

Fusion of Metrology Data for Large-Scale High-Volume Manufacturing of Polymer-based Microfluidic Devices

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ABSTRACT

Metrology of polymer-based microfluidic devices is challenging in the context of large-scale and high-volume production. It is hard for a single instrument to capture all the information necessary for characterizing key aspects or features critical for the functionality of a device, and correcting for errors in the forming process. Multiple instruments are often needed to overcome compromises between (i) range and resolution, or (ii) bandwidth (speed) and resolution. This leads to the challenge of handling the data sets from the multiple instruments, i.e. aligning and integrating the data sets for accurate metrology. Following standard practices in metrology in other contexts, we propose the use of registration markers, or fiducials, formed in polymer samples for aligning the data sets. The design methodology used for fiducials is presented in the context of microfluidic devices. Data sets recorded from sample instruments, an atomic force microscope, interferometer, and confocal microscope are aligned against fiducial markers. As an example metrology situation, we show that more accurate measurements of channel widths are provided if data from multiple instruments are aligned using fiducial markers.

INTRODUCTION

Microfluidics is a growing research field which promises to reduce the scale of large instruments used in biotechnology, pharmaceutical, and other industries onto a single chip [1]. Devices including integrated mechanical, electrical, optical, chemical and other subsystems have been proposed in the literature for achieving complex functionalities, and proof-of-concept implementations have been demonstrated.

While early devices have been made of silicon using traditional semiconductor and MEMS manufacturing techniques, an emerging class of microfluidic devices are being made of polymers. Example polymer materials include poly-methylmethacrylate (PMMA), poly-dimethyl siloxane (PDMS), topaz, and zeonex. The commonly used manufacturing processes include micro-embossing, micro-casting, and micro-injection molding [2]. Multi-layer devices have been created and allow three-dimensional microfluidic structures including complex flow mixing and valving arrangements.

However, current techniques for the creation of these microfluidic devices are primitive and not suitable for

large-scale manufacture. As commercialization opportunities emerge, it becomes desirable to extend the processing capability for such devices to an industrial scale. An ongoing research collaboration between MIT and a Singapore consortium of universities and industrial centers has been established to address the challenges associated with the large-scale and high-volume production of polymer-based microfluidic devices [3].

In order to ensure that the desired functionality of the device is met, critical features of the parts must be made precisely, and the manufacturability of these parts require metrology techniques that accurately characterize the critical features. Additionally, measurements made inline to the manufacturing process must be performed quickly in order to facilitate high volume fabrication.

Metrology plays a critical role in identifying manufacturing errors and is required for process control, which is a key step in large-scale high-volume production. Different metrology techniques applicable in the context of polymer-based devices have been reviewed and compared by our group in [4]. Experimental data captured using three specific instruments - an atomic force microscope (AFM), optical interferometer, and confocal microscope have been analyzed and compared. The metrics used for the comparison include range (in-plane and out-of-plane), resolution (in-plane and out-of-plane), and measurement bandwidth.

Due to their respective merits and limitations, at this time, no single metrology technique is adequate for the characterization of the critical aspects of microfluidic devices. This paper aims to use this fact to motivate the need for techniques to fuse or merge multiple data sets from disparate instruments. While the focus of the paper is toward microfluidics manufacturing, the data fusion methods described in this paper can apply to the broader context of metrology involving multiple data sets.

The rest of this paper is organized as follows. First, we examine the need for data fusion and highlight specific scenarios where data fusion can prove to be extremely useful. Next, we address the problem of aligning data sets in order to fuse them with minimal error. We propose the use of registration markers, or 'fiducials' for the data alignment. We present the design, fabrication, and subsequent data alignment with such markers. Finally, we investigate specific scenarios for data fusion, with data sets from multiple instruments and the use of markers for the data alignment and fusion.

MOTIVATION

In this section, we examine the need for using multiple metrology instruments in characterizing microfluidic devices. We then highlight specific scenarios where integration of data sets taken from disparate instruments is critical in metrology. These arguments lead to a discussion on methods for appropriately aligning the data sets in order to fuse them and capture all the information necessary for characterizing the formed channel on the sample.

a. Need for multiple instruments:

Most metrology instruments used widely in production environments in large-scale manufacturing, such as interferometers or vision-based systems, compromise between (i) range and resolution and (ii) measurement bandwidth (speed) and resolution. Instruments relevant to microfluidic devices in the context of high-volume and large-scale production, such as interferometers, confocal microscopes, and scanning probe microscopes such as AFM also have these compromises [4].

As an example, consider the measurement of a 100 μm -wide channel (see Fig. 1) to a high resolution on the order of nanometers. The width is larger than the lateral spatial range of typical AFMs. Further, an AFM takes a few minutes for a typical scan, and is hence too slow in a production environment. In a high-volume production environment, an interferometer is a preferred choice over an AFM owing to its speed. However, the lateral resolution of an interferometer is too low for capturing the channel topography. Another limitation with interferometer is the poor reflection from channel sidewalls which results in measurement artifacts at the vertical walls (or edges) of a channel.

Thus, for this case, it is evident that using an AFM alone, or an interferometer alone, cannot achieve the desired specifications of large range, high resolution and bandwidth, and accurate measurement of the channel width.

As an alternative, now consider the case in which the AFM and interferometer data are both available for the channel and overlaid against a common frame of reference. This would imply that we have a high resolution measurement of the channel over its entire width.

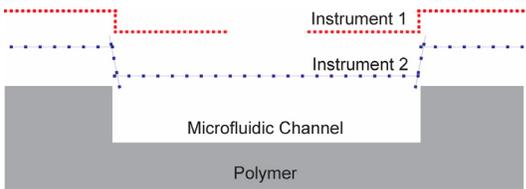


Fig. 1: Cross-sectional view of a channel, with schematic representation of data from typical metrology instruments illustrating the inherent compromise between range and resolution for measurements recorded along a horizontal scan line. Instrument 1, such as an AFM, provides high-resolution and small-range data. Instrument 2, such as an interferometer, provides low-resolution and large-range (field of view) data, and poor sidewall information.

We are interested in such a general problem of metrology, in which multiple instruments are used for the full characterization of device features. Next, we probe further and examine specific scenarios where multiple instruments are needed, and the disparate data sets collected from them need to be integrated, or fused, for accurate metrology.

b. Specific scenarios for data fusion:

Fusion of data sets is commonly used in macroscopic measurements for tasks such as vehicle guidance. In the context of microfluidics metrology, we believe data fusion allows the complementary strengths of different data sets to be analyzed as a 'measurement vector' of different aspects (e.g. height, reflectivity, spectral response, roughness) at each local feature of the sample. We present here three specific scenarios where multiple instruments are needed for accurate metrology. Fusing the data sets after aligning them against reference markers is a critical and necessary step in these scenarios.

b.1. Combining Strengths of Multiple Instruments:

Consider the characterization of a channel formed in a polymer sample, as shown in Fig. 2. The goal is to measure a property, for example, the width w of the channel, over its entire range with a high resolution. Two typical data sets from high-resolution and low-range instruments such as AFM are shown at either end of the wide channel (labeled "Instrument 1"). With these data sets alone, the width of the channel cannot be estimated, since the width is beyond the lateral range of the AFM.

An alternative case is when a low-resolution and large-range data set is captured with an instrument such as an interferometer. As discussed in [4], interferometer measurements are unreliable at vertical sidewalls, and hence the width w cannot be reliably measured (even at a coarse resolution) with the data set from this instrument (Instrument 2 in Fig. 2) alone.

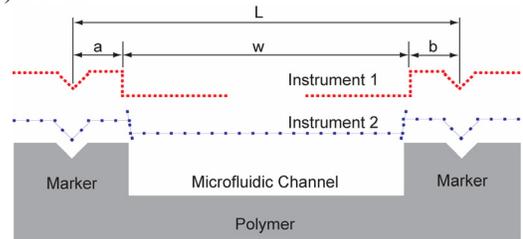


Fig. 2: A channel of width w formed with markers on either side in a polymer sample. Data from Instrument 1 and Instrument 2 are aligned against the marker. The fused data set can be used to extract the precise value of the width of the channel using the relation $w=L-a-b$. Note that with Instrument 1 (such as an AFM) alone, the distance L is unknown and hence w cannot be measured with high resolution. On the other hand, with Instrument 2 (such as an interferometer) alone, the width w cannot be accurately measured due to poor sidewall data.

Data fusion is useful in this situation. A combined data set obtained by fusing the data from both the instruments allows for high-resolution and large-range characterization of the channel. Using alignment markers placed on either side of the

channel, the AFM data set can be used to measure distances a and b , which are defined as the separation between the channel edges and their respective markers in Fig. 2. Using the data set from the interferometer, the dimension L can be estimated by measuring the distance between the markers. Importantly, if the reference marker has a curved profile, sub-pixel information can be determined by interpolating between data points. The reliability of the estimated value of L feeds into the design and fabrication of the reference marker as will be discussed in the later sections of this paper.

The channel width can be measured at a high resolution using the relation $w=L-a-b$. As explained above, this measurement would not have been possible without (i) obtaining data sets from the AFM and the interferometer and (ii) fusing the data sets after aligning them appropriately against reference markers.

b.2. Data Stitching:

Fusing data sets that are all recorded with the same instrument is referred to as data stitching in metrology applications. Reference markers in the overlapping data sets can be used to align them reliably. This idea is shown for a channel formed in a polymer sample in Fig. 3.

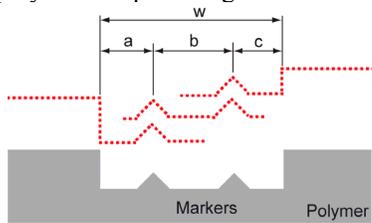


Fig. 3: A channel of width w formed with markers within. Data from a single instrument can be stitched to obtain large-range measurements. In this case, the discrete small-range data sets are lined up against the markers and concatenated. The width w can be measured at a high resolution from the relation $w=a+b+c$.

For the case when the width w of the channel is beyond the range of the high-resolution instrument (for example, AFM) multiple data sets are captured with overlapping portions as shown in the figure. Reference markers, shown as raised conical features formed in the channel, allow for reliable alignment in the overlapped portions. The width of the channel can be measured at a high-resolution from the relation $w=a+b+c$. Note that without the markers, the error in aligning the overlapping data sets could compromise on the accuracy of the measurement of the width w .

b.3. Comparing Instruments against a Reference:

A common task in metrology is comparing any two techniques or instruments for a chosen set of specifications, such as resolution, contrast, or accuracy, against a reference technique or instrument. While a reference instrument such as an AFM can be slow in a production environment, the comparison allows for selecting the best alternative for high-resolution measurement of channel depths or roughness as the polymer samples are formed. Fusing multiple data sets allows for this comparison, as illustrated in Fig. 4.

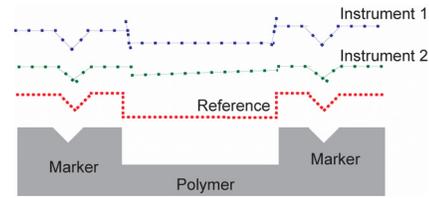


Fig. 4: A channel of width w formed with markers on its either side in a polymer sample. Data sets obtained from multiple instruments can be fused after aligning against the markers. Further, comparison is possible between data sets, say, those obtained from Instrument 1 and Instrument 2 by checking against a reference data set. As an example, roughness profile of the channel obtained with an interferometer and confocal microscope can be compared against an AFM.

In summary, the scenarios illustrated above show specific situations where data fusion is a critical necessity for accurate metrology. The key prelude to the fusion of disparate data sets is their reliable alignment against reference markers, or fiducials. The following section details the design methodology adopted for the implementation of such fiducials.

DESIGN OF FIDUCIALS

The goal of the design is to formulate the metrics for the size, shape and distribution of the fiducials. As an example, the spatial parameters such as height h , width d , and spacing L are illustrated for a fiducial with a rounded top in Fig. 5.

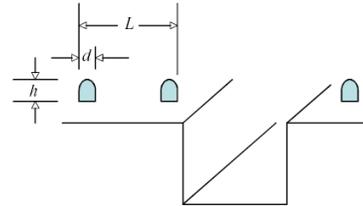


Fig. 5: Spatial parameters in fiducial design.

We begin with examining the set of parameters of interest for the set of instruments being used for the chosen metrology application. In the case of dimensional metrology of polymer microfluidic channels, the parameters of interest are the range (lateral and vertical), and resolution (lateral and vertical). Table 1 shows representative values for these parameters for three instruments – AFM, optical interferometer, and confocal microscope.

Table 1: Representative values for parameters of interest for the set of metrology instruments.

Instrument	Lateral Range	Lateral Resolution	Vertical Range	Vertical Resolution
AFM	$40 \mu\text{m}$	10nm	$4 \mu\text{m}$	$<1 \text{nm}$
Interferometer	$440 \mu\text{m}$	$\sim 0.55 \mu\text{m}$	$2000 \mu\text{m}$	$<1 \text{nm}$
Confocal Microscope	$100 \mu\text{m}$	$\sim 0.25 \mu\text{m}$	$80 \mu\text{m}$	$<0.8 \mu\text{m}$

For fiducials to be recognized by all these three instruments, their lateral size d is dictated by the interferometer, which has the poorest (diffraction-limited) lateral resolution [4]. The spacing L between them is dictated by the AFM since

it has the smallest field of view (FOV) or lateral range. Their height h is limited by the AFM, which has the lowest vertical range.

Mapping instrument parameters to fiducial parameters can be formulated in the frequency domain as well. An approach to modeling each instrument in the spatial frequency domain as a “sampled pass-band” operator is presented in [5]. Here, the spatial frequencies contained in the sample are filtered and discretized by the instrument. This approach can provide a common framework for analyzing capabilities of multiple instruments in diverse metrology scenarios, and also distinguishing spatial frequencies of the sample from instrument effects.

The design of fiducials should also take into account the manufacturing process used. Since vertical sidewall measurements are unreliable with interferometers [4], fiducials with symmetric rounded tops are likely to be a better choice. For example, data from an interferometer can be interpolated finer than its diffraction-limited resolution to identify the peak of a rounded-top fiducial. Embossing high aspect ratio features with lower pressures and hold times can generate under-filled replicas that have rounded tops [6]. In this work, we have explored this approach to form fiducials with widths from 2 to 8 μm , depth of 2 μm , and spaced 20-140 μm apart as detailed in the experimental section.

Another possible approach for manufacturing would be to decouple the fabrication of the fiducials from that of the actual channels on a microfluidic device. This would mean a serial process of manufacturing; errors from the forming channel process can hence be characterized, assuming the fiducials are perfectly formed in another manufacturing step. Advanced lithography techniques such as E-beam lithography, or nano-indentation can be possible options to explore in this context for forming fiducials. In evaluating these techniques, the ability to form rounded-top fiducials should be considered.

EXPERIMENTS

Square PMMA blanks (2.5 cm on a side) were embossed with a custom-built Instron-based hot-embossing machine developed by our collaborators in the Singapore MIT Alliance. The embossing process conditions are as follows: The sample was first heated to a temperature of 130°C and the embossing force was ramped to 1 kN. With zero holding time, the sample was cooled to 90°C to complete the embossing cycle. A 6”-diameter silicon wafer stamp used for the embossing was made by a custom DRIE process for 2 μm channel depth. This depth dimension was chosen so that it is within the range of AFM measurements. A 0.09” thick, 5” square soda-lime glass mask laser-written by Microtronics, Inc. (Newton, PA) was used in the photolithography step in the fabrication of the silicon stamp.

The AFM measurements were captured with a Quesant (Santa Cruz, CA) Q-250 instrument and optical measurements were recorded with a Veeco (Woodbury, NY) interferometer and Zeiss (Göttingen, Germany) laser confocal microscope at SIMTECH and NTU, respectively.

DATA FUSION

Results from data fusion of channels in the wafer measured by the AFM, interferometer and confocal microscope are presented here. With the fiducial markers as reference, the relative orientation and position between different data sets can be determined to facilitate their alignment in three specific scenarios discussed earlier in this paper.

a. Combining Strengths of Multiple Instruments:

A large-range but low-resolution image of a microfluidic device is acquired by a white-light interferometer, as shown in Fig. 6. Since the interferometer cannot provide accurate measurements at the sidewalls, width of the channel cannot be measured accurately. The AFM offers high resolution image capture and can measure the sidewalls more accurately. However, it does not have a large enough lateral range to cover the entire channel. Therefore, high resolution data from the AFM (shown in Fig. 7) can be aligned to the fiducials in the interferometer image, and an accurate measurement of the channel width can be obtained.

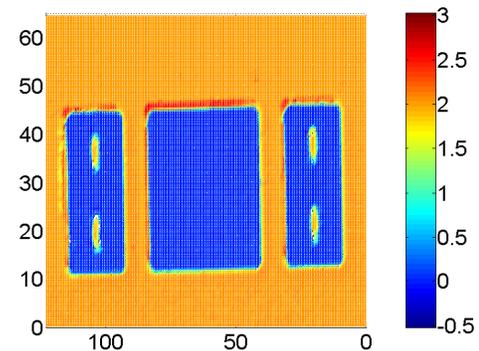


Fig. 6: A large-range but low-resolution image acquired by a white-light interferometer (units are microns).

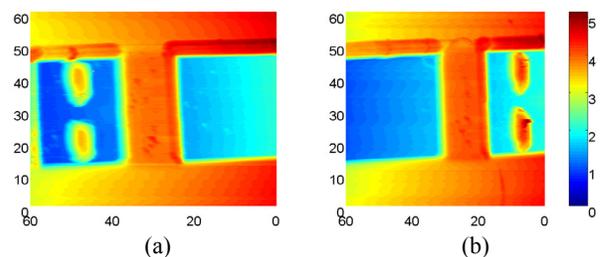


Fig. 7: Left (a) and right (b) parts of the device imaged by AFM (units are microns).

The channel width is estimated from the interferometer data alone to be $44 \pm 1.2 \mu\text{m}$, where the tolerance is determined from the resolution of the data combined with increased uncertainty of the interferometer at a sidewall. Here we note that optical methods tend to overestimate channel width because they are gradient sensitive and stop providing reliable data at sharp changes of topography. However, because the fiducial markers have a rounded profile, low resolution data can be interpolated to acquire a maximum at the fiducial, and this

maximum is used to overlay the high resolution AFM data, shown in Fig. 8.

After the high-resolution data are aligned on top of the large-range data, a profile of the channel width can be obtained, and is shown in Fig. 9. Here we estimate the channel width using the high confidence AFM data, and find that it is $43.75 \pm 0.12 \mu\text{m}$, where the tolerance is calculated from AFM resolution, which is set in this case by the digital-to-analog converter bit-rate of the instrument.

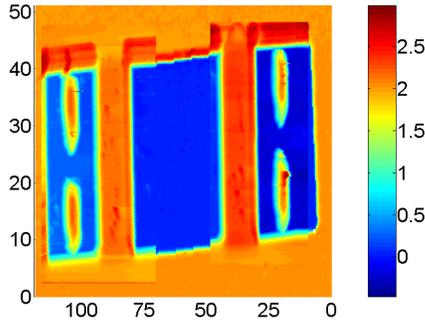


Fig. 8: AFM data are overlaid on interferometer data to more accurately determine the channel width (units are microns).

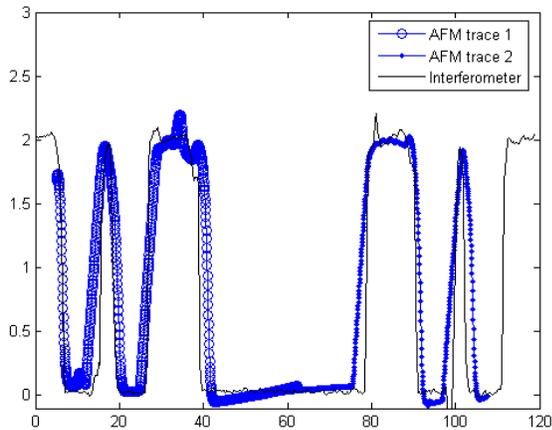


Fig. 9: Cross section data overlaying high-resolution AFM data on top of low-resolution, large-range interferometer data (units are microns). The AFM data (dark traces) are aligned at the peaks of the fiducials. Note that the interferometer overestimates the channel width.

b. Data Stitching:

Due to the limited range (or lateral field of view) of the AFM, the entire profile of a wide channel cannot be obtained directly. Data from the left and right portions of a channel are shown in Fig. 10. To obtain the channel width using only high resolution measurements, the data must be stitched. The two parts both contain the same two fiducial markers that act as the reference in the following stitching operation. By aligning the data to the overlapping fiducials, the channel width is measured to be $81.37 \pm 0.12 \mu\text{m}$, and the stitched data are shown in Fig. 11.

To evaluate the accuracy of data stitching, we use the difference between the same markers in two aligned images as a reference, which denotes the overlapping degree of the two images. Fig. 12 shows the cross sections of the same two

markers from the left and right AFM data sets. The average difference is calculated as $0.086 \mu\text{m}$.

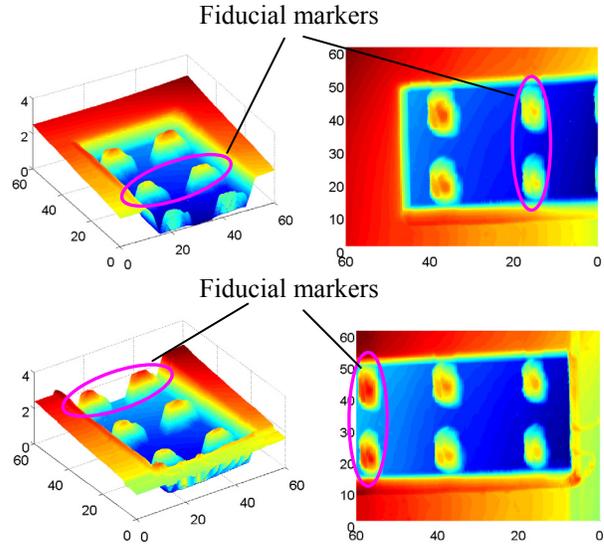


Fig. 10: Left and right parts of the channel as measured by AFM (units are microns).

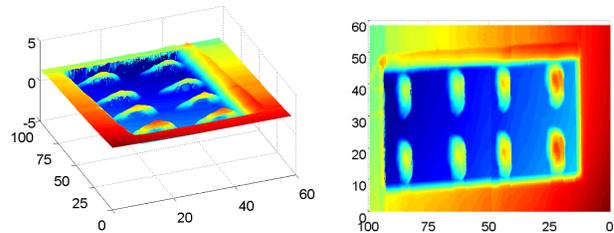


Fig. 11: Data from two AFM measurements are stitched together in one image using fiducial reference markers (units are microns).

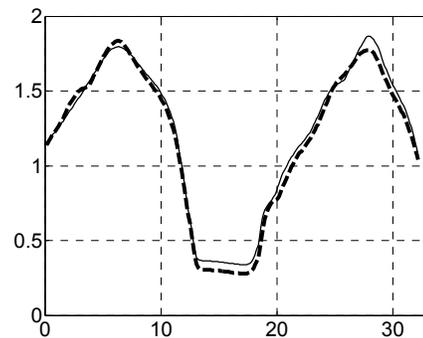


Fig. 12: Cross sections of the same two markers from the left (solid line) and right (dashed line) AFM images (units are microns).

c. Comparing Instruments against a Reference:

In order to obtain guidelines for recommending instruments in various metrology situations, it can be valuable to compare the performance of various instruments to a standard. Toward that end, confocal microscopy data are compared to an interferometer using the AFM as a standard. To ensure that all data are mutually aligned, reference fiducials are used. The same device mentioned above is measured by AFM, white-light interferometer and confocal microscope (whose acquired image is shown in Fig. 13) respectively to compare

the characterization of the three instruments. After alignment against the two markers, the data from three instruments are combined and a cross section is extracted (indicated by the black vertical line in Fig. 13 and shown in detail in Fig. 14).

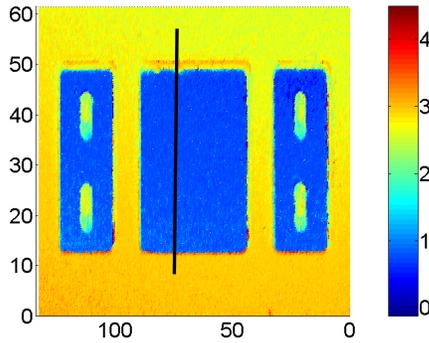


Fig. 13: Image from a confocal microscope (units are microns). The black vertical line indicates the cross section location shown in Fig. 14.

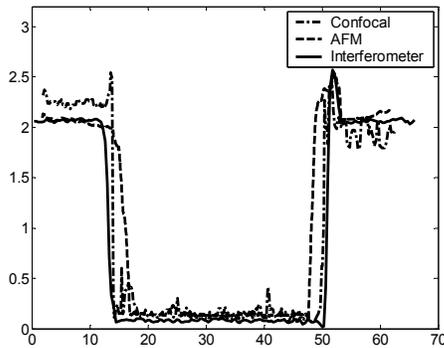


Fig. 14: In order to compare the strengths of multiple instruments, data from an AFM, a confocal microscope, and an interferometer are aligned using fiducial markers (units are microns). Misalignment in the vertical scale is due to a lack of a vertical degree-of-freedom in the preliminary alignment algorithm.

If the AFM data are taken as the normal reference, we can compare the other two instruments. The correlation coefficient between data from the interferometer and AFM is 0.936; the same between that from confocal microscopy and AFM is 0.865.

Several conclusions can be drawn from the data shown above. There is much more noise in the image from confocal microscopy, in which the device surface seems very rough. This is expected from the diffraction-limited resolution of the confocal microscope for vertical imaging. The interferometer data set appears to be less noisy, as expected from the fact that its vertical resolution is not diffraction-limited, but dictated only by the pixel noise in the CCD plane. Further, both the interferometer and confocal microscope cannot generate precise sidewall information. Comparing multiple instruments on aligned data sets enables these kinds of general conclusions, and these recommendations may serve to guide the selection of tools for manufacturers of microfluidic devices.

CONCLUSIONS

In this paper, we have examined the need for fusion of data sets from multiple instruments, and identified scenarios where high resolution measurement of device features over large fields of view requires data sets to be aligned and integrated. For the alignment or registration of the data sets, we utilized fiducial markers fabricated on the device alongside the functional features.

Our experimental investigation focused on the specific scenarios motivated in the paper. The scenarios include combining strengths of multiple instruments, stitching the data from any instrument beyond its range, and comparing one instrument against the other. The framework for the data fusion was carried out for the case of AFM, interferometer, and confocal microscope. Since sidewall measurements from interferometers are unreliable, rounded-top fiducials were made from underfilling of high-aspect ratio channels in the tool. With image-registration and subsequent fusion, the channel widths were measured to be $43.75 \pm 0.12 \mu\text{m}$, as compared to $44 \pm 1.2 \mu\text{m}$ when data fusion is not used. This result shows the promise of the proposed approach, however it should be noted that the alignment algorithm is based on least squares and may itself be a source of error.

Future tasks include (i) investigating edge artifacts from optical measurements, (ii) extending the proposed alignment concept to vertical alignment of data sets, (iii) building on a instrument model approach formulated in [5] for designing fiducials and other applications, and further, (iv) utilizing a spatially tuned pattern of fiducials for characterizing wafer-scale forming errors.

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