

From Miniaturized Bioassays to 3D Imaging of Microfluidic Devices

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Summary:

This paper presents the evolution of capillary-driven microfluidic systems for miniaturized biosensing applications and the subsequent development of a programmable 3D microscopy platform designed to address the optical inspection challenges associated with these devices. The presentation will take the audience from my early work on bioassay development and the associated fabrication and inspection challenges to the founding of Microqubic AG to support the sensor and microfluidics community with dedicated imaging solutions.

Keywords: microfluidics, biosensors, microscopy, inspection, imaging

Background, Motivation and Objective

The development of point-of-care diagnostics using microfluidics requires precise fabrication, fluidic control, reagent integration, and quality assurance. While developing and scaling lab-on-a-chip devices for production is demanding, inspection and quality control remain equally important and are often underestimated in research. Microfluidic devices are commonly fabricated from highly transparent materials such as PDMS, glass, and thermoplastics, highly reflective substrates such as silicon, or hybrid combinations of both. Sealed channels, embedded reagents, electrodes in some cases, and liquid flow further complicate optical inspection. In addition, these devices may be physically large, exceeding the field of view of standard microscopes, while containing features down to only a few micrometers, often combined with variations in channel depth. Conventional microscopes struggle to capture the complex 3D topography and sidewalls of these structures for both characterization and presentation-quality full-device imaging.

Development of Novel Microfluidic Concepts

During my tenure at IBM Research-Zurich, we addressed several of these hurdles by introducing novel microfluidic concepts integrated with dedicated electronic and optical systems. We developed electro-actuated valves enabling programmable stop-and-go flow control from a smartphone [1] (see Fig. 1). We also introduced self-coalescing flow concepts for pulse-shaped reagent delivery [2]. Using ultra-miniaturized chips supporting capillary-driven flow and localized dried-reagent reconstitution, we realized one-step immunoassays [3] and

devices containing up to 10,000 localized biochemical reaction sites [4] (see Fig. 2). This research frequently required custom imaging solutions in our laboratory, including 3D inspection systems.

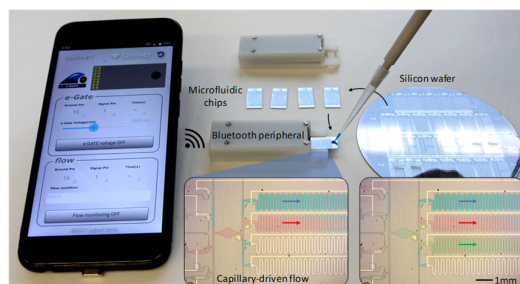


Fig. 1. Programmable smartphone-controlled flow of multiple liquids in capillary-driven microfluidic devices without active pumps.

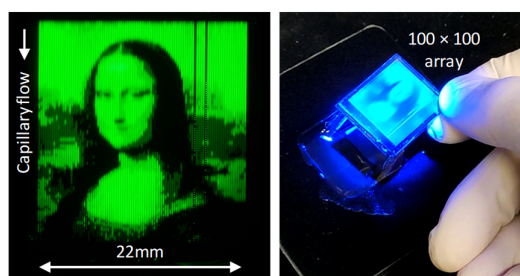


Fig. 2. Localized reconstitution of dried reagents using self-coalescing flow, imaged with a custom-built fluorescence microscope.

Programmable 3D Microscopy System

Imaging requirements in our research motivated me to develop a dedicated programmable 3D microscopy platform. Although high-end 3D microscopes exist, they are typically expensive, difficult to adapt to custom experimental setups,

and not optimized for microfluidic sensors. Driven by the need for a versatile and accessible inspection tool, I initially built a fully motorized microscope prototype using Lego components (see Fig. 3). Following its publication [5], the system attracted significant attention from the microfluidics and sensors communities, highlighting the value of multi-angle optical inspection. This motivated me to found Microqubic AG to commercialize modular, programmable, and affordable 2D/3D microscopes (see Fig. 4). The microscopes incorporate seven motorized actuators enabling X-Y translation, sample rotation, focus, zoom, and camera tilting. To image challenging samples effectively, the system integrates five illumination sources, including a proprietary curved LED matrix and coaxial illumination.

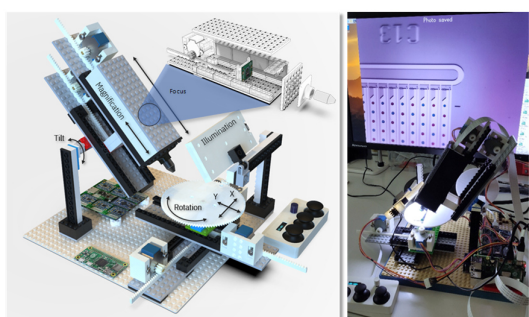


Fig. 3. Motorized Lego microscope developed for imaging microfluidic chips (github.com/IBM/Microscopy).

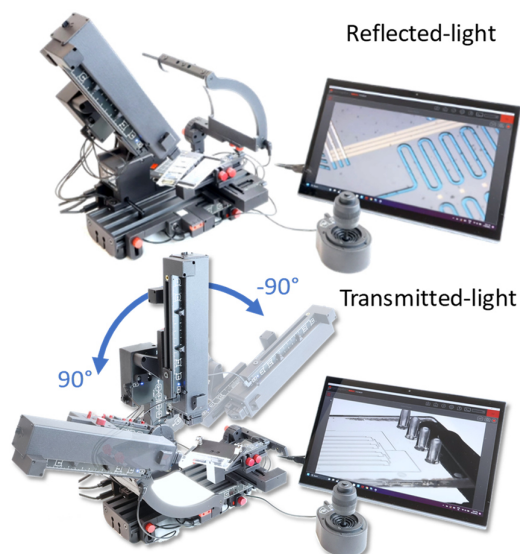


Fig. 4. Microqubic's motorized, programmable, and modular 3D microscope for imaging transparent and opaque microfluidic chips (www.microqubic.com).

Results and System Impact

Combined with MRCL Viewer software developed in-house, the platform supports autofocus, automatic focus stacking, HDR

imaging, 4K video capture, automated imaging and live 2D/3D measurements (see Fig. 5). The systems are now used in more than 100 laboratories across 25 countries and continue to evolve with features such as fluorescence imaging and automated chip inspection.

Historically, researchers have often had to adapt their experimental setups to rigid microscopy systems. Microqubic platforms aim to reverse that traditional paradigm by providing compact and reconfigurable tools tailored to the experiment itself. For the sensor community, this approach enables rapid, precise, and affordable characterization of next-generation microfluidic devices, biosensors, and MEMS.

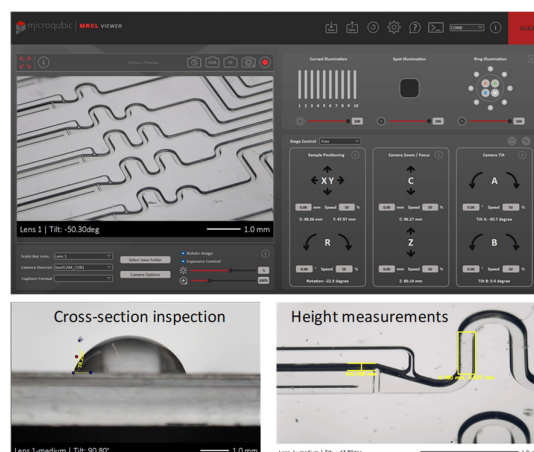


Fig. 5. Microqubic's software supporting advanced features such as 3D measurements, autofocus and focus stacking.

References

- [1] Temiz, Y.*, Arango, Y.*, Gökçe, O., et al., "Electro-Actuated Valves and Self-Vented Channels Enable Programmable Flow Control and Monitoring in Capillary-Driven Microfluidics," **Science Advances**, 2020; doi: 10.1126/sciadv.aay8305
- [2] Gökçe, O., Castonguay, S., Temiz, Y., Gervais T., Delamarche, E., "Self-Coalescing Flows in Microfluidics for Pulse-Shaped Delivery of Reagents," **Nature**, 2019; doi: 10.1038/s41586-019-1635-z
- [3] Hemmig, E., Temiz, Y., Gökçe, O., et al., "Transposing Lateral Flow Immunoassays to Capillary-Driven Microfluidics Using Self-Coalescence Modules and Capillary-Assembled Receptor Carriers," **Anal. Chem.**, 2020; doi: 10.1021/acs.analchem.9b03792
- [4] Temiz, Y.*, Gervais, T.*, et al., "Large-Scale Dried Reagent Reconstitution and Diffusion Control Using Microfluidic Self-Coalescence Modules," **Small**, 2022; doi: 10.1002/smll.202105939
- [5] Temiz, Y., "The lego microscope: A valuable lab tool began as a diy project," **IEEE Spectrum**, 2020; doi: 10.1109/MSPEC.2020.9078448