mu m \) corresponds to a cross section near the top (top is \( z = 180 \mu m \)) and bottom channel walls (z), and 0.0 microns corresponds to the center of the channel. The profiles are parabolic in all cases, but the maximum velocity varies from approximately 0.014 m/s to 0.002 m/s in the region where the edge effects are significant. Profiles from 0-100 \( \mu m \) superimpose confirming quantitatively that in that region the
velocity profile is essentially 2-D. As expected, the theoretical velocity profile for a 2-D structure lies between the maximum and minimum profiles from the 3-D predictions. The results show that for aspect ratios of 7:1 or greater, the 2-D analytical velocity approximation agrees well with the 2-D velocity profile that is characteristic of over 50% of the channel. The agreement improves as the aspect ratio increases.

2.3.2 Pressure Drop

Because of the small dimensions, pressure drops in micro-channels can become very large. Pfund et al. [52] determined the pressure drop over a wide range of channel dimensions where Reynolds numbers ranged from 60-3,450. The Reynolds numbers (0.05-200) for mixing/reaction channels, overall, are lower than those investigated by Pfund et al. [52]. Table 2.3-1 reports dimensions and calculated pressure drops for various segments of the micromixer. The mixing/reaction channel pressure drops are large compared to those for other segments. Figure 2.3-2(d) compares the experimental pressure drops over two micromixers with the theoretical pressure drop expressed by Equation 2.3-2 where \( \Delta P \) = pressure drop, \( Q \) = total flow rate, \( l \) = channel depth, \( h \) = channel width, \( \Delta y \) = length of the channel, \( \mu \) = fluid viscosity.

Pressure sensors upstream of the fluid manifold measured the experimental pressure drops. The theoretical curve in Figure 2.3-2(d) is based on Equation 2.3-2 for 2-D plane poiseuille flow in the mixing/reaction channel. The pressure drop over the fluid manifold and tubing was less than 1 kPa at the highest flow rate tested and was neglected. Figure 2.3-2(d) shows that the simple 2D calculation (Eqn. 2.3-2) accurately predicts the pressure drop over the mixer, especially at lower flow rates. The figure also shows data for two mixers, demonstrating the high degree of reproducibility expected from microfabrication.

\[
\Delta P = \frac{12Q\Delta y\mu}{lh^5} \tag{2.3-2}
\]

2.3.3 Extent of Mixing Determination

Figure 2.3-3(a) shows a semi-log plot of both the experimental and predicted EOM for various average residence times. The mixer achieves 90% mixing in under 10 ms, and 99% mixing by 25 ms. Hence, this mixer would be suitable for eliminating confounding mixing effects for determining reaction rates with half lives > 25 ms.
Figure 2.3-2: Velocity Profile Examination: (a) Top view of the center slice (x-y) of the velocity profile. The scale bar indicates the velocity in m/s. (b) Cross section (z-x) of the mixing/reaction channel after the velocity profile is fully developed. The contour plot shows the depth over which edge effects are significant. (c) 3D simulation comparison with theoretical, 2D velocity approximation for various values of z (d) Pressure drop over mixer modeled as plane poiseuille flow including only pressure drop over mixing/reacting channel compared to experimental result.
Table 2.3-1: Micromixer segment dimensions and pressure drops

<table>
<thead>
<tr>
<th>Channels</th>
<th>Length (mm)</th>
<th>Width (mm)</th>
<th>$\Delta P/Q \ (Pa\cdot s/m^3)\times 10^{11}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short inlets</td>
<td>1.0</td>
<td>0.05</td>
<td>2.7</td>
</tr>
<tr>
<td>Long inlets</td>
<td>6.5/0.5</td>
<td>0.120/0.05</td>
<td>~1.3/1.3</td>
</tr>
<tr>
<td>Focusing</td>
<td>1.5</td>
<td>0.400 to 0.05</td>
<td>0.9</td>
</tr>
<tr>
<td>Mixing/reaction</td>
<td>13.0</td>
<td>0.05</td>
<td>35</td>
</tr>
</tbody>
</table>

Figure 2.3-3(b) shows predicted concentration profiles for two flow rates, 4.0 ml/min and 1.0 ml/min. The profiles represent averages of concentrations at four channel depths from full 3-D simulations. As expected, after 3.18 ms of contact, mixing appears to occur much faster in the center than at the edges because of the high flow rate (4 ml/min). At 12.7 ms residence time (1 ml/min), the edge concentrations have shifted approximately 0.3 units, whereas the center has changed less than 0.1 unit. This results in a more uniform concentration distribution over the channel width. The concentration profile at 12.7 ms corresponds to an EOM of 98%. Nevertheless, variations in the profile can still be resolved in the simulations. This result suggests that CFD simulations could be useful for determining small differences in EOM for applications where high resolution is needed.

2.3.4 Parameters Influencing Extent of Mixing

2.3.4.1 Distribution Effects

In Figure 2.3-3, the flow rates in the outer two channels were $\frac{1}{2}$ the flow rate of the inner channels. This initial condition creates outer channel widths that are approximately $\frac{1}{2}$ the inner channel widths. Figure 2.3-4(a) shows a semi-log plot of the experimental and predicted EOM as a function of contact time for equal flow rates in all 10 channels or, equivalently, layers that are all the same width. The EOM is 95% in 25 ms, whereas by 127 ms, the EOM is only 97%. For comparison, from Figure 2.3-3(a), EOM is at 99% after only 25 ms. This difference in the EOM for a small variation in distribution indicates the critical importance of distribution effects for applications where EOM's of 95% or greater are desired.

Figure 2.3-4(b) shows profiles extracted from full 3-D CFD simulations. Similar to Figure 2.3-3(b), at 3.18 ms of contact, the concentration gradients are distinct. By 12.7
ms, the inner layer gradients are almost completely resolved, whereas the outer layers have shifted only approximately 0.05 concentration units. Even though the inner gradients are resolved, this profile corresponds to an EOM of only 92%.

Figure 2.3-5 is a plot of predictions of the EOM as a function of the distribution of fluid among the channels extracted from 2D models. The flow distribution is controlled by keeping the flow rates equal in the 8 inner and outer 2 channels. The ratio of the two flow rates is expressed as $m_1/m_2$, where $m_1$ is the flow rate in one of the inner 8 channels and $m_2$ is the flow rate in one of the outer 2 channels. The ratio, $m_1/m_2 = 0$, represents a "T" mixer. As $m_1/m_2 \rightarrow \infty$, the profile approaches an 8-channel mixer with 7 mixing pairs. The peaks in Figure 2.3-5 are very broad, indicating that mixing is fairly insensitive to $m_1/m_2$ ratios between 2 and 4. This is an important design consideration for diffusion mixing in microsystems. The results also demonstrate that the lamellar configuration dramatically enhances EOM. For $m_1/m_2=0$ ("T") at a flow rate of 0.25 ml/min, the EOM is only 20%, whereas for $m_1/m_2 \geq 1$, the EOM is at least 80%. The maximum EOM for a particular flow rate scales with the $m_1/m_2$ ratio (Table 2.3-2) — thinner layers are required in outer channels with increasing flow rates.

2.3.4.2 Dispersion Effects

Table 2.3-3 lists the predicted widths of the 9 mixing pairs from the mixer for an average residence time of 3.18 ms, with the profile averaged over the channel depth. The reciprocal of the standard deviation ($\sigma^{-1}$) is a measure of the EOM. For the continuous flow mixer, the laminated layers adjust widths as the velocity profile develops. The $m_1/m_2$ ratio equals 2 to assure proper scaling of the volumetric flow rates of the various layers, but the velocity is higher in the center so the layers are thinner in the center. The thinnest pair is 3.3 µm, and the widest 10.9 µm. The average residence time for the continuous flow is 3.18 ms, but the time is shorter for the inner layers and longer for the outer layers. The residence time and layer width, both a function of position due to the velocity profile, have opposite influences on mixing time. After 3.18 ms, the EOM (as measured by the $\sigma^{-1}$) is higher for intermediate pairs 3 and 7 versus the center and outer pairs. This observation suggests that the competing effects dominate in different regions for these conditions (50 µm channel, $v_{max} = 0.059$ m/s) and result in a higher EOM in
intermediate regions. Independent of the profile and the width of the layer, the average concentrations of the pairs would be expected to be 0.5. The outer pairs deviate the most, with average concentrations of 0.39 and 0.62, respectively.

Figure 2.3-3: Extent of Mixing (EOM) Analysis: (a) Experimental: EOM asymptotes before 100 ms (b) 3D Simulation of concentration across the channel (x-position) 8 mm downstream from mixing front
Table 2.3-2: Location of maximum EOM as a function of flow rates

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>m1/m2</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0</td>
<td>4</td>
</tr>
<tr>
<td>1.0</td>
<td>2.5</td>
</tr>
<tr>
<td>0.25</td>
<td>2</td>
</tr>
</tbody>
</table>

An idealized representation to approximate mixing times can be derived by modeling the flowing fluids as unsteady, stagnant layers of equal width. The governing equation for one stagnant mixing layer may be expressed as Equation 2.3-3 [53] where \( C \) = concentration, \( D \) = scalar species diffusivity, \( t \) = time, \( x \) = position along the channel width and \( C_{mix} \) = equilibrated concentration:

\[
\frac{\partial C(x,t)}{\partial t} = D \frac{\partial^2 C(x,t)}{\partial x^2}
\]  

(2.3-3)

which has the solution:

\[
C(x,t) = C_{mix} + C_0 \sum_{n=1,3,\ldots} \frac{2}{n\pi} \sin \left( \frac{n\pi}{2} \right) \cos \left( \frac{n\pi x}{h} \right) e^{-\left( \frac{n\pi}{h} \right)^2 D t}
\]  

(2.3-4)

The analytical solution (Equation 2.3-4) is based on the pair width, 5.6 \( \mu \)m, which would result if the velocity profile were flat instead of parabolic, given a channel width of 50 \( \mu \)m and 9 mixing pairs. The analytical results in Table 2.3-3 also correspond to a contact time of 3.18 ms. According to the analytical solution, the EOM is 99% after 11 ms, which could be considered a theoretical minimum time for mixing in this system. This result compares reasonably with the experimental and predicted values of 25 ms indicating that analytical approximations could provide first estimates of mixing in these types of mixers.
Figure 2.3-4: EOM - Distribution Effects: (a) Experimental: EOM from maldistribution experiment \((m_1/m_2 =1)\) that asymptotes after 250 ms (b) 3D Simulation of concentration across the channel (x-position) 8 mm downstream from mixing front.
Figure 2.3-5: 2D Simulations: $m_1/m_2$ ratios from 0 (“T” contactor) to 4 compared for various flow rates or average residence times. (Lines are added to guide the eye.)

Table 2.3-3: Mixing layer characteristics

<table>
<thead>
<tr>
<th>Pair #</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>ideal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length ($m \times 10^{-6}$)</td>
<td>10.9</td>
<td>5.8</td>
<td>3.3</td>
<td>3.4</td>
<td>3.3</td>
<td>3.4</td>
<td>3.3</td>
<td>5.8</td>
<td>10.8</td>
<td>5.6</td>
</tr>
<tr>
<td>$\langle$Normalized Concentration$\rangle$</td>
<td>0.39</td>
<td>0.55</td>
<td>0.50</td>
<td>0.42</td>
<td>0.51</td>
<td>0.57</td>
<td>0.50</td>
<td>0.45</td>
<td>0.62</td>
<td>0.5</td>
</tr>
<tr>
<td>$\sigma^{-1}$</td>
<td>6.6</td>
<td>13</td>
<td>30</td>
<td>13</td>
<td>8.3</td>
<td>13</td>
<td>29</td>
<td>13</td>
<td>6.7</td>
<td>5.8</td>
</tr>
</tbody>
</table>

In order to reduce the non-uniformities caused by the parabolic velocity profiles for high aspect ratio structures, the flow rate for each channel would need to be regulated independently, as compared to the inner 8 layer and outer 2 layer regulation presented. Alternatively, rather than relying on pressure-driven flow, electroosmotic pumping, which results in a plug flow profile, could be considered. These approaches may be necessary to achieve shorter and more uniform mixing times.
2.3.4.3 Converging Channel Effects

Figure 2.3-6(a) shows the center slice (z=0) of the top-view of the predicted concentration contours for one component in the micromixer. The inlet conditions are alternating solutions of two components. Figures 2.3-6(b)-2.3-7(a) show channel cross sections in the focusing region at a flow rate of 1.0 ml/min. The positions of the cross sections are indicated on Figure 2.3-6(a). The focusing region serves to reduce the mixing length scales from an average of approximately 44.0 μm to 5.6 μm while avoiding significant increases in pressure drop. The decrease in the mixing pair widths drawn to scale from Figure 2.3-6(b) to Figure 2.3-7(a), and the small contribution of the focusing region to pressure drop, validates the design feature. The slope of the channel walls in the focusing region is 8.5, which does not produce re-circulation or other potentially adverse mixing behavior. Since mixing starts upon contact, some degree of mixing takes place in the focusing regions, as indicated by Figures 2.3-6(b)-2.3-7(a). Figure 2.3-7(a) is at the boundary of the focusing region and the 50 μm channel, where some mixing has already occurred. Another interesting feature is the bell-shape of the contours near the top and bottom of the channel. This may be a result of the serial contacting that results from the radial inlet layers. The two innermost layers contact first because of their locations. Then the fluids in the adjacent channels enter the contacting region, and the flare appears. The addition of streams amplifies the flare. When the outermost layers enter the contacting region, the cycle ends.

2.3.4.4 Edge Effects

Figures 2.3-7(a)-(c) are cross-sections (x-z) of the channel at a flow rate of 1 ml/min. The cross sections correspond to the end of the focusing region, 4 mm downstream, and 8 mm downstream from the focusing region, respectively. These cross sections show the concentration profiles over the channel depth at different channel positions. In general, the EOM is higher near the top and bottom edges because of the longer residence times that result because of the no-slip condition. The exception is in the center (x) of the channel near the bottom and top edges. These conditions result in slower mixing as compared to center (z) regions where the residence time is shorter.
Figure 2.3-6: EOM – Focusing Effects (a) Top view (x-y), center slice (z = 0) of contacting region at 1ml/min from predictions (b) 3-D predictions upon contacting
Figure 2.3-7: EOM –Edge Effects (a)-(c) 3D, predicted pH concentrations (x-z) at different positions (0.0 mm, 4.0 mm and 8.0 mm from the focusing region boundary). High pH = 8.0, low pH=6.4

2.4 Conclusions

The mixing characteristics in a multi-layer liquid-liquid micromixer have been investigated through experiments and simulations. Without optimization, sub-second mixing times can be achieved. With adjustment of operational parameters, the mixer
achieves 99% mixing in less than 25 ms. The good agreement between experiments and simulations demonstrates that the CFD simulation tools could be used to design and optimize multi-layer mixers. Pressure drop in the microfabricated mixer follows predictions for plane Poiseuille flow. Also, the analytical approximation of 99% EOM after 11 ms is the same order of magnitude as the experimental and predicted value of 25 ms, which suggests that the analytical solution can be employed for order-of-magnitude estimations of mixing times for optimized mixers.

The parabolic velocity profile, which is prominent for high aspect ratio structures, causes mixing pairs to have various widths. The velocity edge effects, which are significant over two channel widths, also cause higher EOM at the top and bottom channel edges versus intermediate regions. The converging channel enables faster mixing times while not disturbing the flow field for the lamellar mixing layers. Based on the sub-second mixing times that have been achieved, this work demonstrates a mixer that is suitable for conducting sub-second reactions without contact limitations.
Chapter Three

3 Monolithic Integration of Microchemical System Components

There is considerable interest in monolithic integration – coupling several different components onto one chip [2,7,36,46,54-57]. Integration would facilitate the fabrication of more compact devices than can be achieved using a module-like approach for connecting micro components. Groups have investigated integrating various microfluidic components including channels, valves, pumps, flow sensors, thermal sensors, mixers, dosing systems and optical detectors [2,7,36,46,54-57].

This work describes the fabrication and demonstration of an integrated microchemical system that consists of a mixer, a parallel plate heat exchanger, as well as infrared detection and temperature sensing capabilities. The mixer was described in Chapter Two. A parallel plate heat exchanger and thin film temperature sensors were added to the mixer. Then, all-silicon T reactors were a study platform to identify and understand the issues associated with incorporating infrared (IR) detection into a more complex microreactor. Finally, a microchemical system consisting of a mixer, heat exchanger, temperature sensors, and IR detection capabilities was demonstrated.

3.1 Integration of Thermal Control Components

Mass and heat transfer are two important issues for chemical systems. The issue of mass transfer in homogeneous systems is addressed in Chapter Two. Heat transfer, which involves adding or removing heat often to maintain isothermal operation, is addressed in this chapter. Conventional ways of heating chemical systems include heat exchangers, which use a fluid to transfer energy; heating elements, which rely on heat conduction; or immersion, which is based on convection. To maintain flexibility to either heat or cool, a heat exchanger was chosen over resistive heating previously used for microchemical systems [48].

Not only is it important to control heat transfer, but also it is critical to monitor heat transfer. This is typically accomplished using some kind of temperature sensor, such as a
thermometer, a thermocouple or a thin film sensor. Microfabrication is well suited for thin film sensors so they were employed in this study.

3.1.1 Parallel Plate Heat Exchanger Integration

The first addition to the mixer was a micro-channel heat exchanger to control the temperature of the mixing and reacting fluids. The device is analogous to a double pipe heat exchanger, but it is based on flow through rectangular channels.

Early studies for using parallel plate heat exchangers focused on cooling silicon integrated circuits. For example, Tuckerman et al. investigated the problem of achieving forced convection liquid cooling of planar integrated circuits [58-59]. Their approach was to flow water through high aspect ratio channels directly below the circuits that they wanted to cool. They determined that the heat-transfer coefficient for the coolant limited cooling efficiency. For their design, they found that the substrate temperature rose a maximum of 71°C at a power density of 790 W/cm². Based on these results, they concluded that the heat sink should have applications for ultra high speed Very Large Scale Integrated (VLSI) circuits.

Bier et al. developed a mechanical method for fabricating microstructures [60-61]. The technique is based on shaping foils with precision cutting tools. They subsequently applied their technique to build small, micro heat exchangers made of stainless steel, aluminum alloys, titanium and copper. They achieved volumetric heat transfer coefficients greater than 300 MW/m³K for water-to-water cooling [60]. They also conducted gas phase studies with helium, nitrogen and argon as heat transfer fluids for stainless steel and copper finned heat exchangers. For the stainless steel heat exchanger, they achieved overall heat transfer coefficients as high as 1700 W/m²K [61]. They recognized that heat conduction in the longitudinal direction limited the overall heat transfer coefficient.

Weisberg et al. used microfabrication techniques to fabricate large numbers of compact, high precision microchannels in silicon [62]. They experimentally determined that these types of systems are highly efficient heat exchangers. In addition to their experimental study, they presented a theoretical investigation of heat transfer for their systems.
Gaviilidis et al. recognized that dual catalytic microreactors have the potential to operate isothermally [63]. They conducted a theoretical study of the case for which heat transfer is controlled by balancing simultaneous endothermic and exothermic reactions. The two reactions would occur in alternating channels coated with a catalyst where heat is transferred between the wall that separates the two reaction zones. Calculations with various channel sizes indicated that optimal values exist for efficient reactor operation.

Drost et al. investigated the performance of an integrated microchannel combustor/evaporator [55]. Separate experiments were conducted to develop the combustor and evaporator portions of the device. The preliminary, experimental results in addition to simulation studies were used to design, construct and test an integrated combustor/evaporator system. Results showed that the combustor/evaporator achieved heat fluxes up to 30 W/cm² with good efficiency.

Alepee et al. developed a cooler to couple to a gas-phase, silicon nitride-capped membrane reactor [64]. The cooler operates as either a co or counter-current flow heat exchanger machined in silicon by deep reactive ion etching. The experimental overall heat transfer coefficients were lower than expected because of longitudinal heat conduction.

Ravigururajan et. al studied single-phase flow characteristics of Refrigerant 124 in a parallel plate microchannel heat exchanger [65]. Reynolds numbers ranged from 220 to 1250 and heat fluxes ranged from 30 to 90 kW/m². Data showed an increase in the heat transfer coefficient by factors ranging from 2 to 8 when compared to predictions. Similarly, the corresponding pressure drop increased by factors ranging from 7 to 18 when compared to predictions. The authors indicated that the trend of increasing heat transfer with increasing pressure drop is well established. The increased deviation from predictions is for higher flow rates. The prediction is based on laminar flow so the deviation could be a result of the onset of turbulence.

3.1.1.1 Parallel Plate Heat Exchanger Design

The goal for this heat exchanger design is to maximize the overall heat transfer coefficient (U) expressed in Equation 3.1-1.
\[ U = \frac{1}{\frac{1}{h_1} + \frac{\Delta x}{k_w} + \frac{1}{h_2}} \]  
(3.1-1)

\( U \) is a function of the heat transfer coefficients of the fluids \((h_1,h_2)\), the thermal conductivity of the heat exchanger wall \((k_w)\) and the wall thickness \((\Delta x)\) [66]. As expressed in Equation 3.1-2, \( U \) is inversely proportional to the sum of \( \chi \) and \( \Delta x \) where

\[ \chi = k_w \left( \frac{h_2 + h_1}{h_2 h} \right) \]

\[ U \propto \frac{1}{\chi + \Delta x} \]  
(3.1-2)

The design parameters for the parallel plate heat exchanger are the wall thickness and the fluid channel width. Because \( \chi \) is \(-0.005\) m, the heat exchanger wall would need to be 500 \( \mu \)m before they began to contribute to \( U \). Thus, based on \( U \), the wall thickness is not critical. The limiting factor is the longitudinal conduction, heat loss along the length of the heat exchanger. The longitudinal conduction parameter is expressed in Equation 3.1-3 where \( L = \) length of heat exchanger, \( c_p = \) heat capacity, \( m = \) mass flow rate, and \( A_e = \) conduction area = \( \Delta x \cdot \) depth of the channel.

\[ \lambda = \frac{k_w A_e}{L m c_p} \]  
(3.1-3)

For a thicker wall, the longitudinal conduction parameter becomes increasingly important. Based on these considerations, a 50 \( \mu \)m wall thickness was chosen.

The second issue is the width for the heat exchanger channels. The heat transfer coefficient for the fluid is inversely proportional to the channel width as expressed in Equation 1.1-4 where \( Nu = \) Nusselt number and \( d = \) the channel width [66].

\[ h = \frac{Nu \cdot k_w}{d} \]  
(3.1-4)

Therefore, to increase \( h \) (the only design parameter that significantly impacts the ideal value for \( U \)), the channel width should be small. The lower limit for the channel width is the pressure drop that results from a small channel as previously discussed (See
Chapter Two). The limit previously identified was 50 μm and was chosen as the width for the heat exchanger channels. Based on the design parameters, the estimated overall heat transfer coefficient, assuming negligible longitudinal heat conduction, is ~10^4 W/m²°C.

Figure 3.1-1 shows the mixer with the parallel plate heat exchanger added. Figures 3.1-1(a)-(b) show a top view and aerial view respectively. Figure 3.1-1(c) is a cross section of the reaction and heat exchanger channels. Two channels are located on either side of the reaction channel. An air gap channel was added for insulation of the cooling/heating channel to minimize adverse axial heat conduction. The heat exchanger can be operated in co- or counter-current mode.

Figure 3.1-1: Mixer with Integrated Parallel Plate Heat Exchanger: (a) close-up of the mixer and heat exchanger channels (b) aerial view of the chip (c) cross section of the channels
3.1.1.2 Parallel Plate Heat Exchanger Testing

Figure 3.1-2 shows the test station for the overall heat transfer coefficient determination. The chip shown in Figure 3.1-1(b) is sealed to a plexiglas fluid manifold using compressive force applied to a poly-dimethyl siloxane (PDMS) gasket. Thermocouples are inserted in four chip locations – the channel inlet ($T_{h1}$), the channel outlet ($T_{h2}$), and one heat exchanger inlet ($T_{c1}$), and outlet ($T_{c2}$), as illustrated in Figure 3.1-2. The thermocouples were interfaced with Labview® data acquisition software for continuous temperature monitoring. Water at 0.3 ml/min and room temperature (~20°C) flowed through the reaction channel inlet. Water at 1.5 ml/min and 0°C (~12.5°C upon entering the chip) flowed to each heat exchanger channel co-currently to the reaction mixture. Temperatures and standard deviations for the four monitoring points are listed in Table 3.1-1.

3.1.1.3 Heat Transfer Coefficient Determination

Based on experiments to determine $T_{c1}$, $T_{c2}$, $T_{h1}$ and $T_{h2}$, the overall heat transfer coefficient was calculated as 1420 ± 130 W/m²°C. $U$ is calculated based on Equation 3.1-5 where $A$ = heat transfer area, $q$ = energy transferred, and $\Delta T_{lm} = \log$ mean temperature difference over the heat exchanger. The log mean temperature is expressed in Equation 3.1-6 [66].

$$q = UA\Delta T_{lm} \quad (3.1-5)$$

$$\Delta T_{lm} = \frac{(T_{h2} - T_{c2}) - (T_{h1} - T_{c1})}{\ln \left( \frac{A}{(T_{h2} - T_{c2})^{2}} \right)} \quad (3.1-6)$$

For calculating $q$ to determine $U$, the heat removed from the hot fluid was calculated as expressed in Equation 3.1-7 where $c =$ heat capacity and $m =$ mass flow rate. This value was ~0.1 J as compared to ~0.7 J lost from the cooling fluid. The order of magnitude difference between the theoretical $U$, $10^4$ W/m²°C, and the experimental value, $1420 \pm 130$ W/m²°C, is attributed to longitudinal heat conduction, which was neglected in the theoretical case [67].

$$q = mc\Delta T \quad (3.1-7)$$
Figure 3.1-2: Test Station for Overall Heat Transfer Coefficient Determination
Table 3.1-1: Data for Overall Heat Transfer Coefficient Determination

<table>
<thead>
<tr>
<th>Run</th>
<th>$T_{c2}$ (C)</th>
<th>$\sigma_{c2}$</th>
<th>$T_{c1}$ (C)</th>
<th>$\sigma_{c1}$</th>
<th>$T_{h2}$ (C)</th>
<th>$\sigma_{h2}$</th>
<th>$T_{h1}$ (C)</th>
<th>$\sigma_{h1}$</th>
<th>$U$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.2</td>
<td>0.4</td>
<td>12.4</td>
<td>0.5</td>
<td>17.1</td>
<td>0.5</td>
<td>20.2</td>
<td>0.5</td>
<td>1512.3</td>
</tr>
<tr>
<td>2</td>
<td>14.8</td>
<td>0.7</td>
<td>13.0</td>
<td>0.8</td>
<td>17.4</td>
<td>0.5</td>
<td>20.0</td>
<td>0.6</td>
<td>1415.4</td>
</tr>
<tr>
<td>3</td>
<td>15.7</td>
<td>0.5</td>
<td>12.6</td>
<td>0.6</td>
<td>18.2</td>
<td>0.5</td>
<td>20.8</td>
<td>0.4</td>
<td>1330.1</td>
</tr>
<tr>
<td>4</td>
<td>15.0</td>
<td>0.4</td>
<td>11.6</td>
<td>0.4</td>
<td>17.6</td>
<td>0.4</td>
<td>20.7</td>
<td>0.5</td>
<td>1436.4</td>
</tr>
</tbody>
</table>

$U_{\text{avg}}$ 1423.6
$2\sigma$ 129.8

3.1.2 Thin Film Silicon Temperature Sensors

Small temperature sensors such as the thermocouple are compact and reliable. Nevertheless, micro thermal sensors are of interest because of the ease of fabrication and integration into existing microdevices as well as the capability to monitor temperatures over regions smaller than possible with thermocouples [68]. There are several physical phenomena that are exploited in microsensors to measure temperature. Temperature sensors may be based on diode effects, transistor characteristics, the Seebeck effect – the phenomena that a thermocouple exploits, as well as thermoresistivity [68].

Thermoresistivity, change in electrical resistance with temperature, is characteristic of many metals and doped single or polycrystalline silicon. For this technique, the local temperature of a region is determined by passing a constant current through the resistor, measuring the voltage, calculating the corresponding resistance and correlating that to the temperature. The relationship between normalized resistance and temperature is often linear. This technique is known as resistance thermometry [68].

Srinivasan et al. used resistance thermometry to measure the temperatures for the gas-phase, partial oxidation of ammonia in a membrane reactor [48]. The resistors were fabricating by depositing a 10 nm adhesion layer of titanium and a 100 nm layer of platinum onto a silicon nitride membrane, which capped silicon fluidic channels. The normalized resistance change of the platinum was linear with temperature. Alepee et al. also used platinum temperature sensors for gas-phase reactions in a silicon-nitride capped membrane reactor [64]. Resistance thermometry is used in this work for thermal sensing.
3.1.2.1 Temperature Sensor Design and Fabrication

The temperature sensors for the second generation device are fabricated in the silicon film of a silicon-on-insulator (SOI) wafer. An SOI wafer consists of three layers: bulk silicon (300-550 μm), thin silicon dioxide (~ 1μm) and thin film silicon (1-50 μm). This scheme is convenient because the channels can be etched in the bulk silicon and the sensors are fabricated in the thin film silicon directly beneath the reaction channels. The thin film silicon dioxide electrically insulates the sensors from the bulk silicon and the reacting fluids. There are two design parameters: $R_{\text{sens}}/R_{\text{lead}}$, the ratio of the sensor resistance to the lead resistance, and the base resistance of the resistor. The design constraints were as follows: the sensor length is the channel width, $R_{\text{sens}}/R_{\text{lead}} > 1$, and the chip size must remain the same (2.2 X 2.7 cm).

Given those constraints, the sensor is 10 μm wide, and the leads are effectively 2.5 mm long and 800 μm wide. The actual leads are 10 mm long, but the measurement is made over 2.5 mm. Figure 3.1-3(a) shows a picture of the chip without sensors and Figure 3.1-3(b) shows a schematic of the chip with sensors (not visible from the top of the chip).

The goal for the base resistance was 100 Ω. This necessitated a resistivity of ~0.002 Ω·cm [69]. To achieve this resistivity over the temperature sensing layer, the silicon is doped with phosphorus. Gaseous POCl₃ was the phosphorus source for a doping concentration ranging from $10^{21}$ at the surface to $10^{19}$ at the silicon/silicon dioxide interface. Then, the layer is annealed to smooth the concentration gradient that results from the non-equilibrium diffusion profile.

The sensor fabrication is added to the front end of the process so fabrication of the reaction and heat exchanger channels does not change with the addition of the thin film sensors. Fabrication begins by doping and annealing the blank silicon thin film layer. Then, the layer is patterned and etched to define sensors that are separated from the remaining thin film area by a 10 μm gap. Figure 3.1-3(c) is a photograph of a temperature sensor etched in a 2.2 μm thin film.
Figure 3.1-3: Silicon Temperature Sensor Design (a) picture of a chip without temperature sensors (b) schematic of a chip with temperature sensors (c) picture of a temperature sensor

3.1.2.2 Temperature Sensor Testing

Figure 3.1-4(a) shows the chip mounted for testing, and Figure 3.1-4(b) shows a top view of the teflon block for fluid manifolding. The manifold contains through holes so that contact pins can be inserted to make electrical contact to the chip. The contact pins may be connected to a multimeter or LabView® data acquisition software for the resistance and corresponding temperature measurement. Figure 3.1-4(c) shows the results of an experiment that confirmed the linear response behavior. The temperature coefficient of resistance (TCR), which is the slope of the line given by the normalized resistance versus temperature, is 0.0024/°C for silicon. The experimental value agrees well with the literature value as also shown in Figure 3.1-4(c).
Figure 3.1-4: Silicon Temperature Sensor Testing (a) chip mounted on testing block with electrical contact pins inserted (b) chip mount showing contact pin ports (c) normalized resistance curve for the thin film temperature sensors

3.1.3 Thermal Control Components Demonstration

The alkaline hydrolysis of neat propionyl chloride was performed using the mixer/heat exchanger/silicon temperature sensor system. For the study, only 2 of 3 temperature sensors were functional. Based on measurements with two sensors, a 40°C temperature rise over the channel was eliminated by flowing cooling water through the heat exchanger channels. Two issues emerged from the investigation: (1) the robustness of the fabrication scheme and (2) determination of the extent-of-reaction for chemistries investigated.
After the reaction and heat exchanger channels are etched in the substrate, free standing silicon dioxide or silicon dioxide/silicon membranes should remain. When the thin films are attached to the substrate, the intrinsic stress is not important. However, once the structures are released as membranes, the stress causes the membrane to buckle (shown in Figure 3.1-5) and break. This limitation necessitated the exploration of new fabrication schemes and temperature sensor designs. Prior to choosing a new thermal sensor design, the second issue, determination of the extent of reaction, was addressed.

Figure 3.1-5: Picture of the Buckled Edge of a Feature for the SOI Design

3.2 Investigation of On-Chip Infrared Transmission Detection

One major, technical challenge in the development of the liquid phase microchemical systems has been in the determination of the extent of reaction by separation, quench or detection in the microreactor. The driving factor for the determination is that, typically, the external, fluid chamber volume is much larger than the volume of the microreactor. Consequently, to avoid artifacts one of the following should occur: (1) the reaction reaches full conversion in the microreactor, (2) the reactants and products are separated in the microreactor, (3) the products are detected in the microreactor or (4) the reaction is quenched in the microreactor. Otherwise, the observed reactor volume will be that of the reactor-analytical system interface. Many gas phase reactors and multi-phase reactors employ high temperatures and/or a catalyst. Thus, the reactions are effectively quenched because the reactor effluent is not in the presence of heat and/or the catalyst. However, the liquid phase microchemical system employs homogenous catalysis, if any, and the
reactions occur spontaneously without the addition of heat. Thus, the development of integrated methods of determining the extent-of-reaction is important.

Infrared (IR) detection is a broadly applicable detection method that would prove enabling for monitoring reactions. Guber et al. used stainless steel sheets sandwiched between AgCl discs and fixed in an adapter system for gas phase applications [70]. Researchers investigating liquid reactions have capped microchannel structures with AgCl discs [71], used bare silicon as an IR window and included a spacer [72], or used off-chip IR detection for microchemical systems [73]. For this work, technologies recently developed for the micro-electromechanical systems (MEMS) and microfluidics communities were exploited: deep reactive ion-etching (DRIE) to define fluidic geometries [31] and fusion bonding of two silicon pieces to create hermetic seals for fixed-pathlength transmission cells [74] as illustrated in Figure 3.2-1.

The approach is to fabricate reactors by defining reaction geometries in silicon wafers. The channels are capped by fusion bonding to another silicon wafer. Silicon is IR transparent from ~8000 to 700 wavenumbers so the reactor may be used to detect the presence of reactants and/or products for reactions. This work represents the first known demonstration of using etched and fusion-bonded silicon for on-chip, IR liquid phase detection.

![Figure 3.2-1: Cross Section of a Channel Etched in a Silicon Wafer and Capped by a Blank Silicon Wafer](image)

3.2.1 Materials Issues for Infrared Detection

Increasing the signal-to-noise ratio is a challenge for demonstrating liquid-phase, IR detection using an all-silicon microreactor. Thickness, doping of the wafer as well as reflections from the substrate surface adversely affect transmission. The transmissions of
several Si substrates are compared in Table 1.2-1. All the substrates are polished on both sides, and all data was collected using a Nicolet 800 IR spectrometer.

Of the uncoated samples, optical silicon (undoped silicon with oxygen impurities) has the highest transmission even though the substrate is thicker. Optical silicon substrates with wafer dimensions are commercially available. However, semiconductor (doped) silicon is more widely available and is also commonly used for integrated reactor designs because of its desirable chemical and electrical properties. As expected, Sample 3—lightly doped with boron (p-type)—has a transmission comparable to Sample 1. In contrast, Sample 4, which is much thinner than Samples 1 and 3, does not transmit appreciably because the dopants are excited and absorb the IR light. Generally, resistivities ($\rho$) should be greater than 10 $\Omega$-cm for boron-doped samples and greater than 1 $\Omega$-cm for phosphorus-doped samples. Although the transmission (~40%) obtained using uncoated samples is sufficient for most applications using an anti-reflective (AR) coating increases transmission through silicon. These AR coatings, however, need to be chemically compatible and should not complicate processing of the wafer.

Table 3.2-1: Silicon IR Transmission for Varying Dopant Concentrations

<table>
<thead>
<tr>
<th>Sample</th>
<th>Doping</th>
<th>Coating</th>
<th>Thickness (mm)</th>
<th>Transmission (%) (4000 to 1200 cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>undoped</td>
<td>no</td>
<td>2.0</td>
<td>48.4±5.6</td>
</tr>
<tr>
<td>2</td>
<td>undoped</td>
<td>yes</td>
<td>3.0</td>
<td>81.0±14.7</td>
</tr>
<tr>
<td>3</td>
<td>p-type, $\rho$=10-50 $\Omega$-cm $^*$</td>
<td>no</td>
<td>1.0</td>
<td>41.7±2.1</td>
</tr>
<tr>
<td>4</td>
<td>n-type, $\rho$=0.005 – 0.002 $\Omega$-cm</td>
<td>no</td>
<td>0.5</td>
<td>0.2±0.2</td>
</tr>
</tbody>
</table>

$^*$prior to 1100°C anneal in N$_2$

After choosing the Si substrate, the dielectric boundaries within a system that contains etched channels must be considered. When electromagnetic radiation contacts a dielectric interface of two media with different refractive indices ($n_1$ and $n_2$) reflection occurs [75] as illustrated in Figure 3.2-2. The reflection is a result of the dielectric discontinuity and can be reduced or eliminated at a particular wavelength by coating the substrate with thin dielectric layers. The reflection coefficient (ratio of intensity of
reflected electromagnetic radiation at a boundary between two dielectric media to incident intensity) is expressed in Equation 3.2-1.

\[ R = \left( \frac{n_2 - n_1}{n_2 + n_1} \right)^2 \]  

(3.2-1)

A single, homogeneous antireflection coating that is a quarter wavelength in thickness (Equation 3.2-2 where \( \lambda \) is wavelength and \( n \) is the index of refraction of the coating) is the simplest method for reducing reflections.

\[ t = \frac{\lambda}{4n} \]  

(3.2-2)

Based on this equation, reflectance can not be completely eliminated for a scanning spectrometer. Nevertheless, to achieve zero reflectance at a single wavelength, the index of refraction is expressed in Equation 3.2-3 where \( n_1, n_2 \) are the refractive indices of the bulk layers.

\[ n = \sqrt{n_1 n_2} \]  

(3.2-3)

Materials with the index of refraction indicated by Equation 3.2-3 may not exist for a particular application. Using materials with an index of refraction close to that given in Equation 3.2-3 significantly reduces reflections. Moreover, using materials with an index of refraction between \( n_1 \) and \( n_2 \) and any thickness will reduce reflectance. For this application, the ideal refractive index is \( \sim 1.9 \), which corresponds to silicon nitride. However, silicon dioxide coating technology is more readily available. Thus, to decrease the effect of the interference fringes, the inner and outer surfaces of the chip were covered by a 0.1 \( \mu \text{m} \) silicon dioxide layer. The residual reflectance at the desired wavelength is given by Equation 3.2-4.

\[ R = \left( \frac{(n_1 n_2 - n^2)^2}{(n_1 n_2 + n^2)^2} \right) \]  

(3.2-4)

Figure 3.2-3 shows that the interference fringes decrease significantly with the surface modification of the device. The ratio of the reflection of the coated sample (Equation 3.2-4) to the uncoated sample (Equation 3.2-1) is 0.64 for a single reflection. The multiple reflections with the experimental system leads to additional reduction. In addition to reducing the interference fringes, the oxide layer offers chemical resistance to
the alkaline solutions used in this study and electrical insulation for the Ti/Pt temperature sensors.

![Origin of Interference Fringes](image)

Figure 3.2-2: Schematic of Reflections in the Silicon Channel

3.2.2 T Contactor Study Platform for IR Detection

A T contactor was chosen for developing on-chip IR detection because it is the simplest way to contact two fluids for a reaction. The simplicity of the contacting scheme facilitates the investigation of the central issue, understanding how to perform on-chip IR transmission detection in a microfabricated reactor.

3.2.2.1 T Contactor Fabrication

All-silicon microreactors were fabricated by defining reaction geometries in silicon wafers (Figure 3.2-4). A silicon wafer was coated and patterned with photoresist. DRIE defined the microchannels. Next, the patterned silicon wafer and a blank silicon wafer were RCA cleaned [30]. Then, the wafers were contacted and annealed at 1100°C for 1 hour to complete the bond. After bonding, the microchannel reactor inlet and outlet ports were patterned and DRIE released individual reactors.
3.2.2.2 Testing of T Contactor IR Reactors

Figure 3.2-5 shows the test setup. A commercial IR detection cell holder was used with a Nicolet 800 IR spectrometer. For testing, compressive force sealed the microreactor against a gasket in the cell, and the microreactor was placed in the sample compartment of the IR spectrometer. IR light from the bench passed through the
microreactor to the detector and the transmission spectrum was generated. Liquids were delivered to the reactor using a syringe pump connected to the detection cell by poly-ether-ether-ketone (PEEK) tubing. The fluids were filtered using chemically resistant 0.45 μm filters.

![Diagram of IR Microreactor and Sample Holder](image)

**Figure 3.2-5: Test Station for IR Microreactors**

Prior to beginning an experiment, the depth of the channels was confirmed using the interference fringes that are prominent in the transmission profile of an empty channel [76]. Figure 3.2-6 shows the experimental result and Equation 3.2-5 expresses the relationship between the fringe pattern and the cell depth where \( w_n \) = wavenumber (cm\(^{-1}\)) and \( n \) = number of fringes counted.
\[ L = \frac{5n}{w_1 - w_2} \]  

(3.2-5)

Figure 3.2-6: Transmission Profile to Confirm Cell Depth

3.2.2.3 T Contactor IR Studies Results

Figure 3.2-7 compares the transmission spectra of continuously flowing acetic anhydride obtained using both the microfabricated reactor and a standard CaF\(_2\) crystal assembly with teflon spacers. The two spectra in Figure 3.2-7 are qualitatively in agreement. Thus, it is possible to probe the region from 4000 to 1000 cm\(^{-1}\) using the all-silicon microreactor, and resolve close peaks in the carbonyl region (\(-1500-1900\) cm\(^{-1}\)) where not only anhydrides, but also acid chlorides absorb strongly.

The hydrolysis of propionyl chloride in tetrahydrofuran, shown in Figure 3.2-8, was a model reaction for the liquid phase microreactor. The reaction is fast so appreciable conversion may be achieved for the short contact times that are typical of microreactors. Figure 3.2-9 shows the IR spectra for the hydrolysis of propionyl chloride. The acid chloride peak is at 1791 cm\(^{-1}\) and the product peak (carboxylic acid) is at 1738 cm\(^{-1}\). Figure 3.2-9 also shows that the peaks, separated by only \(-50\) cm\(^{-1}\), may be distinguished. Decline of the reactant peak and the rise of the product peak as contact time is increased (by decreasing flow rates), shows the progress of the reaction. Moreover, quantitative mass balances, as illustrated in Figure 3.2-10, were demonstrated using control samples. The time resolved studies in Figure 3.2-9, also illustrate that this type of detection method is suitable for extracting reaction kinetics.
Figure 3.2-7: Spectrum of Acetic Anhydride for the Microreactor and Commercial Cell

Figure 3.2-8: Alkaline Hydrolysis of Propionyl Chloride

Figure 3.2-9: Progress of the Alkaline Hydrolysis of Propionyl Chloride
3.3 Fully Integrated System

After gaining a thorough understanding of issues associated with on-chip IR transmission detection, a final design, illustrated in Figure 3.3-1(a), was chosen. The platform is the round chip used for the IR studies so that the same holders and fluid manifolds can be used. The mixer and parallel plate heat exchanger previously described were coupled to an IR probing region. IR detection for the conditions of this study requires a probing depth <60 μm whereas the mixing channel is ~400 μm deep to avoid prohibitive pressure drops. A cross section (AA') of the channel that illustrates this profile is shown in Figure 3.3-1(b). Figure 3.3-1(c) shows the inlets to the reactor, and Figure 3.3-1(d) is a schematic of the metal layer. The metal layer consists of a shutter to replace the polymeric gasket used in the previous study and titanium/platinum thin film temperature sensors to replace the silicon sensors previously described.

3.3.1 Fully Integrated System Design

The final design has three features that are different from those previously described: a designated spectroscopic probing region, a coating to reduce reflections described in Section 3.2.1, and Ti/Pt metal for thermal sensing and light attenuation.
Figure 3.3-1: (a) integrated reactor channels (b) AA' cross section (c) inlet ports (d) metal layer

There were three design constraints for the probing region: the overall chip size could not change, the probing area had to be large enough so that the spectrometer signal was sufficient for kinetics studies, and the divergence from the 50 μm mixing channel to the probe area width should not cause recirculation. Based on those criteria, Figure 3.3-1(d) shows that the channel widens from 50 μm to 2000 μm over a length of 1.8 mm, has a constant cross section for 1 mm, and tapers back to 400 μm over a length of 1.0 mm. The outlet channel is 400 μm wide.

In previous studies, a polymeric gasket attenuated the light everywhere but the region of interest. This technique is sufficient, but alignment is difficult to reproduce. Consequently, Ti/Pt shutters have been incorporated. The shutters are aligned to the region of interest using photolithography so resolution in the micron range is achieved. Furthermore, the shutter is fixed so that alignment is always reproducible. In addition to
the metal shutter, platinum resistive temperature sensors were patterned in the metal layer [48].

3.3.2 Fully Integrated System Fabrication

Figure 3.3-2 illustrates the fabrication scheme for the fully integrated system. Fabrication begins with a blank Si wafer coated with silicon dioxide (a). The silicon dioxide is patterned with a mask of the probing region using photolithography and the oxide is etched to define the pattern (b). The wafer is cleaned, coated (c) and re-patterned with the device channels. The silicon is etched to define ~300 μm of the channels (d). Then, the photoresist is removed to uncover the probing region, and the mixer channels are etched an additional 40-60 μm while the probing region is defined (e). Next the silicon dioxide mask is removed, and the processed wafer and a blank wafer are heated to 1100°C in the presence of oxygen so that a 0.1 μm silicon dioxide layer forms on the surface (f). Then the processed wafer and blank wafer are fusion bonded (g). Next, the blank wafer is coated, patterned and etched to define the inlet ports (h). The wafer is flipped and patterned with a ring that is the die size and etched to release each chip (i). Individual chips are then coated and patterned with the negative of the metal layer (j). Titanium and platinum are deposited, and the chips are soaked in acetone to lift-off the metal that is deposited on the photoresist. This step leaves the metal pattern shown (k) and completes device fabrication.

Figure 3.3-3 shows images of the finished device. Figure 3.3-3(a) shows the channels that are imbedded in the two bonded silicon wafers. Figure 3.3-3(b)-(c) are pictures of a chip with and without metal respectively.
Figure 3.3-2: Integrated Microchemical System Fabrication Steps
Figure 3.3-3: Fully Integrated System (a) buried channels (b) top view without metal (c) top view with metal layer

3.4 Conclusions

An integrated microchemical system that consists of a mixer, parallel plate heat exchanger, and thermal and optical sensing capabilities was fabricated. The parallel plate heat exchanger has an overall heat transfer coefficient of $1420 \pm 130 \text{ W/m}^2\text{°C}$. Although comparable to typical heat transfer coefficients for macroscopic equipment, the value was lower than the theoretical value for the microsystem because of longitudinal heat conduction effects in the surrounding Si. Thin film temperature sensors were added to the integrated microchemical system, and the device was used to conduct a highly exothermic reaction. For this application, the heat exchanger was shown to eliminate a $40\text{°C}$ rise in temperature over the reaction channel as evidenced by monitoring with the thin-film, silicon temperature sensors.

On-chip IR transmission detection in an all-silicon T contactor from 4000-1000 cm$^{-1}$ was demonstrated. It was shown that IR transmission detection may be employed to monitor the progress of the hydrolysis of propionyl chloride. Factors that adversely affect the signal to noise ratio for IR transmission detection are doping, reflections, and IR
crystal thickness. AR coatings can increase transmission by 30% when compared to uncoated samples with high resistivities. Moreover, such coatings could reduce interference fringes. AR coatings, however, should be compatible with the fabrication process and the chemistry to be investigated.

A final, monolithically integrated design was defined by using the circular chip platform from the IR studies with the mixer/heat exchanger. A probing region for detection, a metal shutter for accurate and repeatable probing, and titanium/platinum temperature sensors were added. All of the device surfaces were coated with silicon dioxide for three purposes: (1) reduction of interference fringes (2) chemical resistance to alkali-OH and (3) electrical insulation for active metal sensors.
4 Kinetics Study of a Rapid Homogeneous Liquid Reaction: The Alkaline Hydrolysis of Methyl Formate

In the previous chapter, a monolithically integrated chemical system was described. The system consists of a laminar flow mixer, previously characterized for rapid homogeneous mixing (Chapter 2); a parallel plate heat exchanger for temperature control; and, on-chip infrared detection for concentration and subsequent kinetic parameter determination.

In this chapter, the monolithically integrated microchemical system was used for kinetics studies of a rapid homogeneous reaction, the alkaline hydrolysis of methyl formate. This work demonstrates a microfabricated silicon system with on-chip infrared detection for chemical kinetics studies of a reaction with a half life < 1 second. The time for the reaction was varied by changing the total flow rate of the reactants. This type of technique is known as a continuous flow method.

4.1 Liquid-Liquid Continuous Flow Kinetics Studies

Continuous-flow methods are tools for kinetics studies of reactions in solution [77]. After initiation by a mixing step, the reaction proceeds while the liquid flows down a reaction conduit. Detectors placed downstream from the mixing point are used to determine the concentrations of the reactants/products and, thus, the corresponding kinetic parameters. The concentrations are at steady state so the detector does not need to have a fast response. However, a slower detection method requires a larger volume of reagents.

High flow velocities and large conduit cross sections lead to turbulence, which promotes axial mixing and consequent homogeneity of the time axis. Conversely, low fluid velocities and small conduit cross sections lead to laminar flow, which is characterized by a parabolic velocity profile. The parabolic velocity profile and no-slip boundary condition result in an obscuring of the time axis. The obscurity or dispersion experimentally has proven to be less pronounced than is often assumed [77]. Moreover,
the results of a detailed simulation study clearly prove the feasibility of continuous-flow experiments in the laminar flow regime.

Traditionally, fused silica systems have been used for these types of studies. Glass blowing and bonding techniques are well developed so that system fabrication is not an issue. Also, silica is optically transparent for incorporation of UV-Vis detection. More recently, microfabricated systems have been identified for use in continuous flow kinetics studies.

4.1.1 Fused Silica Capillary Systems

Konermann et al. studied cytochrome c folding kinetics by time-resolved electrospray ionization mass spectrometry (ESI MS) [78]. The method combined a continuous flow mixing technique with an electrospray mass spectrometer illustrated in Figure 4.1-1. Reynolds numbers for the experiments ranged from ~2 to 9 for a 75 μm tube diameter. The kinetics were described by two lifetimes of 0.17 ± 0.02 and 8.1 ±0.9 s, which were consistent with the results of conventional experiments previously described in the literature. The technique was also used by Konermann et al. to study the acid-induced denaturation of holo-myoglobin (hMb) following a pH-jump from 6.5 to 3.2 [79] and by Zechel et al. to measure the pre-steady state kinetics of an enzymatic reaction by monitoring a transient enzyme intermediate [80]. In both cases, the kinetic data were in agreement with those determined using conventional techniques.

Shastry et al. described a continuous-flow capillary mixing method to monitor reactions on the microsecond time scale [81]. Reactants flowing in separate conduits contacted, and mixing was enhanced by flow past a platinum sphere. The reaction kinetics were followed by measuring fluorescence versus distance downstream from the mixer, using a Hg(Xe) arc lamp source and a digital camera for detection. Test reactions indicated that mixing was complete with 15 μs of its initiation. The scope of the method was illustrated with an example of a protein folding reaction.

4.1.2 Microfabricated Systems

In the last decade, microfabricated systems have been identified as effective tools for studying the kinetics of fast reactions. Micron and sub-micron scale dimensions that can be realized using micro-fabrication techniques correspond to smaller characteristic
mixing lengths. Smaller characteristic mixing lengths correspond to faster mixing times, and faster mixing times make it possible to determine the kinetics of rapid reactions.

![Diagram of continuous flow mixing coupled with ESI MS](image)

**Figure 4.1-1: Continuous Flow Mixing Coupled with ESI MS**

Hadd et al. used a microfabricated channel network illustrated in Figure 4.1-2 to perform an automated enzyme assay [82]. The enzyme was assayed using a substrate that was hydrolyzed to a fluorescent product. Reaction kinetics were obtained by varying the concentration of substrate on-chip and monitoring the production of fluorescent product using laser-induced fluorescence. Calculated Michaelis-Menten constants compared well with those obtained using a conventional enzyme assay. Moreover, the enzyme assay performed on the microchip reduced the amount of reagent consumed by 4 orders of magnitude over the conventional assay.

Bokenkamp et al. developed a silicon mixer illustrated in Figure 4.1-3 for sub-millisecond quench-flow analysis [37]. The group fabricated the mixer and interfaced it with commercially available quench-flow instrument. The reactants enter inlets A and B shown in Figure 4.1-3. The reaction is quenched by the introduction of acid through inlet C and the fluids exit through D. The reactor effluent is analyzed off-line. They found that, comparatively, dead times as well as reagent volumes were significantly reduced. For the alkaline hydrolysis of phenyl chloroacetate, they measured a second order rate constant of $430 \pm 47 \, \text{Lmol}^{-1}\text{s}^{-1}$ using off-chip UV detection at a half life of $\sim 10$ minutes compared to a literature value of $363 \pm 21 \, \text{Lmol}^{-1}\text{s}^{-1}$ measured using conventional techniques.
Figure 4.1-2: Microfabricated Channel Network for Enzyme Assay (a) substrate (b) buffer (c) enzyme (d) inhibitor (e) waste

Knight et al. described the formation and control of nanoscale, submerged jets using hydrodynamic focusing on a silicon chip illustrated in Figure 4.1-4 [39]. A fluid enters the inlet and is hydrodynamically focused using side streams for rapid diffusion mixing. The technology supports the study of reactions with small reagent volumes and the determination of fast kinetic reactions not accessible with conventional methods. Based on experiments and theory, the authors concluded that they could mix within 10 μs using nano-liter volumes of reagents. These reagent volumes and mixing times are on the order of the requirements for gathering kinetic data previously unattainable due to the limitations of the fastest, conventional, measurement methods.

The T sensor, illustrated in Figure 4.1-5, is a microfabricated system for determination of various parameters including kinetic parameters [83]. This is a recently developed microfluidic chemical measurement device that exploits the low Reynolds number flow conditions in microfabricated channels. The concentration of the target analyte is determined by measuring fluorescence in a region where the analyte and fluorescent indicator have mixed. An analytical model predicted the device behavior from the diffusion coefficients of the analyte, indicator, analyte-indicator complex and kinetics of the complex formation. Diffusion coefficients, local viscosity as well as
reaction equilibria are often unknown. A method for determining these unknown parameters through interpretation of T-sensor experiments was presented.

Figure 4.1-3: Sub-millisecond Quench Flow Device (A) reactant 1 inlet (B) reactant 2 inlet (C) quench flow inlet (D) outlet

Pollack et al. studied the time resolved collapse of a folding protein with a microfabricated, rapid mixing device and small angle x-ray scattering (SAXS) illustrated in Figure 4.1-6 [84]. They described recent work on the protein bovine \( \alpha \)-lactoglobulin where folding was directly observed on the millisecond time scale.

Figure 4.1-4: Microchip with Hydrodynamic Focusing
4.2 Alkaline Hydrolysis of Esters as a Model System

The alkaline hydrolysis of esters is a common model system for the study of rapid reactions. The mechanism is known and the kinetics are second order. The alkaline hydrolysis of methyl formate was studied in this work. A suitable half life for study using the integrated chemical system is on the order of the mixing time, 25 ms, or longer. The half life of a second order reaction is expressed in Equation 4.2-1. It is a function of the rate constant (k), which is a function of the temperature, and the initial reactant concentration (a), where b = concentration of the second reactant and a = b.
\[ t_{\frac{1}{2}} = \frac{1}{k \cdot a} \]  

(4.2-1)

The design constraint for demonstrating the system was to choose a reaction half life close to the mixing time while keeping the reactant concentrations high enough to maintain a good spectroscopic signal-to-noise ratio.

4.2.1 Alkaline Hydrolysis of Esters

Alkaline or acid catalyzed hydrolysis of a carboxylic ester yields a carboxylic acid and an alcohol/phenol [85]. Under alkaline conditions, the carboxylic acid is obtained as its salt. Basic conditions promote the hydrolysis of esters by providing the strongly nucleophilic reagent OH\(^-\). The reaction is essentially irreversible because reaction between a resonance-stabilized carboxylate anion and an alcohol is not favored.

Alkaline hydrolysis involves attack on the ester by hydroxide ion. This description is consistent with the second order kinetics. The hydroxide attacks at the carbonyl carbon to displace the alkoxide ion rather than at the alkyl carbon. This hypothesis is supported by stereochemical and tracer evidence. This kind of bond cleavage may be expected considering the generally greater reactivity of carbonyl carbon.

Also, according to the mechanism, attack by hydroxide ion on carbonyl carbon displaces the alkoxide in two steps with the intermediate formation of a tetrahedral compound rather than in one step. The mechanisms were considered equally likely until isotopic exchange experiments suggested the mechanism illustrated in Figure 4.2-1.

4.2.2 Second Order Reactions

The alkaline hydrolysis of methyl formate is a second order reaction. Equation 4.2-2 describes the general case of an elementary second order reaction where A and B are the two reactants [86].

\[ A + B \rightarrow^{k} \text{product(s)} \]  

(4.2-2)

Once the reaction is initiated, the change in concentration of the two reactants is expressed in Equation 4.2-3 where \( c_i \) = concentration of component i, \( t \) = time, and \( k \) = rate constant.
Figure 4.2-1: Mechanism for the Alkaline Hydrolysis of Methyl Formate

\[
\frac{dc_a}{dt} = \frac{dc_b}{dt} = kc_ac_b \quad (4.2-3)
\]

Equation 4.2-4(a)-(b) expresses the initial concentrations of the reactants \(a, b\) based on the concentration and the extent of reaction \(x\).

\[
a = c_a + x \quad (4.2-4a)
\]

\[
b = c_b + x \quad (4.2-4b)
\]

Substituting the extent of reaction for the concentration yields Equation 4.2-5.

\[
\frac{dx}{dt} = k(a - x)(b - x) \quad (4.2-5)
\]

Separation of variables (Equation 4.2-6) and integration (Equation 4.2-7) yields an expression for the reaction time as a function of the extent of reaction.

\[
\int_0^x \frac{dx}{(a - x)(b - x)} = k\int_0^t dt \quad (4.2-6)
\]
\[ \frac{1}{a-b} \ln \frac{b(a-x)}{a(b-x)} = kt \]  \hspace{1cm} (4.2-7)

Manipulating Equation 4.2-7 yields the linear form expressed in Equation 4.2-8.

\[ \ln \frac{(a-x)}{(b-x)} = (a-b)kt + \ln \frac{a}{b} \]  \hspace{1cm} (4.2-8)

Substituting concentration, the typical measured experimental quantity, for the extent of reaction yields Equation 4.2-9.

\[ \ln \frac{c_a}{c_b} = (a-b)kt + \ln \frac{a}{b} \]  \hspace{1cm} (4.2-9)

Equation 4.2-10 expresses a second order reaction where identical molecules react.

\[ 2A \overset{k}{\rightarrow} \text{product(s)} \]  \hspace{1cm} (4.2-10)

Once the reaction is initiated, the change in concentration of the reactant is expressed in Equation 4.2-11 where \( c_a \) = concentration, \( t \) = time, and \( k \) = rate constant.

\[ -\frac{dc_a}{dt} = kc_a^2 \]  \hspace{1cm} (4.2-11)

Equation 4.2-12 expresses the concentration as a function of time.

\[ c_a = \frac{a}{1 + k \cdot a \cdot t} \]  \hspace{1cm} (4.2-12)

Equations 4.2-13, 4.2-14, and 4.2-15 express three different linear forms of Equation 4.2-11. These equations also apply for the special case of Equation 4.2-2 when \( c_a = c_b \).

\[ \frac{1}{c_a} = \frac{1}{a} + kt \]  \hspace{1cm} (4.2-13)

\[ c_a t = \frac{c_a}{k} + \frac{1}{k} \]  \hspace{1cm} (4.2-14)

\[ \frac{1}{c_a t} = \frac{1}{a t} + k \]  \hspace{1cm} (4.2-15)

The choice of linear forms for plotting varies. Typically, the error associated with the time measurements is small relative to the error in the concentration measurement. Thus, the plotting form may be determined by this factor. The extent of reaction for the experiment is another consideration.
4.2.3 Previous Kinetics Studies of the Hydrolysis of Methyl Formate

The alkaline hydrolysis of methyl formate was studied by Humphreys et al. [87]. The stirred flow reactor technique for measuring reaction rates in solution was modified by injecting one reactant as a pure liquid or as a concentrated solution using a syringe pump. The technique was demonstrated for reactions with half lives as short as 0.6 seconds and specifically, was used to determine kinetic parameters for the alkaline hydrolysis of ethyl formate in 85% ethanol and of methyl formate in water.

Figure 4.2-2 is a plot of data extracted from the literature for the alkaline hydrolysis of methyl formate. The concentration of reactants versus time was determined by quenching the reaction and subsequent titration. The plot shows a good linear fit to the Arhenius equation. The kinetics were determined based on a second order analysis. These data and corresponding data calculated by interpolation are the basis for comparison to literature data throughout this work.

![Figure 4.2-2: Literature Data for the Alkaline Hydrolysis of Methyl Formate](image)

4.3 Isothermal Operation

Isothermal operation is critical for the extraction of rate constants. Based on the standard heats of formation for the reactants and products, the heat of reaction at 25°C was estimated as $-48.5$ kJ/mol. The maximum calculated temperature rise in the system without the heat exchanger and without ambient temperature gradients is $1.1^\circ$C. With heat exchanger operation, the maximum temperature rise is reduced to $<0.5^\circ$C. Thus, it is appropriate to assume that the reactor is isothermal for the conditions of this study.
4.4 Testing

Figure 4.4-1 is a schematic of the testing station for the kinetics studies. The integrated chip is loaded into the sample holder, and the sample holder is placed in the sample compartment of the IR spectrometer. A syringe pump delivers fluids to the reactor, and a pressurized tank delivers fluids to the heat exchanger.

For the study, solutions of 0.5 M NaOH and 0.5 M methyl formate were prepared. The solutions were delivered to alternating inlet channels, and the residence time for reaction was varied by changing the flow rate of the two components. Flow rates were lower than 1 ml/min corresponding to Re < 200 which implies laminar flow.

Infrared radiation was transmitted through the probing region. The absorbance was measured using a Nicolet 800 IR spectrometer.

Figure 4.4-1: Test Station for Infrared Kinetics Studies
4.5 Calibrations

For the hydrolysis reaction studied in Chapter Three, the acid chloride and product peaks were monitored to follow the reaction. For the hydrolysis of methyl formate, the reactant and product peaks were not distinguishable. Consequently, the disappearance of the OH$^-$ peak was monitored to determine the extent of reaction. OH$^-$ was found to absorb distinctly from 1600 cm$^{-1}$ to 2900 cm$^{-1}$ as illustrated by raw data (de-ionized (DI) water as the background) in Figure 4.5-1.

Although there are two peaks for the OH$^-$ absorbance, only the largest peak from 2380 cm$^{-1}$ to 2900 cm$^{-1}$ was considered. Figure 4.5-2 shows absorbance curves for NaOH for various concentrations with DI water as the background. The curves were obtained by flowing the NaOH solution through the reactor and measuring the absorbance. The small periodic variation superimposed on the OH$^-$ signal is caused by the interference in the cell, as discussed in Section 3.2.1. The broad peak in combination with the interference fringes necessitated trapezoidal integration for the calibration curve shown in Figure 4.5-3. The curve is linear at lower concentrations and begins to curve slightly at the higher concentrations. The measurements for this study are within the linear region. Error bars correspond to 2σ for 4 data points at each concentration.

![Absorbance vs. Wavenumber](image)

Figure 4.5-1: 0.313 M NaOH absorbance in an All-Silicon Reactor
Figure 4.5-2: NaOH absorbance in a Silicon Dioxide-Coated Reactor

Figure 4.5-3: NaOH Calibration Curve
4.6 Rate Constant Extraction

Concentration versus time data were obtained for the alkaline hydrolysis of methyl formate at 294 K. A premixed, equilibrated solution was chosen for the background absorbance. Data were obtained by collecting the signal corresponding to a steady state concentration profile at a particular flow rate. The reaction time was calculated as the ratio of the reactor volume to the flow rate through the reactor. Water at 294 K and 1 ml/min flowed through each of the heat exchanger channels to assure <0.5°C deviation from the desired temperature.

Figures 4.6-1 and 4.6-2 are plots of the data based on Equations 4.2-13 and 4.2-14 respectively. The plots are linear, but there is a large error for the most heavily weighted data point. The error for this point was higher because of variability introduced by the syringe pump at lower flow rates. Moreover for Figure 4.6-2, the error in the concentration measurement seems to be magnified because concentration appears on both the independent and dependent variable axis. Figure 4.6-3 is a plot based on Equation 4.2-15. The linearity and error bars suggest that this plot is most appropriate for the data presumably because time rather than concentration appears on both axes.

Table 4.6-1 summarizes the data. All of the plots indicate the correct initial concentration. All of the constants are the same order of magnitude as the literature value, but the plot based on Equation 4.2-15 provides the best estimate of the rate constant. For data where the error in all the concentration measurements is small, Equation 4.3-11 may be appropriate. Uncertainty for the rate constant is based on the confidence interval calculated using the student t test [88].
Figure 4.6-1: Data Regression Based on Equation 4.2-13

\[
\frac{1}{c_a} = \frac{1}{a} + kt
\]

Figure 4.6-2: Data Regression Based on Equation 4.2-14

\[
c_a t = -\frac{c_a}{ka} + \frac{1}{k}
\]
Figure 4.6-3: Data Regression Based on Equation 4.2-15

Table 4.6-1: Rate Constant Determination Results at 294 K

<table>
<thead>
<tr>
<th>Equation</th>
<th>Rate Constant L-mol^{-1}s^{-1}</th>
<th>$R^2$</th>
<th>a</th>
</tr>
</thead>
<tbody>
<tr>
<td>literature</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1.3-11</td>
<td>20.9±5.2</td>
<td>.8742</td>
<td>.250</td>
</tr>
<tr>
<td>1.3-12</td>
<td>21.7±5.4</td>
<td>.8364</td>
<td>.246</td>
</tr>
<tr>
<td>1.3-13</td>
<td>31.0±1.6</td>
<td>.9900</td>
<td>.257</td>
</tr>
</tbody>
</table>

4.7 Temperature Dependent Measurements

The heat exchanger previously described in Chapter Three lowered the reactor operating temperature of the microchemical system for temperature dependent reaction measurements. The pressurized vessel illustrated in Figure 4.4-1 delivered fluids to the heat exchanger because the syringe pump flow rates and volumetric hold-up were too small for this application.
Figure 4.7-1 is a plot of the temperature dependent data plotted according to the linear equation expressed in Equation 4.2-15. The curves shown in Figure 4.7-1 correspond to heat exchanger fluid pressures of 0 psi, 40 psi, and 70 psi with a source temperature of 273 K. A higher heat exchanger fluid flow rate corresponds to a lower reactor temperature. The temperature indicated on Figure 4.7-1 refers to the literature temperature corresponding to the rate constant that was calculated using Equation 4.2-15. The temperatures measured for 0 psi, 40 psi, and 70 psi, were 296 K, 293 K and 290 K respectively. The on-chip temperature sensors were disabled for this study due to inadequate area for contact caused by the congestion of the fluid tubing and sample holder. Instead, the temperatures of the fluids were measured at the outlet of the tubing connected to the heat exchanger outlet. Thus, the discrepancy between the literature temperatures and the experimental temperatures may be due to heat gain of the cooling fluids in route to the reactor and from the reactor to the temperature measurement point.

The curves plotted in Figure 4.7-1 clearly show that the heat exchanger enables kinetic data to be obtained at various temperatures. The shifting of the curves down the y-axis with constant slope is the behavior expected for temperature data plotted according to Equation 4.2-15. Thus, another feature of the liquid-liquid microchemical system, the capability to generate kinetic data at low temperatures (limited by the temperature of cooling fluid – eg. ethanol/CO\texttextsubscript{2} at –78°C) is demonstrated. It follows that the system could also be used to obtain data at high temperatures (limited by heating and handling of heat exchanger fluids).
Figure 4.7-1: Alkaline Hydrolysis of Methyl Formate at Various Temperatures

4.8 Conclusions

Continuous flow methods are tools for kinetics studies. An all-silicon, microfabricated mixer/parallel plate heat exchanger was used to monitor the alkaline hydrolysis of methyl formate. This reaction follows second order kinetics and is fast with a half life of 70 ms for the conditions used in this study. Following the disappearance of the OH⁻ peak was found to be appropriate for monitoring the reaction. OH⁻ exhibits Beer's law absorbance especially at lower concentrations. The interference fringes characteristic of the silicon crystal as well as the broad OH⁻ peak necessitated trapezoidal integration to determine the relationship between the absorbance signal and the reactant concentration.

Using a premixed sample for the background absorbance, the reaction was followed and concentration versus time data were extracted at 294 K. The data were plotted using three different linear forms. The equation with time on both the x and y axes exhibited the most linear relationship. The rate constant that was extracted, 31.0 ±1.6 L·mol⁻¹s⁻¹, was in good agreement of literature value of 30.1 ±0.6 L·mol⁻¹s⁻¹. Moreover, the half life
of the reaction was reduced by an order of magnitude with no sample post processing as compared to the literature study. Temperature dependent data for the reaction were obtained by introducing a cooled fluid to the heat exchanger channels. The shape and parameters for the temperature curves are consistent with the linear equation used for plotting. Thus, the microchemical system can also be used to obtain kinetic data over a wide range of temperatures limited only by the capability to cool/heat and handle the heat exchanger fluid.
5 Heterogeneous Microfluidic Contacting for Encapsulation of Quantum Dots

5.1 Introduction

In the previous chapter, a homogeneous contacting application for the novel microchemical system was described. Typically, the only type of instability characteristic of a homogeneous, isothermal, single component system is turbulence, observed at high Reynolds numbers (Re). Moreover, the flow field for this microchemical system does not exhibit any instabilities due to the small Re associated with operation.

For heterogeneous contacting, the system has the potential to exhibit instabilities at all Re. Therefore, more than one type of flow field may be observed for a given set of conditions. In this chapter, heterogeneous contacting is studied, and segregated flow of immiscible liquids is ultimately used to develop a process for microencapsulation of quantum dots.

Several groups have investigated heterogeneous contacting in microsystems. Burns et al. studied the fluid dynamics of liquid-liquid flow inside a microchannel reactor for separations applications [89]. Their results indicated that stable parallel flow of two immiscible liquid phases could be achieved over a range of viscosities and flow rates. Additional experiments revealed that individual component streams could be split at the end of the contacting channel into two separate output streams with little contamination.

Haverkamp et al. studied the potential of micromixers for contacting of disperse liquid phases [90]. They studied the dispersion of two immiscible fluids in a static micromixer using silicone oil/water systems. Flow rates between 20 ml/h to 700 ml/h were tested. Experiments showed the dependence of the average droplet size and size distribution on geometrical parameters of the micromixer and operating conditions.

Thorson et al. studied dynamic pattern formation in a vesicle-generating microfluidic device [91]. In the study, a heavy oil phase, such as écane, tetradecane or hexadecane, contacted a water solution containing a surfactant. They showed that a microfluidic device can produce intricate, ordered patterns. They also found that self-
assembly of the droplets into patterns varied with relative flow pressures and channel dimensions.

5.2 Theory

The problem of hydrodynamic stability for homogeneous systems is well formulated [92-93]. However, the problem of stability in heterogeneous liquid-liquid systems is not well understood. This is, in part, due to the complexity of the heterogeneous systems. Hydrodynamic stability for a homogeneous system involves only one parameter, Re, whereas hydrodynamic stability for a two phase system involves at least six of the following parameters: \( \alpha = \text{wavenumber}, \ Re = \frac{\delta \nu}{\mu}, \ m = \frac{\mu_1}{\mu_2}, \ r = \frac{\rho_1}{\rho_2}, \ n = \frac{d_1}{d_2}, \ S = \frac{\sigma}{\rho U d}, \ F = \frac{g(\Delta \rho) d}{\rho U^2}, \ \beta = \text{angle of inclination}, \) where \( d \) = layer depth, \( \mu \) = viscosity, \( \rho \) = density and \( U \) = velocity. [92]

There are several classes of instabilities, defined as a function of variations in the parameters previously listed [93]. The microchemical systems in this study are horizontal and shallow so there is no gravity dependence, and the Re is small so there is no turbulence. Consequently, the viscosity-induced instability, studied by Yih, is most relevant to our systems [94]. Yih examined the stability of two superposed fluids of different viscosities in poiseuille flow. Based on numerical calculations, Yih determined that the flows he studied could be unstable at any Reynolds number (no matter how small) due to viscosity differences.

Yih's study was of two layers and, therefore is applicable to at least one of the two systems studied for this work. However, the work may not be directly applicable to the multi layer system that was investigated. Instead, this case could be more like the instability of jet flow treated by Rayleigh [95]. Rayleigh determined that a jet becomes unstable by two modes illustrated in Figure 5.2-1. There is the varicose wave-cylinder where the axis is straight and the sinuous wave where the radius is constant, but cylinder axis has a sinusoidal displacement. In a jet, either wave may be dominant depending on the conditions [96]. Rayleigh found that when the wavelength of the perturbation exceeds the circumference of the unperturbed cylinder, the flow is unstable. This suggests that a smaller cylinder, or thinner layer, is more likely to become unstable. Surface tension is stabilizing and counters fluid break-up. Once the break-up has
occurred, surface tension pulls the fluid into droplet form. The limitation of Rayleigh's study in application to formation of emulsions is that the viscous forces of the bulk fluid are neglected [97].

To overcome this limitation, Taylor's work focused on predicting process targets, such as droplet size, from known input parameters [97]. Based on Taylor's work, the droplet size is estimated as $r \sim \sigma / \nu \varepsilon$, where $r$ is the droplet radius, $\sigma$ is the interfacial tension between the water/oil, $\nu$ is the viscosity of the continuous phase and $\varepsilon$ is the shear rate [91]. The shear rate is estimated as $\varepsilon = 2v / y_o$ where $y_o$ is the channel radius and $v$ is the velocity of the fluid, which leads to $r \sim \sigma y_o / 2yv$ [91].

![Image of modes of jet instability](image)

**Figure 5.2-1:** Modes of Jet Instability (a) varicose wave-cylinder (b) sinuous wave

### 5.3 Contacting Studies and Observations

Contacting studies were conducted to determine (1) the types of flow profiles that exist in regions of interest and (2) when they occur. Water dyed red using phenol red indicator was contacted with various organic phases: hexane, toluene, cyclohexane, and methanol.

Figure 5.3-1 shows the test station. A T contactor with the T etched in Si and capped by pyrex was used for the study. One of the pyrex layers contained drilled holes for fluidic access. A syringe pump delivered fluids to the chip. Pyrex glass is optically transparent so the fluids could be monitored using a CCD camera. The chip sits on a teflon fluid manifold with a viton polymeric gasket for sealing. Flow rates tested ranged from 0.001 ml/min to 2.00 ml/min. The volumetric flow ratios were all 1:1. The T contactor channel dimensions ranged from 200-800 $\mu$m in 200 $\mu$m increments. The inlet channels were half the width of the contacting channel.
Figure 5.3-1: Immiscible Fluid Studies Test Station

Figure 5.3-2 shows the three types of flow profiles that were observed. The images are all at the same flow rate, 0.1 ml/min. For miscible pairs such as methanol water (Figure 5.3-2(a)), the contact line was straight and stable for all conditions. For immiscible fluids, two types of profiles were observed, the wavy contact line as shown in Figure 5.3-2(b) and the segregation of one fluid into another in so-called Taylor cells as shown in Figures 5.3-2(c)-(d).

Occasionally, the wavy interface would steady, but fluid breakup was much more common. No identifiable transition point from the wavy to the segregated profile was observed for the contacting studies. This could be caused by perturbations from the syringe pump that delivers the fluids and/or the condition of the syringe pump.
Figure 5.3-2: Immiscible Fluid Contacting Flow Profiles at 0.1 ml/min for Each Phase: (a) straight contact line (b) wavy contact line (c)-(d) segregated

Figure 5.3-3 shows images of toluene-water contacting in a 1:1 ratio with varying flow rates. The flow rates in Figure 5.3-3(a)-(f) are 0.005, 0.01, 0.05, 0.1, 0.5, 1.0 ml/min respectively for both fluids. It is clear from Figure 5.3-3 that the droplet size scales with the flow rate. This result is consistent with previous studies [91]. Figure 5.3-3(g) is a plot of data extracted from the images in Figure 5.3-3(a)-(f). The droplet size appears linear for low velocities as suggested in previous studies [91]. At higher velocities, however, the relationship does not appear to hold.

The degree of control that was spontaneously achieved for the segregated flow profile was quantified using optical spectroscopy. An optical fiber mounted to the chip or to the fluid manifold guided the light through the channel and subsequently to the spectrometer (Figure 5.3-4(a)). The profile shown in Figure 5.3-4(b) was anticipated. When a water slug passes through the channel, the transmission should be lower versus when an organic slug was passing through because of the phenol red absorbance. The transmission was monitored at 565 nm. The behavior was quantified at a low flow rate to
be within the resolution of the spectrometer, which is $O(\text{milliseconds})$ for the operating conditions used in the study.

![Images of droplet size flow rate dependence](a) 0.005 ml/min, (b) 0.01 ml/min, (c) 0.05 ml/min, (d) 0.1 ml/min, (e) 0.5 ml/min, (f) 1.0 ml/min, (g) droplet radius vs. velocity$^{-1}$ for a-f

Figure 5.3-3: Illustration of Droplet Size Flow Rate Dependence: (a) 0.005 ml/min, (b) 0.01 ml/min, (c) 0.05 ml/min, (d) 0.1 ml/min, (e) 0.5 ml/min, (f) 1.0 ml/min, (g) droplet radius vs. velocity$^{-1}$ for a-f

As shown in Figures 5.3-5 (a)-(b), the predicted periodic profile was observed experimentally. The data seems fairly noisy when viewed for 40 s (Figure 5.3-5(a)), but it is quite well bounded between 10-50% transmission. Looking at a close-up (Figure 5.3-5 (b)) of one area of the data, the behavior is resolved. The period is 200 ms with a standard deviation of 100 ms. Furthermore, a thin film of water surrounds the organic slug, which is perhaps why the transmission does not reach 100%. This observation is
consistent with a previous study on the deposition of a viscous fluid on the wall of a tube [98]. The results also suggest that a two-channel contactor could be used to make a monodisperse emulsion.

![Diagram](image)

Figure 5.3-4: Test Method for Quantification of Droplet Size Control (a) side view of channel with segregated flow (b) predicted transmission profile

Although the contacting study was approached broadly, the work ultimately focused on the segregated profile because it is stable and reproducible in a T contactor. A number of potential applications ranging from the fabrication of multi-layered structures, illustrated in Figure 5.3-6(a), to microencapsulation, illustrated in Figure 5.3-6(b), were considered for the segregated profile. However, microencapsulation was chosen as the focus for this thesis.
Figure 5.3-5: Droplet Size Control Demonstration: (a) transmission profile for 40 s (b) resolved profile for 1 s

Figure 5.3-6: Segregated Flow Profile Potential Applications (a) multi-layer patterning (b) microencapsulation

5.4 Microencapsulation

Formation of emulsions can be treated as a problem in hydrodynamic stability [99]. Emulsions are formed because energy is added to two separate and thermodynamically stable phases. If the system is stable, the perturbation will be damped and the system will
return to its normal state. If the system is unstable, the appearance of the flow is changed completely.

Figure 5.4-1 outlines the steps that allow the microencapsulation of quantum dots. First, two immiscible fluids are contacted. A hydrodynamic instability then causes an emulsion to form. The droplets, which contain the quantum dots and one reactant, contact a solution containing the second reactant. The two components react in a step reaction polymerization to solidify the microcapsule membrane and complete the quantum dot encapsulation.

```
Heterogeneous contacting

Hydrodynamic instability

Emulsion and microencapsulation

Step-reaction interfacial polymerization

Solidify capsule membrane
```

Figure 5.4-1: Steps Leading to Microencapsulation

5.4.1 What is Microencapsulation?

Thies [100] describes microencapsulation as “the envelopment of small solid particles, liquid droplets, or gas bubbles with a coating” resulting in a capsule with a diameter between 1 and 1000 μm. Many terms are used to describe the contents of a microcapsule including core material, internal phase, and payload. The coating material, typically an organic polymer, wax, sugar, etc., which solidifies the capsule, may be called a coating, wall, or shell.

There are several techniques to achieve microencapsulation [100]. The technique used for this study is interfacial polymerization. Figure 5.4-2 shows a schematic of the process. The dispersed phase contains one reactant, and the continuous phase contains the
other reactant. The reaction occurs at the interface and forms a solid wall. Washing and filtration prepare the capsules for use.

![Diagram of Interfacial Polymerization]

Figure 5.4-2: Schematic of Interfacial Polymerization

Microencapsulation has a number of application areas including: pesticides, food additives, pharmaceuticals and graphic arts – the motivation for this study [100]. Carbonless paper is an example of a graphic arts application. Capsules are first printed on a sheet of paper. Dye contained in the capsules is then transferred to another sheet of paper when the original sheet is pressed so that the capsules rupture to leave the appropriate pattern.

A more recent development in the inking application is electrophoretic ink, so called E-Ink [101]. Figure 5.4-3 illustrates the technology. Capsules contain suspensions of black particles and white particles with negative and positive charges respectively in a clear fluid. When a positive field is applied to an area, the black particles move to the top of the capsule, and the area appears dark. Conversely, when a negative field is applied, the white particles move up, and the area appears white. Ultimately, the technology may be useful for electronic paper—paper with circuits so that the text is not permanent, but can be changed by simply changing fields on appropriate particles.

5.4.2 Quantum Dots

Rather than encapsulating dye or passive particles for graphic arts applications, this work focuses on quantum dots encapsulation. Encapsulated quantum dots could potentially replace the black and white particles for applications such as E Ink to produce color instead of the current state-of-the-art black and white displays.
Figure 5.4-3: E Ink Display Technology

Quantum Dots (QDs) are three-dimensionally constrained semiconductor nanoparticles, typically between 1 nm and 100 nm in diameter [102]. They are interesting for their applications—biological tagging, room temperature lasers and electronic displays. Similar to atoms, QDs have a discrete emission spectrum as a result of the quantization of the energy levels available to the electrons. The wavelength of emitted light can be tailored by changing the size and/or composition of the QD.

Encapsulation of QDs, consisting of a cadmium selenide core and a zinc sulfide outer coating, has been demonstrated using microfluidics. CdSe QDs range from 10 Å to 60 Å in diameter [103]. As shown in Figure 5.4-4, when the dots are excited with energy that exceeds the bandgap, they exhibit a size-dependent color emission. The emission wavelength or color scales inversely with the size of the dot. The largest dots emit red light and the smallest dots emit blue light. Although all of the dots are manufactured using the same technique, the green dots are most straightforward to manufacture and, consequently, are used for development of the encapsulation technique.

QDs previously have been captured in a continuous polymer matrix [104] and microencapsulated using batch reactor technologies [105]. However, microfluidics offers several advantages over conventional encapsulation systems such as lower power consumption [90], laminar flow environment for precious and/or fragile materials and the potential for a monodisperse droplet size distribution.
Figure 5.4-4: Photoluminescence spectra of diluted solutions of QDs in hexane: from left (CdSe)ZnS QDs with emission peaks at 514 nm, 594 nm, 626 nm (13 Å, 23 Å, 28 Å core radii), respectively (Courtesy of Jinwook Lee, MIT)

In this work, microencapsulation of QDs using microfluidics is demonstrated. The QDs are encapsulated in a poly-urea shell using an integrated micromixer. The micromixer yields a lognormal particle size distribution with different averages based on operating conditions. The micromixer encapsulated the dots with good efficiency as evidenced by the absence of stray dots in the product samples.

5.4.3 Shell-formation Chemistry

Figure 5.4-5 illustrates the chemistry for the interfacial polymerization. Hexamethyl diisocyanate reacts with hexamethyl diamine in a step reaction polymerization to form a polyurea compound. This chemistry was identified prior to this work [105]. In principle, other chemistries could be used. For example, the isocyanate could be replaced with an acid chloride to make a nylon compound. However, this chemistry is not suitable for the QDs, which require a less harsh environment for a quality light emission.

5.4.4 Systems Testing

In the initial stage of the experiments, droplets were generated using the T contactor shown in Figure 5.3-1. The droplets were too large (>300 μm) to be stable and ruptured instead of forming capsules. Then, droplets were generated as shown in Figure 5.4-6 in the integrated microchemical system previously described in Chapter Three. The contacting layer is much thinner. Therefore, smaller, more stable droplet generation was favored.
Figure 5.4-5: Microencapsulation Chemistry

In each experiment, a 20 vol% isocyanate and 80 vol% toluene solution (A) was added to one set of inlet channels. A 2 wt% SDS and 98 wt% water solution (B) was added to the other set of inlet ports. Droplets were generated upon contact and collected in a vial containing a 2X excess of amine to polymerize the capsule wall. Various water-to-oil flow ratios were tested ranging from 5 to 400. The lower limit on the flow ratios tested was the stability of the droplets generated. If the flow ratio is too low or the droplets are too large, they rupture. The upper limit on the flow ratio is the ability to deliver fluids reliably with the syringe pump. If the total flow rate was too high, it exceeded the maximum back pressure of the syringe pump. If the oil flow rate was too low, the inherent pulsing of the syringe pump caused by the screw turning interfered with droplet formation.

Typically, an experiment began by priming the system with toluene and water. After the system reached steady state, the QD/isocyanate/toluene solution replaced the toluene solutions. Similarly, the SDS/water solution replaced the water solution. The QD droplets were collected in 0.2 ml samples into the amine/water solution. After ~1 minute, the capsules were examined with no magnification and then under 10X magnification to determine the quality of the microencapsulation.
Figure 5.4-6: Microencapsulation Experimental Process Flow

One challenge for the encapsulation was water contamination of the organic solvent leading to pre-polymerization. Consequently, the QDs would be captured into the isocyanate/water while in the syringe so that the capsules were outside of the droplets as shown in Figure 5.4-7. The key was to run the reaction promptly after preparation of the starting solutions.

Figure 5.4-7: Example of Encapsulation with Water Contamination in the Organic Phase

5.4.5 Capsule Characterization

5.4.5.1 Results

Capsules were studied using image analysis software. The details are given in Appendix E. Table 5.4-1 gives a summary of the results for the conditions investigated. QDs were not added to the organic phase during the capsule characterization stage of the study. Although more samples were collected than reported in Table 5.4-1, the quality for some of the samples was not high enough to analyze. A sample that could not be analyzed was one that had many ruptured capsules and/or no capsules. Often, the
ruptured capsules were not micropipetted so the sample images appear much cleaner than the samples.

Table 5.4-1: Summary of Microencapsulation Capsule Characterization

<table>
<thead>
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<th>sample #</th>
<th>flow ratio</th>
<th>total flow rate (ml/min)</th>
<th>mean diameter (µm)</th>
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<tr>
<td>1</td>
<td>20</td>
<td>0.06</td>
<td>22.9</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>0.6</td>
<td>18.0</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>1.5</td>
<td>8.6</td>
</tr>
<tr>
<td>4</td>
<td>256</td>
<td>2.56</td>
<td>9.4</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>3</td>
<td>6.5</td>
</tr>
</tbody>
</table>

The flow rates, flow ratios and particle diameters range from 0.06-3.0 ml/min, 20-256, and 6.5-22.9 µm respectively. The average diameter only varies by a factor of 3 over the wide range of conditions tested, which suggests that the process is quite stable.

The particles produced are typically spherical. Occasionally two particles fuse, but the primary problem with the particle geometry is deformation, as shown in Figure 5.4-8, which may be caused by asymmetric stress at the particles’ walls developed during the step reaction polymerization.

![Example of Deformed Capsules](image)

**Figure 5.4-8: Examples of Deformed Capsules**

**5.4.5.2 Discussion**

Based on the data presented in Table 5.4-1, the particle diameter scales inversely with the flow rate. This result is consistent with studies described previously [90-91] and results from T contactor studies. Figure 5.4-9 shows the Sample 4 particle size
distribution, which is typical for all of the samples analyzed. The capsule diameters range from 1-70\(\mu m\) with an average of 9.4 \(\mu m\) and a log normal size distribution. Figure 5.4-6 shows that 4 of the 5 organic feeds are at similar conditions with a water layer on either side. However, one of the feeds is next to a wall so the environment is different. Thus, a bimodal distribution might be anticipated given the homogenizer geometry. Although there is evidence of an underlying bimodal distribution with a peak at \(~5\mu m\) and another peak at \(~12\ \mu m\), there is still a number of much larger particles. This could be due to droplet fusion or maldistribution among the inner channels – possible because the fluid manifolding is internal.

The mixer with the channels individually accessed was tested, but, because the channels are individually accessed, the syringe flow rate was too low. Thus, the sample quality was bad compared to the integrated mixer.

![Graph: Integrated Micromixer Capsule Size Distribution](image)

Figure 5.4-9: Integrated Micromixer Capsule Size Distribution

Sample 5 was chosen for demonstration of microencapsulation of the QDs because that sample yielded the smallest particle diameter, which was the criterion for choosing processing conditions. Figures 5.4-10(a)-(b) shows a bright field image and the corresponding fluorescent image respectively. Figure 5.4-10(b) shows that the dots are homogeneously distributed in the particle, which gives an even brightness. Stray dots are not detected thus indicating the efficiency of the encapsulation.
Figure 5.4-10: Microencapsulated Quantum Dots Shown in (a) bright field mode (b) fluorescent mode

5.5 Conclusions

The studies reported in this chapter demonstrate that microchemical systems are tools for heterogeneous fluid contacting. Three types of flow profiles are observed: straight, wavy and segregated. For the segregated flow profile, the droplet size exhibited an inverse dependence on flow rate so that at higher flow rates, smaller droplets are formed. The spontaneous control exhibited for heterogeneous contacting lends itself to microencapsulation. Moreover, it is shown that polymer capsules can be formed by contacting an organic phase and an aqueous phase in a multi-layer contactor and collecting the effluent in a vial containing an amine to solidify the capsule wall. These capsules average from 6.5 μm to 22.9 μm depending on contacting conditions and exhibit a lognormal size distribution. It has been shown that the technique can be used to encapsulate QDs, which subsequently give a bright, homogeneous emission of green light. Although demonstration of the technique is thus far limited to QDs, it shows promise for many other materials such as titanium dioxide as well as biological systems.
Chapter Six

6 Conclusions and Recommendations for Future Work

6.1 Conclusions

The focus of this work has been a microchemical system with a multi-layer contactor for liquid-liquid processes. The systems were fabricated using, primarily, silicon and glass in which feature sizes ranged from approximately 10 to 500 \( \mu \text{m} \). The multi-layer contactor consisted of 10 alternating inlets for two components. The fluids entered the contactor, were focused by a converging channel, mixed and reacted in a 50 \( \mu \text{m} \) channel. The fully integrated liquid phase microchemical system consisted of the multi-layer contactor, a parallel plate heat exchanger, IR transmission detection and thin film metal temperature sensors. Quantitative data from these systems were obtained using on-chip optical detection methods, integrated thin film sensors, and off-chip pressure sensors. The chips were tested using a polymer block for fluid manifolding or by bonding tubing and an optical fiber connection directly to the chip. Additionally, flow visualizations and computational fluid dynamics (CFD) simulation tools elucidated system behavior.

For microchemical systems, length scales are short. Consequently, Reynolds numbers are small and the flow is laminar. When two or more streams are contacted in a homogeneous system, the flow is stable. The short length scales of the resulting lamellar stream enable rapid diffusion mixing for applications, such as kinetics studies or reaction-rate-limited operation of fast reactions. Instabilities are often observed for heterogeneous systems. When two or more streams are contacted, the combined flow can be lamellar, broken into alternating “slugs” of fluid, or one fluid dispersed as small droplets in another fluid. The lamellar arrangement has been emphasized for applications such as liquid-liquid extraction and phase transfer catalysis. However, the slug flow could be useful for applications such as multi-layer patterning, and the ability to generate dispersions would be useful for emulsions and encapsulation. Characterization and demonstration of homogeneous and heterogeneous applications of a liquid-liquid microchemical system
were addressed in this work. Specifically, kinetics studies and microencapsulation using microfluidics were investigated.

6.1.1 Sub-second Mixing

The mixing characteristics in a multi-layer liquid-liquid micromixer were investigated through experiments and simulations. Without optimization, sub-second mixing times were achieved. With adjustment of operational parameters, the mixer achieved 99% mixing in less than 25 ms. The good agreement between experiments and simulations demonstrated that the CFD simulation tools could be used to design and optimize multi-layer mixers. Pressure drop in the microfabricated mixer followed predictions for plane Poiseuille flow. Also, the analytical approximation of 99% extent-of-mixing (EOM) after 11 ms was the same order of magnitude as the experimental and predicted value of 25 ms, which suggested that the analytical solution can be employed for order-of-magnitude estimations of mixing times for optimized mixers.

The parabolic velocity profile, which is prominent for high aspect ratio structures, caused mixing pairs to have various widths. The velocity edge effects, which were significant over two channel widths, also caused a higher EOM at the top and bottom channel edges versus intermediate regions of the mixer. Based on the sub-second mixing times that were achieved, this work demonstrated a mixer that is suitable for conducting sub-second reactions without contact limitations.

6.1.2 Monolithic Integration

An integrated microchemical system that consisted of a multi-layer contactor, parallel plate heat exchanger, and thermal and optical sensing capabilities was fabricated. The parallel plate heat exchanger had an experimentally-determined overall heat transfer coefficient of 1420 ± 130 W/m²°C. The experimental value was lower than the theoretical value because of longitudinal heat conduction effects. The heat exchanger eliminated a 40°C rise in temperature over the reaction channel as evidenced by monitoring with thin-film, silicon temperature sensors.

On-chip IR transmission detection in an all-silicon T contactor from 4000-1000 cm⁻¹ was demonstrated. It was shown that IR transmission detection may be used to track the progress of the hydrolysis of propionyl chloride. Factors that adversely affected the signal
to noise ratio for IR transmission detection were substrate doping, reflections, and IR crystal thickness.

A final, monolithically integrated design was defined by using the circular chip platform from the IR studies with the mixer/heat exchanger. A probing region for detection, a metal shutter for accurate and repeatable probing, and titanium/platinum temperature sensors were added. All of the device surfaces were coated with silicon dioxide for three purposes: (1) reduction of interference fringes (2) chemical resistance to alkali-OH and (3) electrical insulation for active metal sensors.

6.1.3 Kinetics Studies
Microsystems operating continuously are tools for kinetics studies. As a demonstration, the monolithically integrated system facilitated monitoring the alkaline hydrolysis of methyl formate. This reaction follows second order kinetics and is fast with a half life of 70 ms for the conditions used in this study. Following the disappearance of the OH⁻ peak was found to be appropriate for monitoring the reaction. OH⁻ exhibited Beer's law absorbance especially at lower concentrations. The interference fringes characteristic of the silicon crystal as well as the broad OH⁻ peak necessitated trapezoidal integration to determine the relationship between the absorbance signal and the reactant concentration.

The reaction was followed using a premixed sample for the background absorbance, and concentration data were extracted at 294 K. The plotting form with time on both the x and y axes exhibited the most linear relationship. The rate constant that was extracted, 31.0 ±1.6 L-mol⁻¹s⁻¹, was in good agreement with the literature value of 30.1 ±0.6 L-mol⁻¹s⁻¹. Moreover, the half life of the reaction was reduced by an order of magnitude with no sample post processing as compared to the literature study. In addition, cooling fluids in the heat exchanger allowed data to be gathered at multiple temperatures. The curves obtained were consistent with literature results for 296 K, 290 K and 284 K.

6.1.4 Microencapsulation using Microfluidics
Not only are microchemical systems tools for kinetics studies, but they are also tools for heterogeneous fluid contacting. Three types of flow profiles were observed: lamination, segregation and dispersion. For the segregated flow profile, the droplet size
exhibited an inverse dependence on flow rate so that at higher flow rates, smaller droplets were formed. The self regulation of the droplet size was quite good. This control lends itself to microencapsulation. Contacting an organic phase and an aqueous phase in a multi-layer contactor and collecting the effluent in a vial containing an amine formed polymer capsules. These capsules averaged from 6.5 μm to 22.9 μm depending on contacting conditions and exhibited a lognormal size distribution. It was further demonstrated that the technique could be used to encapsulate QDs with a bright, homogeneous emission of green light. Although demonstration of the technique was limited to QDs, it showed promise for other materials such as titanium dioxide as well as biological systems.

6.2 Recommendations for Future Work

One of the impediments of microfluidics development has been in understanding the limits of the technology from a practical standpoint. Issues such as failure mechanisms, testing protocols, and packaging should be emphasized. A better understanding of preventing channel obstruction, delivering fluids, solids handling and bubble formation in the context of rapid, exothermic reactions needs to be gained. A thorough distillation of the existing literature in the form of a review may be all that is required. However, it presumed that fundamental studies are necessary. Tools such as confocal microscopy for depth profiling and infrared cameras for thermal and thru-silicon imaging will provide insight.

Once a better understanding of channel obstruction mechanisms and solids handling is gained, the concept of microencapsulation on a chip can be taken one step farther by performing the amine contacting on-chip. Initially, the amine contacting region could be very large – ideally the same order of magnitude as the vial currently used for contacting. The smaller surface-to-volume ratio relative to a traditional microfluidic system would reduce the potential for device failure due to channel obstruction and provide insight into integrating the two steps. Gradually, scaling down the size of the region would reveal issues that need to be addressed to fabricate a device so that all steps are performed on a chip with a moderate footprint and minimal bonded layers. Then, focus should shift to encapsulation of other nanoparticles and biomaterials.
Multi-layer fabrication, the other materials application discussed in this work, will require fundamental studies to confirm concept feasibility.

Microfabrication permits the construction of very complex devices. A few types of contacting and heat transfer schemes are quite popular. For contacting, T, lamellar, bifurcated, and micronozzle contactor designs are preferred. However, much of the design space remains unexplored. Other contactors such as one with tangential inlets, a co-axial contactor (See Appendix F), or mixing over a sphere [81] might prove enabling. Tangential contacting, illustrated in Figure 6.2-1, typically produces a whirlpool that might enhance diffusion mixing while minimizing energy losses associated with impinging flows. A co-axial contactor would allow contacting of two fluids while one fluid is protected from a wall. This type of system could have applications including transfer of viscous fluids [106], rapid mixing [49], and suppression of heterogeneous over homogeneous reactions.

For heating, parallel plate heat exchangers, thin film resistive heaters and mounting chips on heated blocks are accepted methods. The concept of energy integration, running endothermic and exothermic reactions in parallel without adding energy externally, has been explored theoretically but hasn’t been realized experimentally [63]. Other possibilities for heating include using lasers and viscous heating. A laser would allow external, yet local heating without common concerns about electron migration of thin film metals [107]. Pressure drops in microchannels are large. This limitation might be harnessed for viscous heating. Theoretical investigations would be necessary to determine concept feasibility. For cooling, evaporation or adiabatic liquid expansion may be beneficial approaches. Investigation of these and other prospective methods might further expansion of microfluidic applications.
Figure 6.2-1: Schematic of a Tangential Contactor

Alkaline hydrolysis reactions were investigated in this work. Other types of rapid liquid-liquid reactions as well as extractions may also be suitable for microfluidics studies. Ultimately, these reaction systems could be scaled out for chemical production. Doraiswamy and Sharma have identified a number of interesting reactions such as nitrations and alkylations [108].

Another potential area for future research is at the intersection of biology, microfluidics and infrared spectroscopy. Major opportunities for the fusion of the three lie in fundamental studies of protein folding and adsorption as well as clinical chemistry. Pollack et al. investigated the time resolved collapse of a folding protein observed with small angle x-ray scattering [84]. They used a microfluidic mixer with on-chip x-ray scattering monitoring. The testing apparatus was very similar to the system used for chemical kinetics studies in this work. X-ray scattering provides information about the size of the protein, but IR spectroscopy could, presumably, provide more chemical information. For clinical chemistry, progress has been made in using IR spectroscopy for diagnostic, pathological and non-invasive in vivo monitoring [109-111]. Specifically, the comparison of different infrared measurement techniques in the clinical analysis of biofluids has been conducted. IR spectroscopy for biological samples is “reagentless, fast and readily automated [109].” Issues such as interference fringes were encountered in
those studies as well. Once these issues are resolved generally, the technique will be ready for widespread application.

The area of liquid microfluidics is rich with problems to solve. Practical issues need to be addressed and much design space remains to be explored. However, the advantages of microfluidics guarantees the opportunity for impact in applications throughout chemistry, materials, and biology.
7 References


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[87] H. M. Humphreys and L. P. Hammet, "Rate measurements on fast reactions in the stirred flow reactor; the alkaline hydrolysis of methyl and ethyl formate," *Journal of the American Chemical Society*, 78, 521-524, 1956.


8 Appendices

Step-wise sequences of the systems fabricated for this work as well as the experimental protocol for image analysis are detailed in these appendices. Fabrication was performed in the Integrated Circuits Laboratory (ICL) and the Technology Research Laboratory (TRL) at MIT.

8.1 Appendix A: Micromixer Fabrication

Mixer fabrication begins with an SOI wafer or a double side polished silicon wafer (when the inlet ports are individually contacted).

Table 8.1-1: Micromixer Process Flow

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<th>Comments</th>
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<td>clean wafer</td>
<td>acid hood</td>
<td>piranha</td>
</tr>
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<td>TRL</td>
<td>2*</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>3*</td>
<td>coat thin film silicon with 7 μm of photoresist</td>
<td>coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>4*</td>
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<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
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<td>expose for 300 s</td>
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<td>Figure 8.1-1</td>
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<tr>
<td>TRL</td>
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<td>develop</td>
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<tr>
<td>TRL</td>
<td>7*</td>
<td>postbake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
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<td>Equipment</td>
<td>Duration</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>------------------------------------------------------</td>
<td>------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>etch silicon to buried oxide</td>
<td>sts1</td>
<td>200 min</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>strip photoresist</td>
<td>acid hood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>double clean</td>
<td>acid hood</td>
<td>piranha</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>anodically bond drilled pyrex for inlet ports</td>
<td>EV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>anodically bond pyrex cap</td>
<td>EV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>dice wafer</td>
<td>diesaw</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*steps omitted for individually contacted inlets*

Figure 8.1-1: Mixer Inlets Mask
Figure 8.1-2: Mixer Channels Mask

Figure 8.1-3: Mixer Channels for Individually Contacted Inlets Mask
8.2 Appendix B: Integrated Fabrication

Table 8.2-1: Integrated Microchemical System Fabrication

Integrated microchemical system fabrication begins with an SOI wafer with a 2.2 μm thick silicon thin film.

<table>
<thead>
<tr>
<th>Lab</th>
<th>Step</th>
<th>Process Description</th>
<th>Machine</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICL</td>
<td>1</td>
<td>phosphorus dope thin film silicon</td>
<td>POCl₃</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>2</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>3</td>
<td>coat wafer with 1 μm of photoresist</td>
<td>coater</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>4</td>
<td>prebake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>5</td>
<td>expose for 25s</td>
<td>kaligner 2</td>
<td>Figure 8.2-1</td>
</tr>
<tr>
<td>TRL</td>
<td>6</td>
<td>develop photoresist</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>7</td>
<td>postbake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>8</td>
<td>etch silicon to buried oxide</td>
<td>sts1</td>
<td>1 minute</td>
</tr>
<tr>
<td>TRL</td>
<td>9</td>
<td>piranha clean</td>
<td>acid hood</td>
<td>piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>10</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>11</td>
<td>coat with 1 μm of photoresist</td>
<td>coater</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>12</td>
<td>prebake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>13</td>
<td>expose for 300 s</td>
<td>kaligner 2</td>
<td>Figure 8.2-2</td>
</tr>
<tr>
<td>TRL</td>
<td>14</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>15</td>
<td>postbake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>16</td>
<td>etch silicon to buried oxide</td>
<td>sts1</td>
<td>1 minute</td>
</tr>
<tr>
<td>TRL</td>
<td>17</td>
<td>etch oxide</td>
<td>acid hood</td>
<td>BOE</td>
</tr>
<tr>
<td>TRL</td>
<td>18</td>
<td>strip photoresist</td>
<td>acid hood</td>
<td>piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>19</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>20</td>
<td>coat substrate with 10 μm of photoresist</td>
<td>coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>21</td>
<td>prebake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>22</td>
<td>expose for 500 s</td>
<td>kaligner 2</td>
<td>Figure 8.2-3</td>
</tr>
<tr>
<td>TRL</td>
<td>23</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>24</td>
<td>postbake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>Step Description</td>
<td>Equipment</td>
<td>Time</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>------------------------------------------------------</td>
<td>-----------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>mount to a handle wafer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>etch silicon to buried oxide</td>
<td>sts1</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>strip photoresist</td>
<td>acid hood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>double clean</td>
<td>acid hood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>anodically bond drilled pyrex for inlet ports</td>
<td>EV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>anodically bond pyrex cap</td>
<td>EV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>dice wafer</td>
<td>diesaw</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 8.2-1: Temperature Sensors Mask

124
Figure 8.2-2: Integrated Microchemical System Inlet Ports Mask

Figure 8.2-3: Integrated Microchemical System Channels Mask
8.3 Appendix C: IR T Contactor Fabrication

IR T contactor fabrication begins with two double side polished silicon wafers.

<table>
<thead>
<tr>
<th>Lab</th>
<th>Step</th>
<th>Process Description</th>
<th>Machine</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRL</td>
<td>1</td>
<td>clean</td>
<td>acid hood</td>
<td>piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>2</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>3</td>
<td>coat with 7 μm of photoresist</td>
<td>coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>4</td>
<td>prebake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>5</td>
<td>expose 300 s</td>
<td>ksaligner 2</td>
<td>Figure 8.3-1</td>
</tr>
<tr>
<td>TRL</td>
<td>6</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>7</td>
<td>postbake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>8</td>
<td>mount to handle wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>9</td>
<td>etch silicon for 50 μm</td>
<td>sts2</td>
<td>20 minutes</td>
</tr>
<tr>
<td>TRL</td>
<td>10</td>
<td>strip photoresist</td>
<td>acid hood</td>
<td>piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>11</td>
<td>rca clean</td>
<td>rca</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>12</td>
<td>fusion bond blank wafer and etched wafer</td>
<td>EV</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>13</td>
<td>anneal bonded wafer</td>
<td>tubeb2</td>
<td>1 hour/1100°C</td>
</tr>
<tr>
<td>TRL</td>
<td>14</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>15</td>
<td>coat with 10 μm of photoresist</td>
<td>coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>16</td>
<td>prebake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>17</td>
<td>expose for 500 s</td>
<td>ksaligner 2</td>
<td>Figure 8.3-2</td>
</tr>
<tr>
<td>TRL</td>
<td>18</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>19</td>
<td>postbake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>20</td>
<td>mount to handle wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>21</td>
<td>etch silicon inlet ports in etched wafer</td>
<td>sts2</td>
<td>200 minutes</td>
</tr>
<tr>
<td>TRL</td>
<td>22</td>
<td>strip photoresist</td>
<td>acid hood</td>
<td>piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>23</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>24</td>
<td>coat with 10 μm of photoresist</td>
<td>coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>25</td>
<td>prebake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>26</td>
<td>expose for 500 s</td>
<td>ksaligner 2</td>
<td>Figure 8.3-3</td>
</tr>
<tr>
<td>TRL</td>
<td>27</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>28</td>
<td>mount to a handle wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>----</td>
<td>-------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>29</td>
<td>release wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>30</td>
<td>strip photoresist</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

sts2 200 minutes
acidhood / piranha/acetone
photowet

Figure 8.3-1: IR T Contactor Channels Mask

Figure 8.3-2: IR T Contactor Inlet Ports Mask
8.4 Appendix D: Fully Integrated System Fabrication

Fully integrated system fabrication begins with two double side polished silicon wafers.

<table>
<thead>
<tr>
<th>Lab</th>
<th>Step</th>
<th>Process Description</th>
<th>Machine</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICL</td>
<td>1</td>
<td>deposit 0.5 µm of oxide</td>
<td>concept 1</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>2</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>3</td>
<td>coat with 1 µm of photoresist</td>
<td>coater</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>4</td>
<td>prebake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>5</td>
<td>expose for 45 s</td>
<td>ksaligner 2</td>
<td>Figure 8.4-1</td>
</tr>
<tr>
<td>TRL</td>
<td>6</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>7</td>
<td>postbake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>8</td>
<td>etch oxide</td>
<td>acid hood</td>
<td>BOE</td>
</tr>
<tr>
<td>TRL</td>
<td>9</td>
<td>strip photoresist</td>
<td>acid hood</td>
<td>piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>10</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>11</td>
<td>coat with 10 µm of photoresist</td>
<td>coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>12</td>
<td>prebake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>13</td>
<td>expose for 500 s</td>
<td>ksaligner 2</td>
<td>Figure 8.4-2</td>
</tr>
<tr>
<td>TRL</td>
<td>14</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>15</td>
<td>postbake</td>
<td></td>
<td>30 minutes/90°C</td>
</tr>
<tr>
<td>TRL</td>
<td>16</td>
<td>Mount to a 6&quot; handle wafer</td>
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<td></td>
</tr>
<tr>
<td>TRL</td>
<td>17</td>
<td>Etch Si</td>
<td>sts2</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>18</td>
<td>Strip photoresist and dismount from handle wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>19</td>
<td>Mount to a handle wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>20</td>
<td>Etch silicon using oxide mask</td>
<td>sts2</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>21</td>
<td>Strip oxide</td>
<td>Acid hood</td>
<td>BOE</td>
</tr>
<tr>
<td>TRL</td>
<td>22</td>
<td>Rca clean</td>
<td>Rca</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>23</td>
<td>Grow thermal oxide on blank and etched wafer</td>
<td>Tube a2</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>24</td>
<td>Fusion bond blank and etched wafer</td>
<td>EV</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>25</td>
<td>Anneal bonded wafers</td>
<td>Tubeb2</td>
<td>1 hour/1100°C</td>
</tr>
<tr>
<td>TRL</td>
<td>25</td>
<td>HmDS</td>
<td>HmDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>26</td>
<td>Coat with 10 μm of photoresist</td>
<td>Coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>27</td>
<td>Prebake</td>
<td>30 minutes/90°C</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>28</td>
<td>Expose for 500 s</td>
<td>Ksaligner 2</td>
<td>Figure 8.4-3</td>
</tr>
<tr>
<td>TRL</td>
<td>29</td>
<td>Develop</td>
<td>Photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>30</td>
<td>Postbake</td>
<td>30 minutes/90°C</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>31</td>
<td>Mount to a handle wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>32</td>
<td>Etch silicon inlet ports in blank wafer</td>
<td>Sts2</td>
<td>200 minutes</td>
</tr>
<tr>
<td>TRL</td>
<td>33</td>
<td>Strip photoresist</td>
<td>Acid hood</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>34</td>
<td>HmDS</td>
<td>HmDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>35</td>
<td>Coat with 10 μm of photoresist</td>
<td>Coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>36</td>
<td>Prebake</td>
<td>30 minutes/90°C</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>37</td>
<td>Expose for 500 s</td>
<td>Ksaligner 2</td>
<td>Figure 8.4-4</td>
</tr>
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<td>Develop</td>
<td>Photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>39</td>
<td>Postbake</td>
<td>30 minutes/90°C</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>40</td>
<td>Mount to a handle wafer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>41</td>
<td>Release wafers</td>
<td>Sts2</td>
<td>200 minutes</td>
</tr>
<tr>
<td>TRL</td>
<td>42</td>
<td>Strip photoresist/dismount released die from handle wafer</td>
<td>Acid hood</td>
<td>Piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>43</td>
<td>HmDS</td>
<td>HmDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>44</td>
<td>Coat with photoresist</td>
<td>Coater</td>
<td>AZ (image)</td>
</tr>
</tbody>
</table>
TRL 45 prebake
TRL 46 expose for 45 s
TRL 47 postbake
TRL 48 flood exposure
TRL 49 develop
TRL 50 deposit Ti/Pt
TRL 51 metal lift-off

ksaligner 2
hot plate
ksaligner 2
photowet-gold

reversal)
25 minutes
Figure 8.4-5
~2 minutes
5 minutes

100Å/ 300Å

Figure 8.4-1: Fully Integrated Microchemical System Probing Region Mask
Figure 8.4-2: Fully Integrated Microchemical System Channels Mask

Figure 8.4-3: Fully Integrated Microchemical System Inlet Ports Mask
8.5 Appendix E: Sample Preparation and Image Analysis

After the sample is collected, it is mixed and a 0.7 μl sample is placed on a microscope slide. Pictures of the sample are grabbed at different positions so that all of the capsules are captured. Scion Image, image analysis software, was used to determine the capsule diameters. The software fits the particle outlines to major and minor axes of an ellipse and calculates the area of the particle. The particles are spherical so the major
and minor axis should be equal to the particle diameter. The particle diameter was calculated as \((4\times A/\pi)^{1/4}\) where \(A =\) capsule area and \(\pi = \text{pi}\).

Figure 8.5-1 shows an example of an image before (a) and after (b) processing. With proper thresholding, the software selects only the capsules. The software assigns each capsule a number for future reference. Also, the software can be programmed to select only capsules within a certain size range (e.g. 5-6 \(\mu\text{m}\)).

For most samples, the capsule density was so high that the samples needed to be diluted before the images were captured. Figure 8.5-2 (a) shows an example of a sample that was too dense prior to dilution. The particles are overlapping so it is not possible to get an accurate count of particle diameters. Figure 8.5-2 (b) shows the particles after a 3X dilution in water. No particles are overlapping so the analysis is correct. The 3X dilution standard was employed for all sample analysis.

![Figure 8.5-1: Image Analysis (a) raw image and (b) processed image](image1)

![Figure 8.5-2: Processed Images (a) undiluted (b) diluted](image2)
8.6 Appendix F: Co-Axial Contactor

A co-axial contactor in which one fluid is completely shielded from an outer wall by a second fluid was fabricated. Figures 8.6-1, 8.6-2 and 8.6-3 illustrate the mask layers. Figure 8.6-4(a) shows a schematic of the nozzle with an inset optical micrograph of the actual nozzle. Figure 8.6-4(b) shows a cross section of the nozzle. The system is fabricated in silicon and capped by PDMS. Two aqueous solutions, with and without a fluorescent dye flowed through the outer channel and nozzle respectively. Cross sections of the channel indicated in Figure 8.6-4(b) are shown in Figures 8.6-4(c)-(e). At the nozzle exit, the fluorescence indicates that the fluid is shielded from the wall. A short distance down the channel, the fluorescein is quenched due to molecular diffusion of the fluorescein from the outer layer to the inner layer.

Co-axial contactor fabrication begins with two double side polished silicon wafers. Each step is performed on both of the starting wafers. However, after Step 5, the two wafers are exposed with different masks—one of which has the inlet port for the nozzle.

Table 8.6-1: Co-Axial Contactor Process Flow

<table>
<thead>
<tr>
<th>Lab</th>
<th>Step</th>
<th>Process Description</th>
<th>Machine</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICL</td>
<td>1</td>
<td>deposit 0.5 μm of oxide on one side of 2 wafers</td>
<td>concept1</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>2</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>3</td>
<td>coat with 1μm of photoresist</td>
<td>coater</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>4</td>
<td>prebake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>5</td>
<td>expose for 45 s</td>
<td>ksaligner2</td>
<td>Figure 8.6-1(a)</td>
</tr>
<tr>
<td>TRL</td>
<td>6</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>7</td>
<td>postbake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>8</td>
<td>etch oxide</td>
<td>acidhood</td>
<td>BoE</td>
</tr>
<tr>
<td>TRL</td>
<td>9</td>
<td>strip photoresist</td>
<td>acidhood</td>
<td>piranha</td>
</tr>
<tr>
<td>TRL</td>
<td>10</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>11</td>
<td>coat with 10 μm of photoresist</td>
<td>coater</td>
<td>AZ 4620</td>
</tr>
<tr>
<td>TRL</td>
<td>12</td>
<td>prebake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>13</td>
<td>expose for 500 s</td>
<td>ksaligner2</td>
<td>Figure 8.6-2(a)/(b)</td>
</tr>
<tr>
<td>TRL</td>
<td>14</td>
<td>develop</td>
<td>photowet</td>
<td></td>
</tr>
<tr>
<td>TRL</td>
<td>Step Description</td>
<td>Comment</td>
<td></td>
<td></td>
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<td>---------</td>
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<td></td>
</tr>
<tr>
<td>15</td>
<td>postbake</td>
<td>30 minutes/90°C</td>
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<tr>
<td>16</td>
<td>mount to a 6” handle wafer</td>
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<tr>
<td>17</td>
<td>etch Si</td>
<td>sts2</td>
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<td></td>
</tr>
<tr>
<td>18</td>
<td>strip photoresist and dismount from handle wafer</td>
<td>acid hood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>continue to etch using oxide mask</td>
<td>sts2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>strip oxide</td>
<td>acidhood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>RCA clean</td>
<td>rca</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>fusion bond 2 etched wafer</td>
<td>EV</td>
<td></td>
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<tr>
<td>23</td>
<td>anneal bonded wafer</td>
<td>tube b2 1 hour/1100°C</td>
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<tr>
<td>24</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
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<tr>
<td>25</td>
<td>coat with 10μm of photoresist</td>
<td>coater AZ 4620</td>
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<td></td>
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<tr>
<td>26</td>
<td>prebake</td>
<td>30 minutes/90°C</td>
<td></td>
<td></td>
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<tr>
<td>27</td>
<td>expose for 500 s</td>
<td>ksaligner2 Figure 8.6-3(a)</td>
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<tr>
<td>28</td>
<td>develop</td>
<td>photowet</td>
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<td></td>
</tr>
<tr>
<td>29</td>
<td>etch Silicon top outer channel</td>
<td>sts2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>strip photoresist</td>
<td>acid hood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>HMDS</td>
<td>HMDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>coat with 10 μm of photoresist</td>
<td>coater AZ 4620</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>prebake</td>
<td>30 minutes/90°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>expose for 500 s</td>
<td>ksaligner2 Figure 8.6-3(b)</td>
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<td></td>
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<tr>
<td>35</td>
<td>develop</td>
<td>photowet 4 minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>etch bottom outer channel</td>
<td>sts2    200 minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>strip photoresist/dismount released die from handle wafer</td>
<td>acid hood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>punch holes in inlet PDMS</td>
<td></td>
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<tr>
<td>39</td>
<td>bond blank PDMS cap and inlet ports layer</td>
<td>O₂ plasma</td>
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</tbody>
</table>
Figure 8.6-1: Co-axial contactor Nozzle Mask: (a) full mask (b) top view of nozzle area (c) Step 9 cross section
Figure 8.6-2: Co-axial Contactor Masks for Outer Channel Portion Nearest the Nozzle:
full mask for outer channel half with (a) and without (b) an inlet (c) top views of
nozzle areas for a,b (d) Step 12 cross section (e) Step 17 cross section (f) Step 20
cross section (g) Step 23 cross section
Figure 8.6-3: Masks for Outer Channel Half Farthest from the Nozzle: full mask for outer channel half with (a) and without (b) an inlet (c) top views of the nozzle portion of a,b (d) Step 30 cross section (e) Step 39 cross section
Figure 8.6-4: Co-axial Contactor (a) schematic and optical micrograph (inset) of nozzle area (b) cross-section of co-axial contactor indicating z positions for c-e (c) cross section at z = +50 μm (d) cross section at z = +150 μm (e) cross section at z = +170 μm