Chapter

Microfluidic Flow Sensing Approaches

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Abstract

Precise flow metrology has an increasing demand in many microfluidic related applications. At the scale and scope of interests, Capillary number instead of Reynold number defines the flow characteristics. The interactions between fluid medium and flow channel surface or the surface tension, cavitation, dissolution, and others play critical roles in microfluidic flow metrology. Conventional flow measurement approaches are not sufficient for solving these issues. This chapter will review the currently available products on the market, their microfluidic flow sensing technologies, the technologies with research and development, the major factors impacting flow metrology, and the prospective sensing approaches for future microfluidic flow sensing.

Keywords: Microfluidics, Flow sensing, Thermal time-of-flight sensing, MEMS sensing, Flow metrology, Cavitation, Dissolution, Interface

1. Introduction

Microfluidics is a broad terminology covering various disciplines and scopes while focusing on life science, biochemical and chemical applications. It applies to the devices that process fluids at a dimension below the millimeter scale, and the maximum fluidic volume is within milliliters. Current applications are more related to fluids from microliters to nanoliters in volumes [1, 2]. Two devices in the late 1970s marked the birth of microfluidics. IBM first reported the inkjet printer heads [3] in 1977, and now millions of such units have been shipped worldwide, enabling color printing into every corner of human life. Another device is the micro gas chromatography made on a 5 cm silicon wafer by Stanford University in 1979 [4]. This *lab-on-a-chip* concept has spiked a great enthusiasm and many research activities to miniaturize the analytical instrumentation for wider usage. However, due to its system issues, its progress is less pronounced. Still, progress made on the key components allows its commercialization success with the products now offered by a few companies such as Agilent and Thermo Fisher. The *Organs-on-chips* [5] approaches utilize microfluidic devices to culture living cells for modeling physiological functions of tissues and organs, making microfluidics a unique tool to enrich our understanding of life sciences and to assist the research and assembly of new drugs. Nevertheless, despite tremendous activities in the past 40 years and many applications proven to be feasible, commercialization is limited. Today's microfluidics is yet the well-established one for implementation but excellent academic approaches and science and technology tools [6–11].

The majority of applications of the current microfluidics are for liquid handling other than the gaseous materials. DNA/Gene analysis and point of care disease diagnosis are extensively studied with microfluidic devices [12–15]. The microfluidic devices can integrate both active and passive elements inside the fluidic channels, enabling the polymerase chain reaction devices that help the DNA amplification. The detailed analyses of the DNA samples become possible. Such information is critical for identifying diseases and understanding the origins of the abnormality to the search for possible recovery routes. The other important and advantageous benefits of these microfluidic-based diagnostic devices are fast processing time with small sample volume. These features are combined with today's communication infrastructure, making the remote diagnosis a fascinating scenario. However, current devices are still less sophisticated to acquire the necessary data for the desired tasks. Most of the devices available are based on colorimetric or optical images or limited electrical signals. These data are similar to the analog ones in the electronic age. Additional *digital* sensors will have to be integrated into the microfluidic device for diagnostic quality data acquisition. If the massive deployment of such devices were realized, the foreseeable heavy burdens of the medical systems for the aged societies worldwide would be significantly alleviated, and many lives of human beings could be saved. Drug delivery is another major application for microfluidics [16–18]. In addition to the fluid handling channels and mixers, drug delivery will require a more complicated system that would involve precision metrology, biocompatible carriers, actuation, execution, and feedback. Reliable, low-cost, and commercially available devices will be the keys for future precision drug delivery implementations. The processing of the fluids at a small scale also provides fundamental new tools. It makes it possible to design and fabricate new materials with special functions that the conventional approaches could never succeed. These new materials, including organics, polymeric microparticles, nanostructured materials, and composites, are also the focuses of current microfluidic applications [19].

Microfluidics advancement, on the other hand, greatly relies on the device fabrication technologies of micromachining. The earlier simple passive microfluidic chips having the only microchannels are no longer the mainstream but components of the current devices. A sophisticated microfluidic chip would have both passive structures and active components, which is a challenge for the micromachining process technologies that do not have standard protocols. The multi-discipline features further complicate the availability of process tooling. Fortunately, microfluidics' growth is parallel with the significant advancement in the MEMS and LSI/VLSI IC industry. With ever-improving micromachining device fabrication technologies, the microfluidics once was only viable on a 2″ wafer, and now 8″ and even 12″ wafers are being routinely produced. Many more foundries are available with specialized alternative substrates of glasses, plastics, polymers, and even papers. In recent years, 3D printing, precision micro-injection, laser processing, hot embossing [20–23], and other alternative tools also greatly enriched the variety of microfluidic devices. The progress significantly solves the issues for chemical and bio-compatibility and, in some cases, for commercialization, but the cost to fabricate a desired microfluidic chip is still far from satisfactory. Moreover, the interactions among the device components and the fluids are also likely and sometimes are mandatory, adding additional requirements for better materials and fabrication technologies. Several key components, including microfluidic channels, microvalves, micropumps, needles, mixers, and sensors, are considered the necessary ones for the desired microfluidic chip or system. These relatively complicated components and the substrate make the process compatibility with the electronics a dilemma. Therefore, package, interface, and system design will become critical for the device's final footprint, manufacturability, and successful deployment.

The inkjet printer head that handles the ink droplets remains an outstanding example of a successful microfluidic application. The envisioned microfluidic future in life science and others are still missing a bridge, mostly from the ease of reach and cost-effectiveness [9, 24–26]. The research data for the current microfluidic market have excluded the inkjet applications, addressing only the diagnostic devices and pharmaceutical and life science tools [27]. Nevertheless, by comparing the market reports from the same market research firm issued a decade ago to the current data, one could find that even the most optimal old forecast has nothing to beat the real growth. On the other hand, today's multi-billion dollar market and the double digital growth predicted by various market research firms are more from the companies making the system level products but not the direct values of the key components. These data for the value-added systems are, in a sense, could deceit the current research focus on components. While the system level products enable various applications, the lack of a miniaturized, standalone, performance dramatizing, and cost-effective device would not maintain the expected or envisioned phenomenal growth. In this chapter, standalone flow sensor products for microfluidics will be discussed, including the technologies, standards, factors that will impact the performance, integrations, and manufacturability or scalability.

Microfluidic studies have covered a huge spectrum of processes. For this chapter's limited space, only continuous flow sensing technologies are discussed with applicable pulsed flow features. Droplet flow, nanofluidic flow, microfluidic manipulation or handling, and biological and chemical-related flow phenomena will not be addressed.

2. Microfluidic flow sensing technologies

Microfluidic sensors are critical components for a complete system. Many research works on sensors have been dedicated to the biomedical and chemical sensing development based on electrochemical, optical, mass, or magnetic sensing principles. Electrochemical sensors are mostly studied and often composed of several electrodes that are easy to fabricate together with the microchannels. This limited integration with a simple configuration allows a fast response with reasonably good sensitivity and enables multiple reagents on a single microfluidic chip. The electrode embedded inside a microfluidic channel can also be used for cell counting and estimate the flow volume. With the assistance of a miniaturized LED, pH measurement could be achieved as well [28–31]. However, many of the proposed biosensors or chemical sensors are very specific, and most are research-orientated, as being determined by the catalytic or affinity properties of the biological recognition agent in a particular study and the sensor itself requires a sophisticated electronic system for readout or analysis. The standalone or large scale commercial applications are yet to emerge.

Flow meters using traditional thermal capillary and Coriolis measurement are commercially available for micro flow measurement before the microfluidics being intensively studied. Researches on microfluidic flow sensing approaches are for miniaturized, cost-effective, and integrable products. In this scope, both flow and pressure sensors have been extensively studied [28]. In some cases, the differential pressure sensor can be used for flow measurement. Flow measurement is one of the most important factors in microfluidic handling for data analysis and precise system control. Without the knowledge of the fluid quantity in the process, analytical results would not be easy to establish the needed and convincing statistics. The conventional flow sensors might be the first commercially available standalone

sensing products for microfluidics. The technologies are still limited, and their package formality is bulky and far off the cost target for the desired microfluidic system. Many studies proposed integrating flow sensors into the microfluidic system. However, there are still many factors that impact data acquisition. The existing sensor products on the market also have some unsolved reliability issues in applications. The commercialization route to a well-performed and cost-effective sensor is yet to be demonstrated.

The available flow sensors applied to microfluidics are classified as thermal and non-thermal sensors [1]. Thermal flow sensors have been applied to small flow measurement for both gas and liquid before the microfluidic concept emerged. Therefore thermal flow sensors are mostly studied and applied in microfluidic applications, and products with various thermal sensing principles are commercially available. Coriolis microfluidic sensor is a non-thermal sensor, and it has an even higher cost. Other "non-thermal" flow sensors are mostly at the research stages. Before the form factor, cost, and reliability issues can be solved, large scale applications are still not possible.

2.1 References and standards

For the traditional flow sensors, the metrology characteristics will hardly enable a self-calibration. Therefore, a primary standard or a reference defined by an international norm governs the manufacture of a flow sensing product with specific sensing technology. The same should then apply to microfluidics. Demanding to establish an international standard for microfluidics has long been proposed [32, 33]. Still, only in recent years, an international microfluidic association has been established, and an international standard (ISO) working committee has been organized with a serial of workshops [34]. It has been proposed that the new ISO standard for the microfluidic shall be having four sub-standards, including *flow control* that addresses the key components of valves, pumps, and sensors for the system; *Interfacing* that is to standardize the connectors and other interfaces; *modularity* that will regulate the integration and *testing methods* that will define the methodology of the metrology and other related testing issues. Such a task is still at an earlier stage, and additional time will be need before the standards become available.

Several efforts to establish a primary standard or a traceable reference system for flow metrology in microfluidics applications have been made in the past years [35–37]. The widely adapted primary standards are the gravimetric and volumetric principle. The comparison of such standards among different European national metrology institutes indicated an uncertainty (k = 2) ranging from 0.05 to 6% for the flow rate ranges of 17 nl/min to 167 ml/min. Still, most of them can have uncertainties within 0.1% [35]. In the reported reference system, the flow generation is critical and requires a stable flow system in the sub microliter per minute flow. Other special effects such as evaporation must be considered, especially when approaching nanoliter per minute flowrates. Degassing through the system and preventing external vibration, and testing environmental control are also critical to ensure the measurement is repeatable and accurate. The flow generators used in these institutes include metallic bellow, precision syringe pump, and gear pump. Because the gravimetric measurement is achieved with high precision balances, the system is a uni-directional open loop. For sub microliter per minute flowrates, laser interferometry has been used as an alternative precise reference for the desired accuracy [38]. However, for high volume applications, a faster closed-loop calibration would be preferred. It could also result in good accuracy using a gear pump and high precision Coriolis meter with an accuracy of ±0.2% as the reference standard [39].

For almost all flowrate ranges in microfluidics, the Reynold numbers are within 1000, indicating that the flow of interests is within the laminar flow regime. Therefore in a desired large dynamic range, the flow profile would not be the same at the different flowrates, which adds complexity to maintain the measurement accuracy. Meanwhile, the flow channels are small in micrometer dimensions. The interfaces between fluid and channel wall become pronounced, which differ from those described for laminar flow by Moody Diagram in the classic fluid dynamics. Besides, cavitation would play a critical role, and dissolution will also contribute to metrology. These are among the new challenges for the on-going metrology standards for microfluidics.

2.2 Thermal flow sensing

The thermal mass flow measurement using calorimetric capillary sensors has been used to measure a very low flow to nanoliter per minute for quite a long time [40]. The sensors are composed of thin metal wires winded outside the wall of a tiny tube of a micrometer in diameter. The tube is usually made of thermally conductive materials such as stainless steel or fused silica. These sensors normally require a higher power to ensure the heat transfer resulting in a small dynamic measurement range and a low accuracy towards the low measurement end. The required manufacture process makes these sensors very costly without being able to be volume produced. Integration of such a sensor into a microfluidic system would be unlikely. In the following discussions, only micromachined sensors will be addressed. The micromachined sensors are mostly made on silicon or glass substrate. A microheater and plural numbers of sensing elements are deposited on a membrane structure, and the air or gas-filled cavity below the membrane provides the desired thermal isolation. The tiny sensing elements enable a fast response time. The membrane is frequently made with silicon nitride or silicon nitride and oxide combination. The sensing elements can be metals with a large temperature coefficient such as platinum, nickel, tungsten, or in the case for the process compatibility, doped polycrystalline silicon is used instead. The micromachined thermal flow sensors' structure has no moving parts, and the surface can be treated with various passivation and post-process coating for better reliability. The micromachining process for the flow sensors is well established today. Most MEMS foundries have the necessary equipment for manufacturing such sensors, which allows a very favorable cost and makes it possible for high volume applications. The first micromachined thermal flow sensor made for microfluid is used in micro gas chromatography [4]. It is for gaseous flow and not a standalone product and only manufactured in a minimal quantity as the OEM product. The commercially available micromachined thermal microfluidic flow sensors for liquid were incepted in the last decade. These commercial products utilize different thermal sensing principles [41–43] that cover the three major technologies with thermal calorimetry, anemometry, and thermal time-of-flight approaches. There are some research activities on other thermal flow sensing designs, such as thermal capacitive utilizing the temperature dependence of dielectric constants, [44] and temperature dependence of the PN-junction in a diode [45]. The measurement scheme of flowrate with these alternative thermal sensing designs could also be classified into the above three thermal sensing principles. **Figure 1** is the graphic illustration of these three measurement principles for the typical micromachined thermal flow sensors on a silicon substrate.

2.2.1 Calorimetric flow sensing

The majority of the current micromachined commercial thermal flow sensors are utilizing the calorimetric principle. Most successful applications are for gaseous

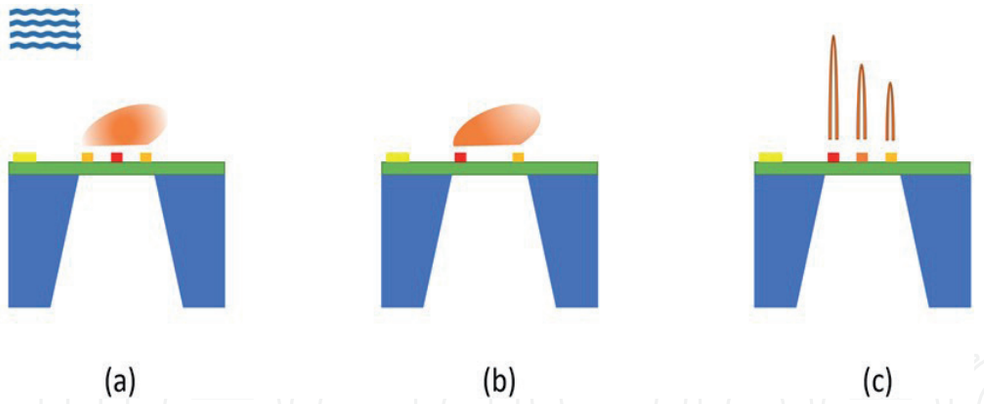

Figure 1.
Graphic illustration of the micromachined thermal flow sensors (on silicon) with the flow sensing principles: (a) calorimetry; (b) anemometry and (c) thermal time-of-flight.

fluids, of which the automotive airflow sensors for fuel control are the dominant application. The structure showed in **Figure 1(a)** is a typical one for a micromachined calorimetric mass flow sensor on which a microheater is placed at the center of the membrane. Two temperature sensors are made symmetrically at the up and downstream of the microheater. These two temperature sensors can be simple resistors of identical resistance values or identical thermal-piles. There are a variety of approaches to realize data acquisition. The commonly used ones are either to keep the microheater at a constant heating power or to maintain a constant temperature from the up and downstream sensor and then measure the heat transfer or temperature differences between the measurements of the up and downstream sensors as the flowing fluid will take away the heat from the microheater resulting in a heat redistribution. By calibration, such heat transfer can be correlated to the mass flowrate of the fluids. In this approach, the measurement is susceptible to low flowrate. As its nomenclature indicates, the measurement is dependent on the fluidic thermal properties of thermal capacitance and thermal conductivity. The thermal sensing using the resistor-based microheater and resistor sensing has the intrinsic temperature effects associated with the environmental conditions, which need to be compensated for better accuracy. For this purpose, another sensor placed on the substrate (the yellow element shown in **Figure 1**) is used to gauge the environmental temperature and correct the resistance value due to environmental temperature variations. The detailed theoretical interpretation and governing physics can be found in the literature as well as the international standard [1, 46].

The major challenge of applying the micromachined thermal sensor to meter microfluidic is the package. For the gaseous sensors, the membrane often has openings that balance the surface's fluidic pressure against the membrane deformation. The change of the membrane position will greatly impact the measurement as the sensor position will be significantly altered with membrane flatness changes. However, for microfluidic measurement, the opening will be detrimental once the liquid-filled up the cavity underneath the membrane. Therefore, the commercially available approach [41] for the package is to have the sensor placed outside the channel with the sensor's surface close to the outer channel wall. Therefore, the channel will need to be thin enough and have good thermal conductivity for heat transfer effectiveness. One of the selections of the channel is a fused silica tube. As the membrane that supports the sensing element is typical with a thickness of 1 micrometer, attach the think tube to the sensor is a very tedious process with a high cost. In addition, compared to the applications for gaseous fluids, the thermal wall of the fused silica also reduces the sensitivity of the sensor, leading to a significantly smaller measurement dynamic range (<50: 1), which is certainly not desired for

microfluidic applications. The commercially available calorimetric microfluidic sensors offer a typic <40:1 dynamic range with the lowest detection flowrate of 7.5 nL/min and the best accuracy of ±5% of reading at the full scale. There are also concerns about the constant thermal power at the channel's specific area during the measurement in practical applications. This will be discussed later in detail.

2.2.2 Anemometric flow sensing

The first micromachined thermal flow sensor on silicon is made with the anemometric flow sensing principle [47]. Thermal anemometry is also known as energy dissipative sensing, and its measurement scheme is relatively simple, as shown in **Figure 1(b)**. Only one sensing element is placed downstream. Alternatively, the sensing element can also be placed upstream, as the measurement of the fluidic flowrate is only from the microheater (a sensing element). The temperature sensor is used as a fluid temperature reference. Therefore, instead of measuring the fluidic flow-induced changes of the temperature profile at the centralized microheater with calorimetry, the anemometry measures the heat loss due to the forced convection. In this case, with the supporting control circuitry, adjusting the microheater power will allow the measurement to be much easier for higher flowrates. Simultaneously, the sensitivity at low flow will be lower compared to the sensing principle of calorimetry. Another character of the anemometry is that its correlation with the fluidic thermal properties has a larger nonlinear effect resulting in the difficulties to apply a constant fluidic conversion factor for correction of the flowrate data when the measured fluid has different thermal properties from those of the calibration fluid. For the same reason, the temperature compensation scheme for the anemometry is more complicated than that for the calorimetry.

One commercially available anemometric microfluidic flow sensor, per the structure described in the company's webpage, [43] also takes the package approach similar to the earlier mentioned one of the calorimetric microfluidic sensors. The sensor is placed at the outer wall of a thermally conductive fine quartz glass tube by machining the tube surface into a smooth flat. Instead of a single micromachined sensing chip, two chips are used. A special glue was applied to attach the chip to the quartz tube's flat surface, forming a close contact for the required heat transfer. The heater chip and temperature chip are separated at a certain distance forming the configuration of an anemometer. The heat transfer needed for the measurement provided by the sensor is achieved via thermal diffusion. These package approaches are also similar to the traditional capillary thermal mass flow sensors, where the hot wires are winded onto the surface of a special stainless tube. However, the micromachined sensor will have a much lower heating temperature than those by the capillary sensor. Because of the heat diffusion, control the heat for the low flowrate measurement would be very challenging, resulting in a small dynamic range and large measurement errors (full-scale error rate) towards the low detection limit. The current offered anemometric microfluidic flow meter has a guaranteed dynamic range of 50:1 with the lowest detectable flowrate of 100 μL/min and the best accuracy of ±5% of reading.

2.2.3 Thermal time-of-flight flow sensing

Both the calorimetric and anemometric flow sensors require a calibration of the real fluid for the desired precision or metrological accuracy, as the fluidic properties will have a nonlinear response in the full dynamic range. The limited dynamic range and the accuracy would not be desirable for the precision requirements for many microfluidic applications such as drug infusion. Also, these flow sensing products

could only provide mass flowrate measurements. The microfluidic applications would appreciate additional fluidic information such as fluidic concentration, physical or even chemical properties of the fluids at the same time. To this end, thermal time-of-flight sensing technology offers much of the competitive advantages. The thermal time-of-flight sensing concept can be traced back to the late 1940s [48] and has been an interest in many subsequent research works [49–51]. The thermal time-of-flight sensing measures the heat transfer transient time as well as the responses at each sensing element. Several sensing elements can be placed downstream of the microheater. Consequently, this approach can measure additional parameters other than the flowrates [52]. The sensor works with a thermal pulse or modulated thermal wave signals. Compared to calorimetry or anemometry, the transient time-domain data are much more immutable to the background interferences. Despite the advantages, a commercially available thermal time-of-flight flow meter is not seen until the past decade [42]. One reason could be that the microheater must possess a mass as small as possible for the needed thermal response to enable the measurement scheme. In the traditional approach, such a tiny wire is extremely vulnerable for reliability in actual applications. On the other hand, pure time-of-flight will only measure the flow velocity. In contrast, the other parameters require advanced and complicated electronics that are not readily accessible until recent years. Nevertheless, the sensor build and package limitation will still lead to a non-pure time-of-flight, and calibration will be required to remove those effects. On the other hand, these effects can also be used to provide additional fluidic information. For the microfluidic applications, the microheater is driven with a modulated microheater, the constant heating spot in the flow channel is therefore eliminated. The sensor outputs flow velocity as well as fluidic mass flowrate and the additional data of the fluidic properties, making the thermal time-of-flight technology an ideal approach for the desired microfluidic flow measurement applications.

Figure 2 shows a typical structure of a micromachined thermal time-of-flight sensor chip [53]. The micromachined process has a wide spectrum of materials selection to allow the sensor with excellent thermal isolation while not sacrificing reliability. This is particularly important for the thermal time-of-flight sensing that requires a super-fast thermal response. The blue materials showed in **Figure 2(b)** can be silicon or glass substrate. The gray colored block will be for thermal isolation. For example, a 10 ~ 15 μm parylene conformal layer will provide the properties of the good material of stiffness and robustness for the application. The green-colored materials need to have good thermal conductivity while excellent surface passivation for reliability. Ideal materials include multi-layered silicon nitride or silicon carbide. Underneath the microheater and sensing elements, a cavity will enhance the thermal performance of the sensor chip. The brown-colored elements are for microheater and sensing elements. One sensing element is placed directly on the substrate to measure the environmental temperature that provides the compensation of the microheater's temperature performance and control. In the photo shown in **Figure 2(a)**, the central element has another sensing element at the proximity of the microheater, which is used to fine-tune the microheater temperature or power with those other physical properties such as thermal conductivity can be precisely acquired.

The heat transfer in the thermal time-of-flight configuration is measured by the temperature T with time t in the flow direction x of non-uniform temperature distribution, determined by the flow medium's conductivity and diffusivity. The working principle can be expressed as below, [52].

$$\frac{\partial T}{\partial t} = \frac{k}{\rho c}\left(\frac{\partial^2 T}{\partial x^2}\right) - V_x\left(\frac{\partial T}{\partial x}\right) + \frac{Q}{\rho c} \tag{1}$$

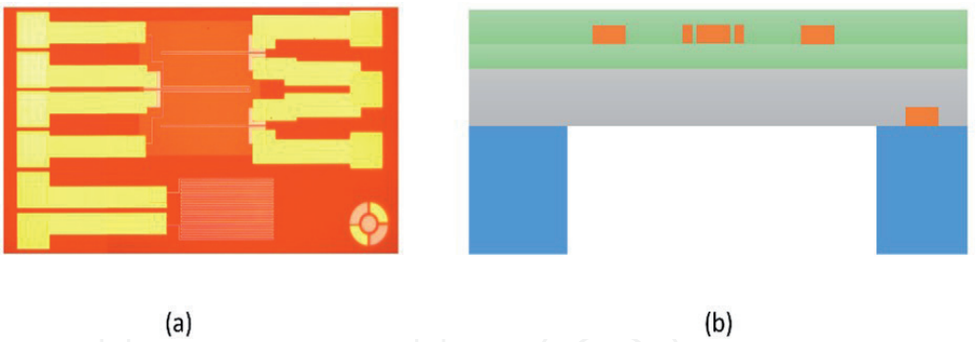

Figure 2.
Example of a micromachined thermal time-of-flight sensing chip: (a) optical photo of the chip, top view; (b) cross-section schematic.

Where Q is the heat generated by the microheater that is normally modulated with a square or sine wave, k is the thermal conductivity, ρ is the density, c is the heat capacity of the flow medium, and V_x is the fluid velocity. With one dimensional approximate, the fluid velocity, V_x, between the microheater and the sensing element would be determined by fluid thermal conductivity k, thermal diffusivity α, and the modulated heat Q, [54].

$$T = \frac{Q}{4\pi kt}\exp\left(-\frac{(x - V_x t)^2}{4\alpha t}\right) \tag{2}$$

Therefore, if the sensor only has a microheater and a sensing element pair, the measurement will still be dependent on the flow medium properties. The microheater and the sensing elements all have the fluidic dependent response that needs to be removed for the complicated fluids. Simple calibration with the conventional fluid can be applied for the fluid measurement without losing the metrology accuracy. A micro-machining process' advantages allow placing multiple sensing elements on the same chip without adding any cost that makes it possible to have the measurement independent of the fluidic properties. The thermal time-of-flight will not be a simple flow velocity measurement. The measured changes in the amplitude are directly proportional to the heat transfer between the microheater and the sensing elements that will provide the mass flowrate similar to the calorimetric or anemometric approach per the data acquisition process. The time-domain data yield additional information, which allows the acquisition of additional fluidic thermal dynamic properties such as thermal conductivity and specific heat. In the microfluidic flow measurement, the liquid is generally non-compressible. The pressure effects of compressibility can be considered secondary. Compared to the gaseous fluids, liquid has a much large heat capacitance making the sensing element resistance-related temperature effects less pronounced. And most importantly, with the multiple sensing elements on a single chip, the measurement dynamic range can be substantially extended. A practical 7500:1 dynamic range can be achieved with two or three pairs of sensing elements.

2.3 Coriolis flow sensing

Coriolis mass flow sensing principle has been well documented, and the first commercial product was introduced to the market in 1977 by Micro Motion. It is a true mass flow sensing technology with very high precision by utilizing an exciting

tube which fluid is flowing through, and the tube oscillates artificially. The changes of the tube oscillation in time and space are a direct measure of the mass flow. One advantage of the Coriolis sensing approach is that the fluid density can be simultaneously determined from the oscillation frequency of the measuring tube. But it also requires a minimum density of fluid such that the resolution of the oscillation can be registered. It also suffers a high-pressure loss and a smaller dynamic range. The high cost of the measuring tube manufacture sparked the attempt with micromachining, and the first research paper was published in 1997 [55]. With the micromachining process, the MEMS Coriolis mass flow sensor can be well applied for microfluidic flow measurements. The commercially available Coriolis meters sensors via micromachining either consists of a silicon microtube via silicon wafer fuse bonding and an integrated temperature sensor [56] or a silicon-rich silicon nitride tube coupled with a strain gauge readout [57, 58]. The micromachined Coriolis sensor using silicon nitride tube has a thin tube wall of about 1.2 μm and is much lighter than the silicon tube. Hence, the light-weighted tube would have a smaller mass than the fluid it measures that simplify the package, and leads to the possibility to measure the fluids at ambient pressure. The demonstrated Coriolis sensor could measure liquid mass flow, density, and temperature (if a temperature sensor is integrated) simultaneously. Another advantage for the MEMS Coriolis mass flow sensor is that it usually operates at a much higher resonant frequency with substantially less vibratory influences from the environments than those for the traditional Coriolis mass flow technology.

Like the MEMS thermal mass flow sensors, the micro Coriolis mass flow sensor also requires clean fluid. Even fine particles can damage or clog the sensor, considering the measuring tube's tiny channel. Besides, the sensor will not function well in liquid with high viscosities and liquid with chemical reactions. The high-speed liquid flow may also alter the performance of the sensor unless bypass configuration is applied. The superior true mass flow accuracy of a Coriolis sensor is overshadowed by its footprint, complication in the package, and cost in the manufacturing process that diminishes high volume and/or disposable applications, which would be a necessity in some microfluidic applications for cross-contamination prevention. The fluidic property independence measurement characteristics also limit its measurements only for flowrate and density. Other fluidic property measurements will require integrating additional sensing elements, further enlarging the sensor footprint, indicating an even higher cost for the final product manufacture. Therefore, although the micromachined Coriolis sensor's demonstration has been over two decades, the applications are still very limited.

2.4 Other microfluidic flow sensing technologies

Flow sensors are likely the ones that can be made with the most versatile technologies and are vastly selectable to the applications. More than twenty different physical measurement principles are commercially available on the market for flow metrology. However, for microfluidics, the options are limited. Other than the commercially available thermal mass flow sensors and Coriolis flow sensors, micromachining advancement offers opportunities for many studies with a wide spectrum of technologies applied for microfluidic flow sensing. But commercialization of many of those is still in question. Some selected researches micromachined flow sensing technologies are discussed below.

2.4.1 Acoustic microfluidic flow sensing

In addition to micromachined thermal and Coriolis sensors, micromachined ultrasonic sensors are also commercially available. Ultrasonic flow sensing is one

of the well-documented technology for flow metrology with high accuracy. By measuring the time differences of the ultrasonic signals propagating in the opposite direction of a fluidic medium, the flow speed can be accurately measured. Therefore, it has the advantage of a pure velocity measurement independent of the fluidic properties. As a sound propagation, it will not require direct contact with the fluids that it measures, or it is non-invasive, which is very attractive for microfluidic related medical applications. However, it will normally require dual transducers placed in opposite directions or at a certain angle with respect to a reflector. This prevents the reduction in footprint and cost. For the microfluidic applications, its signals reduce significantly at the low flow speed, and it is also very sensitive to the fluids where cavitation or dissolution may exist. The current commercially available ultrasonic flow meters for microfluidics have about a 50:1 dynamic range and a detection limit of 300 μL/min [59]. Some research indicated that the ultrasonic transducer could be integrated into the microfluidic channel, but the capability for flow metrology is yet to be demonstrated [60].

Acoustic device applications in microfluidics are mostly for fluid handling, and surface acoustic wave (SAW) sensing and actuation is another approach that can be integrated into the microfluidic channels [61]. Some efforts were also made to measure the flowrate with the SAW devices. It has been reported that a micromachined interdigital transducer (IDT) could direct the fluidic droplets via the excited acoustic streaming that is fast and material independent [62]. In another study, [63] a SAW sensor with dual symmetrical IDTs made on a 30 mm by 30 mm square quartz crystal substrate was used to measure the flowrate in a designed channel by recording the delay times and the corresponding frequencies. A close to a linear correlation between the phase shift from the delay time and flowrate was established. The SAW sensors can be independent of the fluidic properties; however, they require a much larger footprint, and temperature compensation is also complicated compared to thermal sensing approaches.

2.4.2 Differential pressure microfluidic flow sensing

Measurement of flowrate with differential pressure is one of the oldest flow sensing technologies. Micromachined differential pressure sensors have been well established and are widely available on the market at a very low cost. Most sensors are made on a silicon nitride membrane or diaphragm with the piezoresistive sensing elements at the edges of the membrane or with a capacitance measuring principle for the low differential pressures [64, 65]. The advantages of a differential pressure sensor for flow measurement are lower power consumption and relatively easy installation with fewer effects on the flow conditioning. They are also independent of the fluidic properties. The microfluidic flow regime is purely laminar, and the pressure loss is linear with the flow velocity. However, limited by its sensitivity, the measurement dynamic range of a differential pressure sensor is normally small. In particular, for microfluidic applications, the pressure drop at a tiny distance may not even generate enough sensitivity for the measurement. The dependence of the microfluid's pressure loss on the dynamic viscosity also requires a temperature sensor at the proximity for the needed compensation. Other phenomena such as cavitation or multi-phase flow will have a big impact on the measurement of the pressure and hence the accuracy of the deduced flowrate.

Flow measurement with drag force is an alternative pressure-related flow sensing approach. Due to the size restriction, such a sensor does not favor being placed inside the microfluidic channel. However, in an ideally integrated microfluidic system, there will be valves and other actuators. The drag force-sensing approach could be combined with the actuation parts in the system. A typical drag force

sensor is to utilize a cantilever or a diaphragm [66]. The mechanical deflection can be read out with an optical microscope or photodiode. Another approach to measuring the deflection is to utilize the piezoresistive or piezoelectric elements embedded at the positions where maximal deformation could occur at the designed cantilever or diaphragm. To increase the measurement sensitivity, the Fabry Perot spectrum's fringe shift was used to measure the cantilever movement correlated flowrate, which, however, complicated the data acquisition and limited the package options [67]. The materials used to make the micro-cantilevers are silicon nitride, SU8, and polydimethylsiloxane (PDMS). An integrated micro-cantilever inside the microfluidic channel via the microfluidic favorable PDMS process achieved a capability of detecting 200 μL/min flowrate but only have a small 5:1 dynamic range [68]. Most of the micro-cantilevers measure microliter per minute flowrate, even though nanoliter per minutes sensitivity was reported, but the required optical readout often makes the fine readings and subsequent digitization a challenge [69]. While piezoresistive or piezoelectric configuration is more preferred as no optical assistance in readout will be needed. On the other hand, as the piezoelectric cannot detect a static flow, piezoresistive is considered a better choice. The cantilever sensors are more sensitive than diaphragm sensors, but there are still concerns for their reliability and repeatability per the moving cantilever. The sensitivity of these sensors also requires meaningful pressure or critical mass to activate the deformation of the cantilever or diaphragm. Such pressure is not necessarily existing in the microfluid subject to measurement.

2.4.3 Microwave microfluidic flow sensing

The non-invasive approach is always preferred in microfluidic applications, for which life science is the major focus. A microwave microfluidic flow sensor is reported [70] to achieve a large dynamic range of 1-300 μL/min with a high resolution of 1 μL/min. The detection of the flowrate with the microwave is via the measurement of a membrane that was a part of a microfluidic channel and on which the fluid is flowing over, causing the deflection of the membrane. Therefore, it could also be a type of differential pressure sensing. The measurement element is the microwave resonator that detects the effective capacitance because of the changes in the deflected thin membrane's effective permittivity due to the channel pressure changes by the flowing fluid at different flowrates. This configuration is much easier to be packaged with the microfluidic channel, and it is a true noncontact detection that can be miniaturized compared to the optical assisted readout. The microwave flow sensor is consisting of two critical components. One is the microfluidic channel with the membrane that was micromachined with PDMS soft lithography and replica molding. PDMS is a preferred material for microfluidics for its compatibility, and more importantly, it is transparent to microwave with a low loss. The membrane is about 1.5 to 3 mm in diameter and 100 μm in thickness, strong enough to hold the fluidic pressure inside the microfluidic channel. Simultaneously, it is thin enough for the sensitivity of the resonator function needed for the measurements. The second component of the flow sensor is the microwave resonator, designed into an open-ended half-wavelength ring resonator with a microstrip structure on a high-performance microwave substrate made of a 35 μm copper layer on top and bottom surfaces. The resonator operated at a 4 GHz resonant frequency. The fabrication is via the cost-effective conventional printed circuitry board processing. However, the integration with the microchannel made strong application dependence and difficulties in controlling the cost. Also, the metrological performance of this sensor was not well documented.

2.4.4 Optical microfluidic flow sensing

Optical flow sensing is attractive to the microfluidic application for its non-invasive and high accuracy features. Laboratory flow measurements such as particle image velocimetry, infrared thermal velocimetry, and laser interferometry are reported for microfluidic metrology studies [71–74]. These optical technologies are all having complicated bulk settings and require the microfluidic channels to be optically transparent. While the miniaturization efforts continue to focus on microfluidics, optofluidics is now a dedicated field for the studies of the combined optics and microfluidics with targeted miniaturized optical integration sensing functions into a single microfluidic chip. In a microscale optical flow sensor report, [75] an optical fiber structure was fabricated in the form of a drag force cantilever to measure the microfluidic flow. A stripped single-mode optical fiber was positioned across a microfluidic channel and aligned with a multi-mode fiber receiver. The microfluidic flow in the perpendicular directions will displace the fiber cantilever tip, causing the light intensity change at the aligned receiver. The reported sensor had achieved a measurement dynamic range over 60:1 and a minimal detection of 7 μL/min. However, the making of the sensor would be quite complicated with the fiber alignment, and direct contact of the flowing fluid with the fiber cantilever is also required. In another report using the optical approach for flow sensing, miniaturized fluorescence sensing is attempted for micro molecular tagging velocimetry in microfluidics [76], but these methods are not cost-effective and yet to reach the small footprint.

In an alternative optical sensing approach, [77] a collimated light beam was employed to excite the surface plasmon resonance at a gold film on top of a polymethyl methacrylate (PMMA) microfluidic channel. The fluidic flow will cause the temperature redistribution inside the microfluidic channel, which alters the refractive index above the metal film. The refractive index is inversely proportional to the temperature. By acquiring and analyzing the image of the excited surface plasmon, the flowrate could be measured. However, since surface plasmon resonance is very sensitive to temperature, and the response is nonlinear, a full functional measurement scheme and affirmation of metrology parameters will need additional efforts.

2.4.5 Impedance based microfluidic flow sensing

The impedance flow sensing principle is also a topic in the studies for microfluidics. The electrical impedance flow measurement has the advantage of simplicity. The configuration has fewer requirements for environmental parameter compensation and can be applied to a wide range of fluids. A cascade finger structure of the electrical impedance sensor could help the measurement accuracy of pulsed flow. However, the electrical impedance measurement is strongly dependent on the fluid properties and is only applicable to conductive fluids. In a report [78] of an electrical impedance microfluidic flow sensor, the simple two surface electrodes are embedded inside a microfluidic channel. An alternating current signal was applied across the microfluidic channel. The fluid is equivalent to a diffuse layer capacitance impedance or the parallel capacitance impedance, and the electrode forms the serial capacitance impedance with the fluid. By optimizing the applied voltage frequency, the measured impedance can be well correlated to the flowrate. The reported data achieved a 50 nL/min detection limit and about 10:1 dynamic range.

In another approach, the measurement of the magnetic impedance of a hair microfluidic flow sensor offers the ultra-low-power option [79]. The sensor was made by depositing a giant magnetoimpedance (GMI) layer on top of a glass substrate. A PMMA master pillar mold was then applied to the pre-formed magnetic

nanocomposite of permanent magnetic nanowire and PDMS mixture on the GMI layer. The formed flow sensor was placed inside the microfluidic channel. When the fluid flows through the pillars, the flow will force the pillars to bend, resulting in the change of the magnetic field sensed by the GMI layer and output the signals that can be correlated to the flowrate. The results showed a measurement of the water flow speed up to 7.8 mm/sec and a resolution of 15 μm/sec with a typical power of 31.6 μW. The study also indicated that by optimizing the parameters, the power could be further lowered to about 80 nW.

3. Factors impacting the microfluidic flow sensing

The flow metering at the microfluidic scale is quite different from those in a large pipeline. Many factors that may be trivial in the conventional fluidic dynamics become critical for microfluidic metrology. In this section, some critical factors are discussed.

3.1 Microfluidic channel and fluid interactions

In the classic fluidic dynamics, the Moody chart indicates that at laminar flow, the friction factor is inversely proportional to Reynolds number where only viscosity of the fluid plays the role and diffusion is normally not in consideration. In the dimension of a microfluidic channel, the surface area relative to the volume is dramatically larger than those in a large pipe. For the flow speed of interests, factors such as surface tension and diffusion are all having their critical contributions to the microfluidic flow metrology. The capillary number then would be much more important than the Reynolds number [80]. Besides, the majority of microfluidic processes are water-based. Water has a molecular size of about 0.27 nanometer, and it is dipolar in nature. Water interaction with the solid surface is inevitable, and such interaction will be pronounced as interaction will involve a significant portion of the total volume of the microfluidics. Most of the solid surfaces at the microscale would be imperfections that are full of defects with dimensions larger than the water molecule. Water viscosity is also very sensitive to temperature in the applicable ranges. These effects will be even more pronounced in the biological fluid case where the electrolyte is often present as the chemical state of the surface would be altered, either by ionization of covalently bound surface groups or by ion adsorption [81]. Hence, to ensure the accuracy in the flow measurement for microfluidics, the interactions between fluid and solid channel surface must be considered, especially for the long term repeatability, reproducibility, or reliability.

The detailed studies on the fluidic handling and flowrates impacted by the fluid and microchannel interactions are not well documented. However, in a few reports on the long-term stability of the commercially available calorimetric flow sensors for microfluidics, it was reported that the measurement accuracy tended to have a time-dependence. The long-term *drift* was always towards negative directions with a more pronounced deviation at the full-scale flowrate. For example, one report [82] tested the reproducibility of several commercial calorimetric flow sensors of the identical model for the time dependence in water. It was found that although the sensor to sensor performance was inconsistent, the accuracies of all sensors *drifted* towards negative with time, with −25% deviations at the full-scale flowrate in about 5 months. Although the report did not speculate the reasons for the deviations, this phenomenon could be a direct reflection of the water interactions with the microfluidic channel walls. The sensor chip was fixed to a fine tube with a machined flat surface in the product package. It would difficult to guarantee the consistency

of such attachment. The heat transfer was from a microheater with a constant heat diffusion at a fixed glass wall area. This area with a constant heat might promote the interaction between water and any defective sites on the inner channel surface, forming an interface with water-filled pinholes that could percolate laterally, reducing the thermal responses because of the wetted surface condition compared to the dry one at the calibration. Hence the measurement would be gradually moving towards the values with negative deviations.

3.2 Microfluidic cavitation

Cavitation is often known as a detrimental phenomenon in high-speed flows that leads to mechanical damages at the flow path. However, it can also be utilized for industrial processing in classic fluidic dynamics. In microfluidics, cavitation inception is via the diffusion of dissolved gas into the available nuclei. It can occur even at a pure Stokes flow, but the cavitating flow will not normally lead to mechanical defectiveness due to the relatively low energy release, but it can dramatically generate the local flow speed spike. Cavitation has become a growing research topic in microfluidics. It is not only because the cavitation flow is inevitable in many applicable microfluidic flow conditions, but it can also be employed as a tool for microfluidic manipulation such as pumping and mixing via the control of cavitation size alternation. The cavitation can harvest and release energy upon collapse in the microfluidic process. The removal of cavitation can be done with properly designed materials for the microfluidic channels [83–86].

The cavitation presence will greatly impact the measurement reproducibility or accuracy for any flow sensors regardless of the measurement principles. The calibration setup for a microfluidic meter normally requires a degassing device in serial to the calibration line, and degassing is always performed before the start of calibration [39]. The cavitating flow is in fact a two-phase flow. Therefore when a flow sensor calibrated at a cavitation-free condition is applied to measure a cavitating flow, the measurement deviations will be inevitable. The current tools of the cavitation studies are visualization approaches such as colorimetry or via high-speed camera for which a transparent flow channel will be required to collect the data. However, in practical applications, the channels are often opaque. Therefore, it is of interest to have additional measurement approaches that can alert *in situ* when the cavitation is present in microfluidics. In some applications such as drug delivery, the infusion with cavitating fluids into a human body will be very harmful, not just for the uncertainties in totalized delivered drugs. Of the flow sensing technologies discussed above, the thermal sensing approach could be a viable tool to detect cavitation while correcting the quantified microfluidic delivery. **Figure 3** shows the response of a thermal time-of-flight sensor used to detect the bubbles inside the microfluidic channel. (**Figure 3**, Left) The channel design can be found in a previous report [87]. As the two air bubbles (one big and one small) pass through the channel sequentially, the fluidic properties that the sensor senses will be drastically different from those of the pure liquid. In the case of water with air bubbles, the smaller thermal conductivity and substantially lower density for the mixture will prompt a faster heat transfer resulting in a recorded positive flowrate spike. With additional sensing elements to capture the flow speed of the fluid, the time of the burst spike can be used to estimate the sizes of the bubbles. Further, the gas properties inside the bubble might also be detected per the calibration of the sensing element thermal response to the fluid. While in another case, the sensor could also be applied to study the cavitation (**Figure 3**, right). The as-calibrated thermal time-of-flight sensor will normally have an accuracy within ±1%. After calibration in DI water and subsequent verification, the same sensor was kept at the same microfluidic channel at null flow

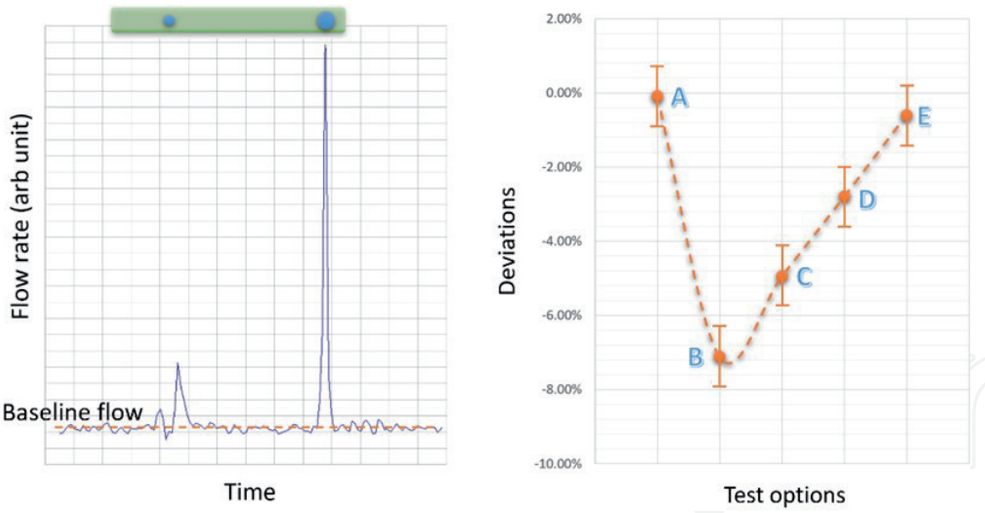

Figure 3.
Left - Example of the response of a micromachined thermal time-of-flight sensor to air bubbles passing in a DI-water microfluidic channel; and right – shows the same sensor response at 20mL/min flow to the channel conditions: A – as calibrated DI water; B – tested after sensor powered on in a null flow DI water channel for 48 hours; C – After B test and degassing for 15 minutes; D – after C and full scale full (30mL/min) flow for 30 minutes; E – after D, the channel dried with N_2 and re-test.

condition with a 5 Vdc power applied for 48 hours. The sensor was then re-tested for the registered accuracies by referring to a high precision mechanical syringe pump in serial. One sees that a huge negative deviation of about −7% was recorded (Test B). This could be likely because the sensor's surface had been populated with small air bubbles due to the prolonged constant heat that promoted the bubble nuclei growth and air diffusion. When the flow was started, the drag force might force the collapse of these bubbles causing the cooling that led to the negative deviations. This was further supported by the fact that after degassing the flow microchannel for 15 minutes where the same sensor was installed. After the observed negative deviations, re-measurement of the flow accuracy with the identical procedure, the deviation was reduced (Test C). The deviation was further reduced by running the flow at the full scale for another 30 minutes (Test D). And finally, the sensor recovered to the original precision by dried the sensor surface with nitrogen and the re-test with the same procedure after degassing (Test E), which would effectively eliminate the cavitation by bubbles.

3.3 Microfluidic dissolution

While manipulating the microfluidics inside the designated microchannel, mixing two or more fluids is a common practice. The mixture of the fluids, depending on the physical properties, can be miscible or immiscible. The miscible fluids will result in a fluid with a new *concentration*, while the immiscible fluids will lead to a *Two-phase* fluid. For the gas–liquid mixture, cavitation discussed in the previous section or bubbles will very much likely be formed depending on how dissolvable the gas into the liquid will be. Many studies have been dedicated to the gas–liquid mass transfer, particularly to the Taylor flow-related bubble forming, flowing, and separating, [88] oil-in-water emulsions [89], and other phase-separated immiscible fluids such as carbon dioxide dissolving in various fluids [90]. A gas such as air dissolution in water can decrease nucleation temperature, making the enlargement of the bubble nuclei of water resulting in cooling [91].

Microfluidic dissolution phenomena impose big challenges in metering the flow for a desired metrological accuracy, either with immiscible or miscible fluids.

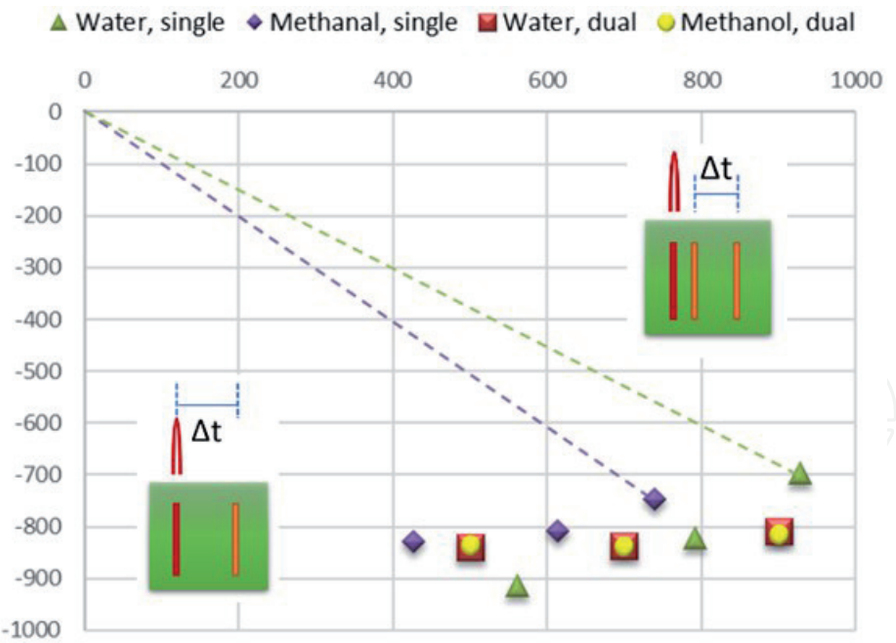

Figure 4.
Thermal time-of-flight measurement of deionized water and methanol flow rates.

The dual-phase or multi-phase flow for the immiscible fluids would involve various liquid–liquid, gas–liquid, liquid–gas–liquid, and supercritical fluid flows beyond the capabilities of the conventional flow sensing approaches. Even with the miscible fluids, the microbubbles would likely present in all cases. The changes in the mixture's density and physical properties will lead to completely different heat and mass transfer, which will significantly deviate the metering values that are always reference to those at the calibration conditions. Optical or image processing would help understand the physical or even chemical process, but it would not help improve the flow measurement accuracy. Therefore, new flow sensing technologies are required for metering these types of microfluidics.

Figure 4 shows the polar plots of a thermal time-of-flight sensor measurement of the deionized water and methanol, respectively, at 3 individual flowrates of 1, 3, and 5 mL/min. The flowrates were set via a precision syringe pump. The sensor's microheater was modulated with a sine wave, and the phase-shifts at the sensing elements were recorded for the flowrate calibration. The fluidic dependent measurement can be seen for the single sensing element configuration as indicated by the differences in measured polar angles between water and methanol. With the dual-sensing elements, the measurements of the two polar plots are overlapped. Therefore, the water calibrated sensor can be directly applied to measure another fluid with different fluidic properties. For the fluidic mixing process with miscible fluids, this dual thermal time-of-flight sensing approach can provide a more desirable measurement than the other thermal sensing approaches. Moreover, as each sensing element's data can be individually acquired, the sensor can also output any changes in its measured fluid. The concentration of the dual miscible fluids can be deduced from the thermal properties measured by comparing the data in the registers at the calibration.

4. Application example: Control of drug infusion

Drug infusion has been in medical practice for over 300 years. Precision control of drug delivery is getting increasing attention in recent years. In a European

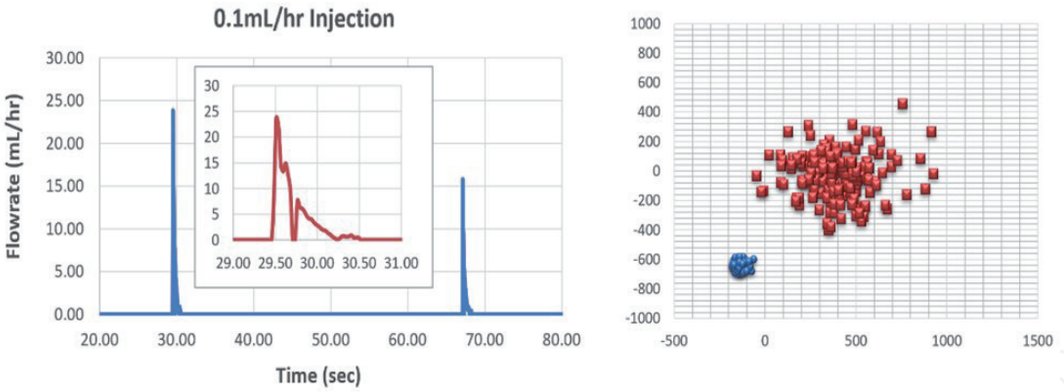

Figure 5.
Drug infusion example: left – commercial infusion pump (Alaris 8100) output at 0.1 mL/hr; and right comparison between the outputs at 20mL/hr by Alaris (red) and a precision syringe pump (blue, KD Scientific Legato 210) measured by a thermal time-of-flight sensor.

Metrology project for drug delivery [92] conducted in 2015, several commercial flow meters with Coriolis, thermal, and differential pressure measurement principles were assessed for metrological performance. However, even the comparisons were made with high precision syringe pumps, some deviations were reported. In practice, many of the devices serving drug infusion are utilizing peristaltic pumps, which have much lower accuracy than the precise syringe pumps [93]. Comparing the peristaltic pump performance and a precise syringe pump can be found in **Figure 5**, the right plot, which is the polar measurements by a thermal time-of-flight sensor at a set point of 20 mL/hr. The red dots are from the peristaltic pump having a large dispersion of the actual flow speed, and the blue dots are from the high precision syringe pump. Therefore, with most of the current drug infusion pumps, the accuracy might not be well controlled since the delivering flow speeds are quite scattered, and a precision sensor is needed to provide the feedback for a close loop. **Figure 5** left plot shows a real-time output of a commercial drug infusion pump Alaris 8100 with a nominal 0.1 mL/hr. delivery speed. From the expanded insert, one sees that the delivery is actually with a pulsed dosage having a wide spectrum of speeds, and the nominal speed is achieved via the adjustment of the time intervals between any of the two pulsed doses. Therefore, the *flowrate* measurement of the flow speeds becomes meaningless, whereas the totalized values would be the ones to provide the real amount of delivered drugs. In an earlier report, [94] a thermal time-of-flight sensor with dual sensing elements suspended in a micromachined microchannel showed a dynamic range of 1000:1 could be achieved. However, to gauge the conventional infusion applications, a sensor with a fast response time of fewer than 3 msec while having a large dynamic range of at least 4000:1 will be needed to meet the requirements for control of total dosage within 5% deviations. A thermal time-of-flight sensor can indeed achieve these conditions with multiple sensing elements.

5. Concluding remarks

Metering the microfluidic flow is critical for many microfluidic applications requiring precise control of the desired microfluidic process or handling. Precision in the flow metering will also improve the performance of the current instrumentation, including the widely applicable drug infusion apparatus, which are nontrivial for the advancement in the medical application and general applications in microfluidics. At the dimensions of interest, current flow sensing technologies are not

fully capable of serving the demands. Factors such as fluid and channel interface/interactions, cavitation, and dissolution play critical roles in impacting microfluidic metrology. Additional sensing elements must be integrated with the current flow sensing approaches to compensate, assist, and enhance the flow metrology. In a most recent review, [95] many available technologies can be used to acquire the microfluidic thermodynamic properties such as viscosity, density, diffusion coefficient, solubility, and phase equilibrium directly from the microfluidic channels on a chip. However, many of these technologies are bulky, costly, and not easily integrated with the microfluidic channels. They also often require a transparent microfluidic channel, which would not be readily available in real applications. Although the advancement of micromachining in both the process tooling and application technologies greatly enrich the options for microfluidic flow sensing, a capable device is yet to be demonstrated. The recently developed thermal time-of-flight sensing technologies for microfluidics offer a multiparameter capability and unprecedented dynamic measurement range. The surface acoustic wave flow sensing as a simple yet non-invasive approach is also very promising. Integrating with additional sensing elements and decomposing the acquired information might provide additional viable tools serving to understand, advance, and better control the microfluidic process and handling.

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