

Measuring Sealed Micro Fluidic Devices — Yes, It Can Be Done!

DR. DIANE HICKEY-DAVIS,
DR. IAN HOLTON

How deep, flat or wide is your closed channel micro fluidics device after fabrication? A way to measure enclosed micro fluidics accurately and quickly.

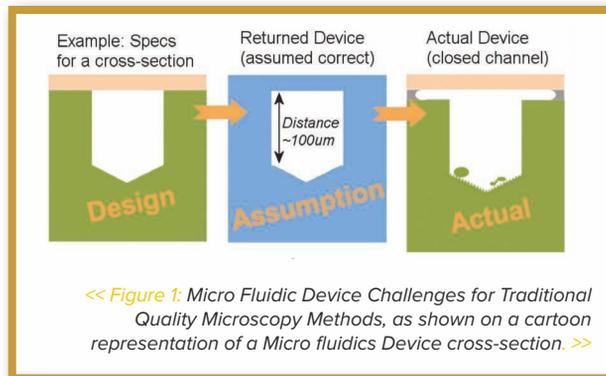
On the cover of “Nature” in March 2014 were the words, “Practical Microfluidics,” indicating that micro fluidics technology was moving mainstream, and in summer 2015, ResearchAndMarkets.com estimated the Global micro fluidics market to be \$3B, and increasing by 19% through 2020. However, becoming ‘practical’ and mainstream comes with some significant manufacturing challenges, specifically for quality assurance, when the fabrication of the device is often separated from the users of the device.

Ensuring quality in micro fluidic devices — a challenge for traditional microscopy

Micro fluidics operate on specific flow dynamics, pressure points and mixing streams, which require very precise simulations of volume and flow. However, in the manufacture of micro fluidic devices, precision to the micron level is affected by surface roughness, mating practices, and surface treatments, and material spoil from manufacturing processes. Achieving post-production performance to match pre-production simulation results is near impossible; and to determine why the results don’t match requires determining the exact measurements of the post-production device.

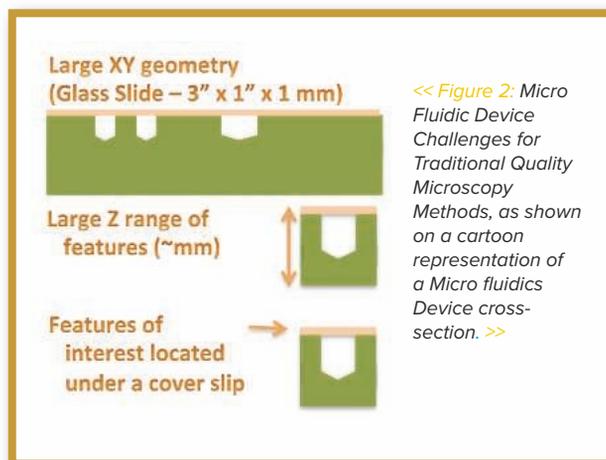
Additionally, R&D devices are often manufactured on glass, but mainstream production is done on softer materials like PDMS. Maintaining similar geometries on PDMS poses a really big challenge. Having the capability to measure closed micro fluidic devices on both glass and PDMS is critical for optimising the transition from R&D to production.

Traditional quality methods — using optical microscopy or profiler probes to confirm specifications — may not work with micro fluidics. Large XY geometries and millimeters deep substrates (chips / glass slides) are not in the sweet spot for those methods. Additionally, quality control processes must be developed to be fast and specific in determining if a product meets specifications.

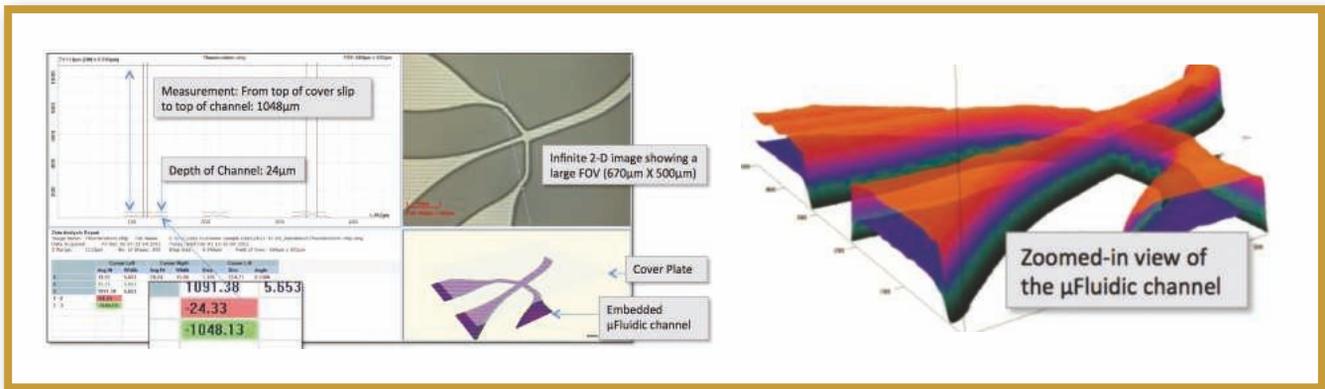


The three-dimensional nature of micro fluidic devices also creates challenges for probe-based measurement techniques. Trenches can be hundreds of microns deep, so quality process must measure not only the distance of the trench, but also the depth. And finally, after final assembly, the finished device must also be quality controlled, so a method to look into a closed trench is essential.

Three specific challenges arise for quality methods using traditional microscopy (figure 2):



Large XY Geometry — micro fluidic devices typically are the size of a glass slide, and in terms of microscopy, are quite large. The ability to analyse specifications across a whole chip device could be time-consuming and painstaking, but is a requirement for quality processes.



<< Figure 3: Measurement of the depth of a channel (above) on a closed 'lab-on-a-chip' device. This optical technique allows a large XY area (over a half-mm²) & deep Z height (over 1 mm deep to the channel) in a single scan as well as providing multi-surface imaging (right). Images courtesy of Zeta Instruments (www.zeta-inst.com). >>

Large Z range of features (~mm) — Because micro fluidics channels are often moving more than just fluid, including cells, the dimensions in the third dimension are quite significant, sometimes in the mm range. Features of interest located under a cover slip — for quality processes, measurements at the completion of the process are critically important. However, for a finished micro fluidic device, this means looking INSIDE the device.

Microscopy Solution Requirements for Quality Control

Quality processes for micro fluidic devices should strive to meet certain criteria:

Be non-contact and non-destructive – Because of the requirements of the medical industry, once manufactured, contact with other surfaces needs to be minimised. Contact profilometers would not be able to analyse the inside of a closed channel.

Cost Effective – Unlike the semiconductor industry, the cost per device does not justify a huge investment in metrology equipment. Any tool being used for these measurements needs to meet the economic constraints of the industry.

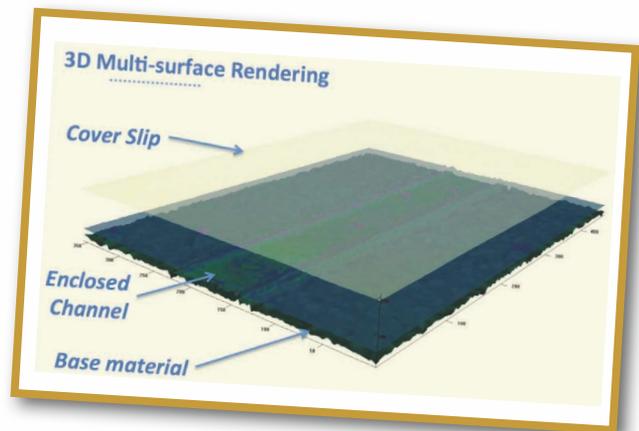
Optical – Of the three micro fluidics materials typically used, two materials (polymers and glass) are transparent to white light, making an optical technique a cost-effective measurement technology. Silicon, the far distant third choice for a micro fluidic device material, could also benefit from an optical technique.

Fast – For any production, quality assessments should be quick. A few minutes to confirm that a device meets or exceeds specs are all that can be tolerated.

Quality Control of finished micro fluidic devices

In 2009, two veterans of the metrology industry, James Xu and Ken Lee, developed the Confocal Grid Structured Illumination (CGSI) technique. This technique evolved confocal microscopy to enable measurement of difficult surfaces and also image in true color. While the CGSI technique is used for a multitude of surface analysis applications, it is uniquely suited for imaging sealed micro fluidic devices, as shown in figure 3.

A number of advancements in the CGSI technique, called ZDots on the Zeta 3D Optical Profiler used for the images in this article, enable this “see-into-a-closed-channel” ability, as show in figure 4. To demonstrate, two case studies and two application examples are presented on page 18.



<< Figure 4: High light throughput optical design images multiple layers simultaneously in less than a minute. Image Courtesy of Zeta Instruments. >>

**CASE STUDY:
Animal Reproduction**

ORGANISATION:
A company using micro fluidics in animal reproduction

SITUATION:
The company designed the chip, then sent it out for fabrication. The fabrication company returned the chip, supposedly made to the specifications. Neither the supplier company nor the customer had a tool to measure the actual dimensions, post-fabrication.

PROBLEM:
Device was not performing to simulation. Unknown reason.

SOLUTION:
Using CGSI (ZDot) technology on a Zeta 3D Optical Profiler, the company was able to determine within 15 minutes (several scans across the device) that the part was not manufactured to specification, and that the mechanical polishing process used by the manufacturer created significant variation device-to-device.

**CASE STUDY:
Collapsed channels**

ORGANISATION:
University Fabrication team

SITUATION:
The fabrication team makes devices for a number of both internal and external customers. These devices range from prototypes to pilot development. Finished devices did not perform to customer specifications.

PROBLEM:
Unable to measure closed micro fluidics device to identify problem.

SOLUTION:
Using this technology, analysis of closed cells showed that in some places, the PDMS had collapsed, as shown in the before and after images in figure 5.

APPLICATION EXAMPLE:
Deep Trench

APPLICATION:
Measuring an open trench (no coverslip).

NEED:
Measure the accuracy of the etch manufacturing step for quality purposes, and as a go/no-go gate for further processing.

PLANNED DEPTH:
300 μm

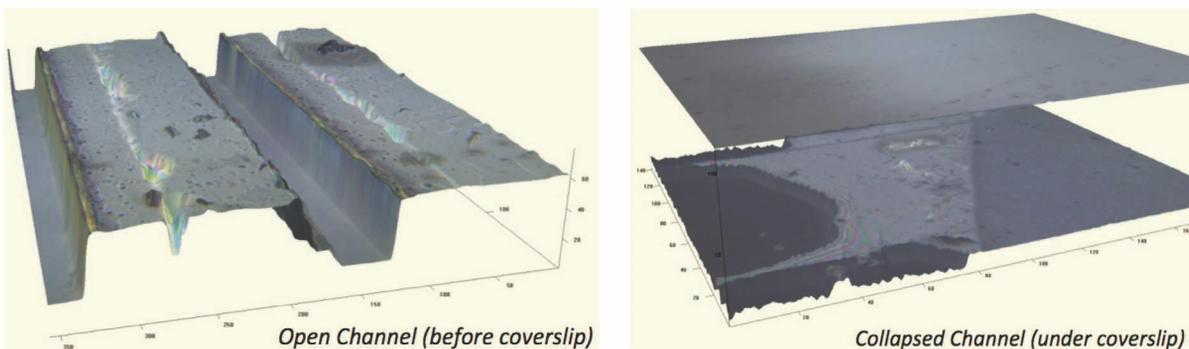
ACTUAL DEPTH:
296.5 μm as shown in figure 6
The CGSI technique can be accurate up to ± 10 nm
This application is typically not possible for other profiling technologies.

APPLICATION EXAMPLE:
Measuring the Accuracy of the CGSI (ZDot) method

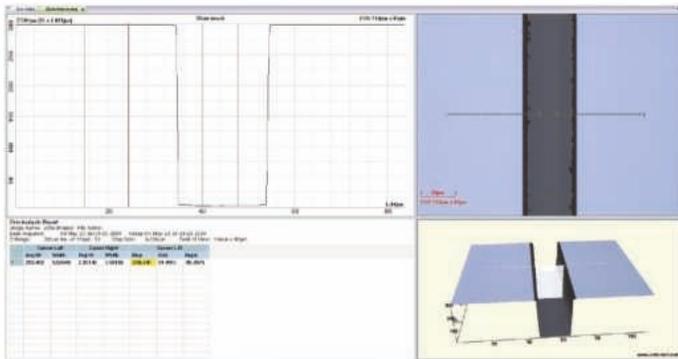
Using a solder bump on a passivated, transparent substrate, the measurement using a CGSI technique is compared to a stylus profilometer. Contact profilometer measures 76.91 μm , CGSI instrument (Zeta Optical Profiler) measures 77.33 μm .

Figure 7 shows both the contact profiler result and the optical profiler result. Correlation is better than 50 nm. This type of application – the measurement over the centerpoint of a half-sphere – would typically take many passes of a stylus profilometer to confirm that the highest point was actually reached, which could take significant time. For optical profilers not using ZDots, the combination of a passivated, transparent substrate and a shiny solder bump would present significant imaging challenges. Using an instrument utilising the CGSI technique enables this accurate measurement quickly.

The CGSI (ZDot) technology enables quality control of the entire manufacturing process of micro fluidic devices, including after the device channels have been enclosed.



<< *Figure 5: Images showing a channel before and after application of cover slip, in a micro fluidic device made via photolithography in PDMS, then covered with a flat piece of PDMS. After the application of the coverslip, the channel collapsed. While easily visible on this Zeta Optical Profiler using CGSI technology, the collapsed channel had previously been a mystery to the university lab fabricators. Images Courtesy of Zeta Instruments. >>*



<< Figure 6: Application example of the measurement of a deep trench. Image courtesy of Zeta Instruments. >>

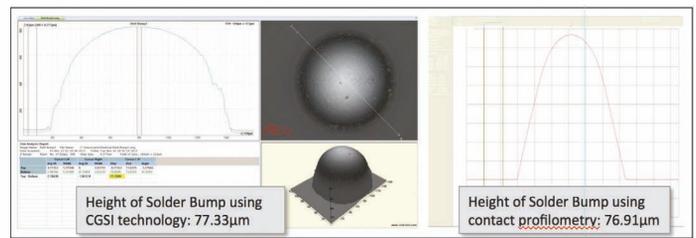
In addition, the CGSI (ZDot) technology has other benefits as well:

- True colour imaging (beneficial for many biological and manufacturing applications) to determine sources of contamination
- In conjunction with software, automated detection and measurement of patterned substrates at multiple process steps can be measured quickly during manufacturing.

As the micro fluidics markets grow, and the outsourcing of manufacturing of device substrates increases, quality assurance both on the part of the manufacturer and the customer will become critical. Technologies like CGSI will fill a need for micro fluidics quality control.

Dr. Diane Hickey-Davis obtained her Ph.D. in Materials Science and Engineering at the University of Florida, studying MEMS fabrication and ion-implantation into materials such as man-made single crystal diamond. She has worked professionally in business consulting, strategic sales & marketing management, and new product development of MEMS devices. She currently works with several start-up companies as a transition executive and consultant.

Dr. Ian Holton obtained his Ph.D. in Physics at the University of Liverpool, and currently works to solve customer problems using innovative compositional analysis, electron microscopy and 3D profiling. He can be reached at sales@acutance.co.uk.



<< Figure 7: Comparison of the accuracy of the CGSI imaging method with contact profilometry, using both to image a solder bump on a passivated, transparent substrate. Images courtesy of Zeta Instruments. >>

DESIGN PROTOTYPE FABRICATE BOND* PACKAGE SHIP REPEAT

* Ambient Temperature Bonding (ATB) provides a unique and unparalleled method to hermetically bond microfabricated structures using silicon-to-glass, metal-to-glass, glass-to-glass combinations without use of adhesives or high temperatures. The temperature of the bulk substrate does not increase even one degree Celsius above ambient temperature. Think of the possibilities.