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Modeling of misalignment effects in microfluidic interconnects for modular bio-analytical chip applications

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Abstract

Minimizing misalignments during the interconnection of microfluidic modules is extremely critical to develop a fully integrated microfluidic device. Misalignments arising during chip-to-chip or world to chip interconnections can be greatly detrimental to efficient functioning of microfluidic devices. To address this problem, we have performed numerical simulations to investigate the effect of misalignments arising in three types of interconnection methods: a) end-to-end interconnection b) channel overlap when chips are stacked on top of each other and c) tube-in-reservoir misalignment occurring due to the offset between the external tubing and the reservoir. For the case of end-to-end interconnection, the effect of misalignment was investigated for 0, 13, 50, 58, and 75% reduction in the available flow area at the location of geometrical misalignment. In the channel overlap interconnection method, various possible misalignment configurations were simulated by maintaining the same amount of misalignment (75% flow area reduction). The effect of misalignment in a tube-in-reservoir interconnection was investigated by positioning the tube at an offset of 164 μ m from the reservoir center. All the results were evaluated in terms of the equivalent length of a straight pipe. The effect of Reynolds number (Re) was also taken into account by performing additional simulations of aforementioned cases at Re ranging between 0.075 – 75. Correlations were developed and the results were interpreted in terms of equivalent length (Le). Equivalent length calculations revealed that the effect of misalignment in tube-in-reservoir interconnection method was the least significant when compared to the other two methods of interconnection.

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1. Introduction

Microfluidics has become one of the fastest growing technologies over the past two decades. The ability to modularize these microfluidic devices by assembling various components to accomplish wide range of functionality has proven to be indispensable. A typical modular device consists of functional modules for sample preparation, purification, detection to name a few [1, 2]. Once assembly is achieved these modular devices can be used to accomplish wide range of functions [3, 4]. To accomplish certain functionality, often these devices rely on transport of fluids or reagents from one chip to the other through fluidic interconnects. A variety of fluidic interconnection schemes have been reported using interlocking finger joints for vertically stacked modules [5], stacking modules by silica capillaries [6], plasma assisted bonding [7] or O-rings [8]. However, providing fluidic interconnections for efficient transport encompasses several challenges since these interconnects should be designed to operate with minimal requirements such as being leak free, having low dead volumes and minimal pressure drop. Other parameters like ease of use and biocompatibility may also need consideration depending on the application. As mentioned, one such critical requirement to achieve successful integration of a microfluidic chip for biological and chemical applications is the minimization of pressure drop. The pressure drop in these microfluidic devices can occur in various flow situations like valves, reaction chambers, T-junctions, mixers, bends and corners, tubing reservoir junctions etc. In addition, one of the major sources of pressure drop is the possible misalignment of interconnected microchannels when chips are connected end-to-end, stacked on top of each other or connected through tube in reservoir. For example in the case of extreme misalignment between a tubing and a microchannel in a pressure driven flow, it was shown that there is an additional pressure drop of 800 Pa when compared to the case with no misalignment for the same flow rate [9]. The misalignments occurring during the alignment of polymer microfluidic chips can be upto 100 μm in the extreme cases [10, 11]. Misalignments can have adverse effect in both pressure driven flows and electrokinetic flows by causing sudden transition in flow area. In electrokinetic flows, misalignments often cause changes in electric field, pressure drop and flow rates. The effect of sudden area changes in electrokinetic flows have been shown [12, 13] to drastically distort velocity profile causing increased dispersion. In a recent work [14], we have reported the effect of these sudden transitions in electrokinetic flows and developed correlations to estimate potential drop, pressure drop and flow rate. In addition, we also quantified the increased dispersion and loss of sample resolution in electrokinetic flows when sudden geometric transition arises during fluidic interconnections. However, to the best of our knowledge, the effect of misalignments on the flow pertaining to fluidic interconnection has not been studied. Owing to the extreme importance of quantifying the misalignments in the assembly of modular devices, in the present work, numerical simulations of pressure driven flows were performed to investigate the possible effects of geometrical misalignments in three different interconnection methods: end-to-end interconnection, interconnection through channel overlap and tube-in-reservoir interconnection.

2. Numerical Simulations

Numerical simulations were performed using FLUENT™. The governing equations are the continuity equation and Navier Stokes,

$$\vec{\nabla} \cdot \vec{v} = 0 \quad (1)$$

$$\rho \left(\frac{\partial \vec{v}}{\partial t} + \vec{v} \cdot \vec{\nabla} \vec{v} \right) = -\vec{\nabla} P + \mu \vec{\nabla}^2 \vec{v} \quad (2)$$

which were solved to resolve the full three dimensional flow field in the microchannel. Here ρ is the fluid density (assumed water properties), $\vec{v}$ is the velocity, P is the pressure and μ is the viscosity of the fluid. Although majority of microfluidic devices employ low Reynolds number flows, there are several microfluidic applications where high Reynolds numbers are encountered. For example, in transdermal drug delivery, piezoelectric actuators are used to produce temporally controlled high Reynolds number ($\sim Re=100$) micro-scale fluid streams for skin penetration, vesicle formation and drug targeting applications [15]. In applications such as valveless pumping for integration onto microfluidic lab-on-chip (LOC) systems or chip cooling, micropumps are used to achieve Reynolds numbers in the range of 100-500 [16]. In addition, high Reynolds numbers are also encountered in microfluidic LOC platform for fluid delivery [17]. In our current work, to expand the dynamic range of the data, the

Reynolds number (Re) was varied between the range 0.075 $\leq Re \leq 75$ where $Re = \frac{\rho V D_h}{\mu}$, with

D_h being hydraulic diameter (i.e. $D_h = \frac{4A}{P}$ where A is the cross-sectional area and P is perimeter). For the inlet boundary condition, a constant velocity corresponding to the Reynolds number was specified at the inlet of the microchannel. A no slip boundary condition was imposed on all other boundaries and zero gauge pressure was specified at outlet. The no slip boundary condition and the simulations are very valid as the Knudsen number (Kn) is < 0.001 for the length scales used in the current work and hence within the continuum limit. For example, such types of modeling and simulations have been employed to model the effect of roughness on the friction factor in microchannels [18, 19, 14]. In the current work, the grid for simulations was varied between 0.5 million cells to 2 million cells depending on the misalignment configuration and the flow behavior at different Reynolds numbers. The mesh was sufficiently refined and grid convergence checked in all the cases to ensure that the results are grid independent.

3. Modeling

3.1. Misalignment effects in end-to-end interconnection

The simulation domain shown in Fig. 1a consists of two channels with rectangular cross section and connected by an end-to-end interconnection scheme. The length, width and depth of the channel were $L=1000\mu m$, $w=50\mu m$ and $H=150\mu m$ respectively. A geometrical mismatch was introduced at the junction of the two channels so as to cause a reduction in the available flow area at the mismatch plane as shown in Fig. 1b. The cross sectional area of

the channel was denoted by A_1 and the reduced available flow area due to the misalignment at the mismatch plane was denoted by A_2 . Similar cross-sectional area convention (i.e. A_1 & A_2) was employed for all interconnection schemes. The effect of misalignment was

investigated for varying flow area ratios ($\frac{A_1}{A_2}$) of 1: 1, 1.14: 1, 2: 1, 2.4: 1 and 4: 1 where the ratio $\frac{A_1}{A_2}=1$ corresponds to the case of no geometrical misalignment (i.e. 0%) and $\frac{A_1}{A_2}=4$ corresponds to extreme case of geometrical misalignment (i.e. 75% reduction in the available flow area). To account for the effect of geometrical mismatch on the flow behavior, the Reynolds number in each case was varied between 0.075 $\leq$ Re $\leq$ 75 i.e. Re=0.075, 15, 25, 37.5 and 75.

3.2. Misalignment effects in interconnection through channel overlap

The effect of geometrical misalignment in the case of interconnection through channel overlap was investigated. This type of misalignment frequently occurs during the alignment of two fluidic chips. For example, Fig. 2 shows the case of two microfluidic chips being aligned through V-grooves which is a case of interconnection through channel overlap. The misalignment in such cases can be upto $103 \pm 6 \mu\text{m}$ in the direction of X-axis and $16 \pm 4 \mu\text{m}$ in the direction of Y-axis [11]. Additionally, such type of channel overlap interconnection scenarios could arise in vertically stacked modular devices for high throughput applications [20] where fluid needs to be transported from one chip to the other efficiently. We have previously developed assembly tolerance model to predict assembly accuracy from the variations in geometry of passive alignment structures using Monte Carlo methods and achieved good agreement with experiments and simulations [21]. However, it also is important to model the effect of these misalignments on the pressure drop. Numerical simulations can be greatly aid in developing correlations to optimize fluidic design in such situations. To model the misalignment through channel overlap interconnection scheme, several possible configurations were studied. The top view of various misalignment configurations possible when chips are stacked on one another are shown in Fig. 3 and given the nomenclature from M1 to M6. The dimensions of the channels considered had width of $50 \mu\text{m}$, depth of $150 \mu\text{m}$ and a length of $1000 \mu\text{m}$. In Fig. 3, the dimensions of the channel and the misalignment offset are given in terms of the width (i.e. $1000 \mu\text{m}$ length is depicted as $20w$ with width being $w = 50 \mu\text{m}$). The configuration M1 has an area ratio $A_1: A_2 = 3:1$ while the cases M2, M3, M5 and M6 have an area ratio of 4:1. In order to quantify the effects of misalignment, all these cases were compared against configuration M4 that had the maximum available flow area at the mismatch plane i.e. $A_1: A_2 = 1:1$.

3.3. Misalignment effects in tube-in-reservoir interconnection

The misalignment arising between tubing and a reservoir had been dealt in the present study owing to its importance in fluidic interconnection. Often the drilled hole is not located exactly at the center of the reservoir, resulting in an offset from the center. This type of misalignment can also arise during the bonding of the external tubing to the chip. For example, Fig. 4a and 4b show the simulated models for the case of perfect alignment between the center of reservoir and tubing and the case of offset between centers respectively. The case of perfect alignment is an ideal one, which is seldom obtained during

interconnection. In order to estimate the amount of misalignment commonly occurring in practice, PMMA (Poly-methyl methacrylate) chips were hot embossed using a Jenoptik HEX 02 (Jena, Germany) on 1.5 mm thick PMMA sheets (Plexiglas MC, Altulals, Inc., Philadelphia, PA, USA) with a brass mold insert. The chips were drilled using a drilling machine (MicroLux, Japan) with 5000 rpm and #70 or #71 drill bits (Carbide drill, Kennametal Inc., Latrobe, PA USA) at 5000 rpm. The drilled chips were cleaned using ultrasound (Branson, Danbury, CT, USA) with 90% demonized water (DI water) mixed with 10% Isopropyl alcohol (IPA). A 1/32 inch PEEK tube (IDEX Health & Science LLC, Oak Harbor, WA) was connected on the drilled chip for the tubing and investigate the offset under a microscope. One extreme case of offset between tubing and reservoir obtained are shown in Fig. 5a and 5b. It can be observed from Fig. 5b that the tubing offset from the center of the reservoir can upto as 164 μ m. To accurately simulate the misalignment in tube-in-reservoir interconnection, the dimensions of the tubing and reservoir used in the simulation (i.e. 85 μ m and 500 μ m radii respectively) were comparable to the ones shown in Fig. 5a and 5b., These values were reasonable as variations in the radius of the tubing due to the manufacturing tolerance are expected and can be upto $\pm 6.35\mu$ m. For example radius of the tubing shown in Fig. 5b (i.e. 93 μ m) differs by $\sim 5.5\mu$ m from the tubing radius shown in Fig. 5a (i.e. 87.5 μ m). For all the cases simulated, the fluid in the channel was assumed to have the properties of water.

4. Results and discussions

When an incompressible fluid flows through the misalignment, the abrupt area change causes a drop in pressure at the mismatch plane. This pressure drop at the location of the misalignment can be written analogous to the drop due to sudden expansion or contraction [22] as

$$\Delta P_M = P_{12} - P_{23} \quad (3)$$

where P_M is the pressure drop at the mismatch plane, P_{12} and P_{23} are the pressures at the locations shown in Fig. 6. The pressure drop P_M can be quantified in terms of the equivalent length of the straight pipe [23] as

$$h_m = \frac{\Delta P_M}{\rho g} = f \left(\frac{L_e}{D_h} \right) \frac{\bar{V}^2}{2g} \quad (4)$$

where h_m is the head loss due to the geometrical mismatch and f is the friction factor evaluated in the straight part of the channel. L_e , D_h , $\bar{V}$ are the equivalent length of a straight pipe, the hydraulic diameter and the average velocity in the channel. The friction factor f was calculated in terms of the flow rate Q as [24]

$$f = \frac{4\Delta P}{\rho L Q^2} \frac{h^3 w^3}{h+w} \quad (5)$$

The pressure drop from eq. (3) enables the calculation of the equivalent length from eq. (4). The results for the considered three types of interconnection methods were interpreted in terms of the non-dimensional equivalent length of a straight pipe. The equivalent length L_e was non-dimensionalized by the hydraulic diameter D_h . All the interconnection schemes were simulated for varying Reynolds numbers. For the first case of end-to-end interconnection, Fig. 7 shows the Reynolds number dependence of A_1 equivalent length at

flow area ratios of $\frac{A_1}{A_2}=1.14:1, 2:1, 12:5, 4:1$. As expected, the drop in pressure P_M

increases with flow area ratio $\frac{A_1}{A_2}$ and it can be observed that the equivalent length can be

more than 20 hydraulic diameters for the extreme case of $\frac{A_1}{A_2}=4:1$ and $Re=75$ (i.e. $P_M \approx 22\text{KPa}$), owing to the irreversible energy loss at high Reynolds numbers. The recirculation regions due to the misalignment at an extreme case of area ratio and Reynolds number shown in Fig. 8 corroborate the increased pressure drop. To quantify the misalignment in an end-to-end interconnection scheme it is necessary to estimate the

pressure drop for any case of area ratio $\frac{A_1}{A_2}$ and Re . Briefly, the non-dimensional equivalent

length $\left(\frac{L_e}{D_h}\right)$ was first scaled by $\left[\left(\frac{A_1}{A_2}\right)^2 - 1\right]$ and non-linear curve fitting on the data was

performed to develop a correlation of equivalent length as a function of area ratio $\frac{A_1}{A_2}$ and

Reynolds number Re i.e. $\frac{L_e}{D_h} = f\left(\frac{A_1}{A_2}, Re\right)$. The motivation for scaling the equivalent length

by $\left[\left(\frac{A_1}{A_2}\right)^2 - 1\right]$ arises from applying the energy balance and continuity before and after the misalignment junction [23]. In addition, the sudden reduction in the flow area due to misalignment could be modeled as an incompressible flow through an orifice [25] where the

$$C_D = \frac{Q}{A_1 \sqrt{\frac{2(P_1 - P_2)}{\rho \left[\left(\frac{A_1}{A_2}\right)^2 - 1\right]}}}$$

discharge coefficient is given by with Q being the volumetric flow rate. It can be seen from the discharge coefficient expression that pressure differential is

scaled by $\left[\left(\frac{A_1}{A_2}\right)^2 - 1\right]$. To that end, the resulting correlation obtained for $\frac{L_e}{D_h} = f\left(\frac{A_1}{A_2}, Re\right)$ in the end to end interconnection is

$$\frac{L_e}{D_h \left[\left(\frac{A_1}{A_2}\right)^2 - 1\right]} = 2.52 \times 10^{-5} Re^2 + 0.0095 Re + 0.4894 \quad (6)$$

Thus, eq. (6) can be used as a design rule to estimate the pressure drop for a given Reynolds number and a given misalignment area ratio $\frac{A_1}{A_2}$ in the end-to-end interconnection scheme.

In the second type of channel overlap interconnection, the configurations M1 to M6 were simulated for Reynolds numbers ranging from 0.075 to 75. Fig. 9a and 9b shows both non-scaled and scaled equivalent length for the configurations from M1 to M6. It can be seen from Fig. 9a that the equivalent length is the highest for configuration M3 ($A_1:A_2 = 4:1$) while it is lowest for M4 ($A_1:A_2 = 1:1$). This is expected since $A_1:A_2 = 1:1$ corresponds to the case with the highest available flow area and hence lowest pressure drop. As discussed previously, the increase in equivalent length with Re can be attributed to the recirculation regions formed because of the misalignment, thus resulting in increased dissipation (see Fig. 10). The interesting thing to note from Fig. 9b (scaled equivalent length) is that the scaled equivalent length is independent of the configuration as almost all the curves overlap on top of each other. It can be seen that the scaled equivalent length of M1 is slightly higher when compared to other configurations (Fig. 9b). Though M1 had lower pressure drop as expected due to its low area ratio ($A_1:A_2=3:1$) in comparison to the other configurations ($A_1:A_2=4:1$)

(Fig. 9a), the scaling of non-dimensional equivalent length by $\left[\left(\frac{A_1}{A_2} \right)^2 - 1 \right]$ results in a slightly higher value. Nevertheless, the curve fitting to develop a correlation is very applicable considering the scaled equivalent length of M1 (~2.75) differs from M3 (~2.34) by less than 15% even at Re=75. As done in the end-to-end interconnection, curve fitting on the data in the channel overlap interconnection was performed and the correlation which is a function of area ratio and Reynolds number was,

$$\frac{L_e}{D_h \left[\left(\frac{A_1}{A_2} \right)^2 - 1 \right]} = -2.48 \times 10^{-6} \text{Re}^3 + 0.00033 \text{Re}^2 + 0.013 \text{Re} + 0.4999 \quad (7)$$

As the pressure drop is independent of the configuration, eq. (7) can be used to estimate the pressure drop in a modular device for all the configurations depicted in Fig. 3 if the Reynolds number and misalignment area ratio is known in prior.

In the Tube-in-reservoir interconnection method, the case of tubing offset from the center of the reservoir was compared to the ideal case of perfect alignment of tubing and the reservoir. The direction of the flow was from tubing to the channel. Based on the experiments on the offset discussed previously (i.e. ~164 μm), for simulation purposes we considered an even extreme case with 250 μm offset from center of the reservoir. The equivalent length was calculated as discussed previously by the vertical distance between the pressure variation in the channel before the reservoir and the variation in tubing after the reservoir. The calculations can be based either on the hydraulic diameter of the tubing or the hydraulic diameter of the channel. In our work, the equivalent length calculations were based on the channel

$$h_{\text{Reservoir}} = \frac{\Delta P_{\text{Reservoir}}}{\rho} = f_{\text{Rect}} \left(\frac{L_e}{D_h} \right) \frac{1}{2} \bar{V}_{\text{Rect}}^2 \quad (8)$$

where $h_{\text{Reservoir}}$ is the head loss due to the reservoir is, f_{Rect} is the friction factor in the straight part of the channel and $\bar{V}_{\text{Rect}}$ is the average velocity in the rectangular channel.. It

can be seen that the effect of pressure drop in the tube-in-reservoir interconnection method is insignificant when compared to end-to-end interconnection or channel overlap (Fig. S1

supplemental material). For example, at $Re=75$, the maximum value of $\frac{L_e}{D_h}$ for Tube-in-Reservoir interconnection is 1.69 which is insignificant when compared to any of the cases

of interconnection methods. The maximum value of $\frac{L_e}{D_h}$ can be upto 21 in end-to-end interconnection while it can be upto 35 in the case of interconnection through channel overlap. Hence we can conclude that the interconnection through tube-in-reservoir has the least effect on the pressure drop of all the interconnection methods.

5. Conclusions

The effect of geometrical misalignment through numerical simulations has been investigated for three types of interconnection methods: end-to-end interconnection, channel overlap and interconnection through Tube-in-reservoir. In the End-to-End interconnection, the effect of misalignment was evaluated by varying the available flow area ratio and the results were interpreted in terms of the equivalent length of the straight pipe. The Reynolds number dependence was seen by varying the Reynolds number from 0.075–75. There was a drastic increase in the pressure drop as the available flow area decreased and this was found to be enhanced at higher Reynolds numbers. A correlation was developed to estimate the pressure

drop as a function of available flow area ratio ($\frac{A_1}{A_2}$) and the Reynolds number Re . It can also be concluded that the effect of misalignment becomes important for flow area ratios greater than 2:1. In the second case of interconnection through channel overlap, numerical simulations were performed for various possible configurations. The interesting aspect from these simulations is that the effect of geometrical misalignment was found to be independent

of the configuration and is only a function of the available flow area $\frac{A_1}{A_2}$ and Reynolds number Re . Taking this into account a correlation was developed for non-dimensional equivalent length as a function of amount of misalignment and the Reynolds number. This can be used in estimation of the pressure drop in modular devices where interconnection through channel overlap is one of the most popular methods.

The effect of misalignment in third case of interconnection through tube-in-reservoir has been investigated by comparing the ideal case of perfect alignment between tubing and reservoir to the extreme case of 250 μ m between center of tubing and reservoir. It was found that the effect of tube-in-reservoir was insignificant when compared to interconnection through end-to-end and channel overlap.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

A) 3-D View of the simulated channel with an end-to-end interconnection. The dimensions of the channel are shown in terms of the width “w” which was $50\mu\text{m}$. B) Reduction in the available flow area due to the misalignment with A_1 being the original cross-sectional area and A_2 being the reduced flow area due to the misalignment.

Figure 2.
Possible scenario of misalignment due to channel overlap occurring during the alignment of two microfluidic chips using V-grooves.

Figure 3.

Top view of various possible misalignment configurations (M1 to M6) in interconnection through channel overlap. The corresponding flow area ratio $A_1:A_2$ for each configuration is also shown.

Figure 4. 3-D model of simulated model with tube-in-reservoir interconnection having **A)** perfect alignment **B)** 250µm offset between centers of tubing and reservoir. All dimensions are given in µm.

Figure 5.

Experimental images showing the **A**) minimal offset between tubing and center of the reservoir to be $\sim 7\mu\text{m}$ (i.e. close to the ideal case of perfect alignment) **B**) one extreme case where the offset between tubing and reservoir center can be $\sim 164\mu\text{m}$.

Figure 6.
Pressure drop(P_M) due to sudden change in flow area at the interconnection junction.

Figure 7.

Non-dimensional equivalent length ($\frac{L_e}{D_h}$) as a function of Reynolds number for various flow area ratios in an end-to-end Interconnection scheme.

Figure 8. Streamlines showing the recirculation region at $Re=75$ $A_1:A_2$ and $= 4:1$ in an end-to-end interconnection scheme.

FIG. 9a

FIG. 9b

Figure 9.

a) Non-dimensional equivalent length as a function of Reynolds number for various flow area ratios in a channel overlap Interconnection scheme **b)** Scaled equivalent length as a function of Reynolds number for various flow area ratios.

Figure 10. Streamlines showing the recirculation region at $Re=75$ in configuration M5 (i.e. $A_1:A_2 = 4:1$) with a channel overlap interconnection scheme.