Advanced microfabrication with two photon polymerization (2PP) towards developing in vitro diagnostic lab-on-chip platform (#22rl-060)

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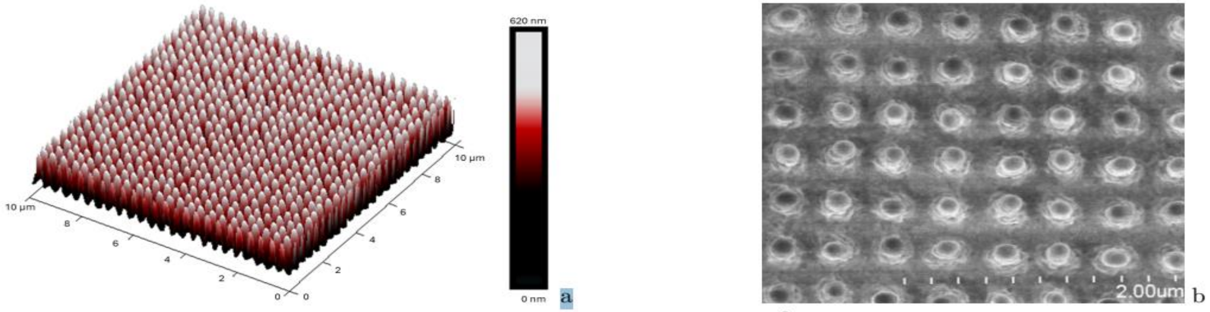
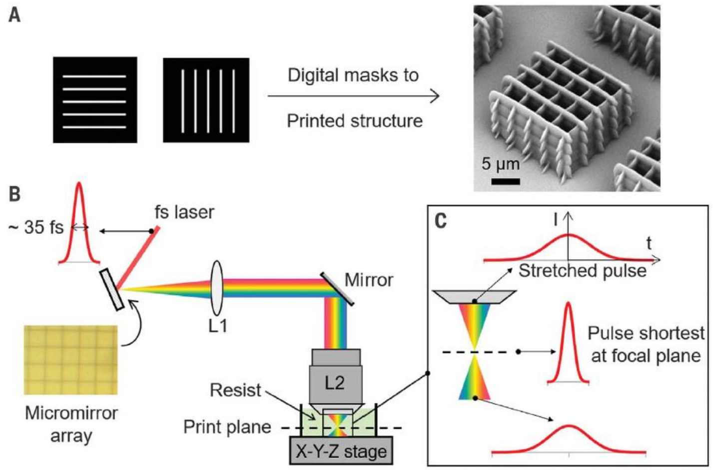
Project objectives

1. Development of the state-of-art additive microfabrication platform for achieving breakthroughs in high throughput, high resolution and high surface quality layer-by-layer fabrication of photonic components for bio-sensing applications
2. Develop and validate a novel type of fully integrated and 3D-printed lab-on-chip platform for SERS based bio-identification of hemoglobin variants for the diagnosis of diabetes
3. Establish multi-photon polymerization manufacturing and Raman spectroscopy-based bio-sensing capabilities at Yerevan State University (YSU)



Chalyan, Tatevik, Mehdi Feizpour, and Heidi Ottevaere. "Two-photon polymerized nanopillars for surface-enhanced Raman spectroscopy." *Optical Sensing and Detection VIII*. Vol. 12999. SPIE, 2024.



Saha, Sourabh K., et al. "Scalable submicrometer additive manufacturing." Science 366.6461 (2019): 105-109.

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Bacterial identification in SERS-integrated microfluidics using CNN-driven 2D classification of 1D spectra

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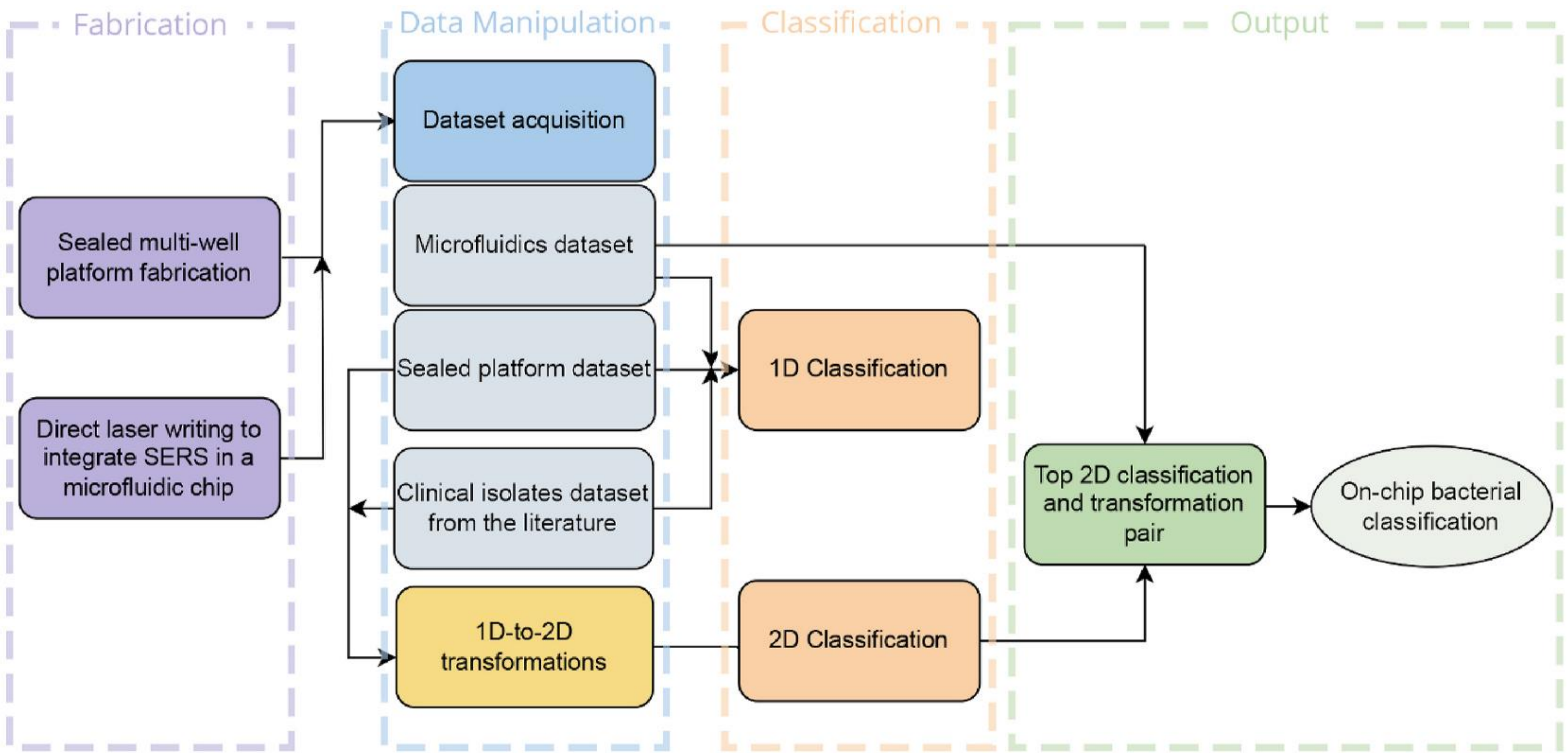
Bacterial classification

ABSTRACT

Bacterial sensing involves complex and variable samples that require advanced handling and analytical methods. To address these challenges, machine learning—especially deep learning—and SERS-based microfluidics have shown great promise. While previous studies have majorly focused on 1D spectral classification, the use of 2D representations of SERS spectra has not yet been explored, particularly for on-chip bacterial identification. In this work, we introduce a novel framework that combines SERS-enabled microfluidics with optimized 2D convolutional neural networks (2D-CNNs) for bacterial classification. SERS integration inside microfluidic chips was achieved through direct laser writing, enabling custom active areas and efficient on-chip measurements. We systematically evaluated nine distinct 1D-to-2D spectral transformations, with spectrogram and continuous wavelet transform yielding test accuracies of 99 % and 97 %, respectively, on controlled datasets. Using transfer learning, we achieved 100 % accuracy on the on-chip dataset, demonstrating the model's adaptability to new data. In contrast, other transformations, like pairwise distance and autocorrelation, performed below 93 %, indicating their limited ability to capture subtle spectral features. This framework offers high sample control, parallelization, and the potential for expanding the bacteria database, making it ideal for low-data-volume situations such as rare infections. Further development and testing across strains, environments, and practical challenges can further improve our approach's reliability for real-world diagnostics.

The workflow of the CNN-Driven 2D Classification of 1D bacterial spectra



SERS spectra measurement in the sealed multi-well platform

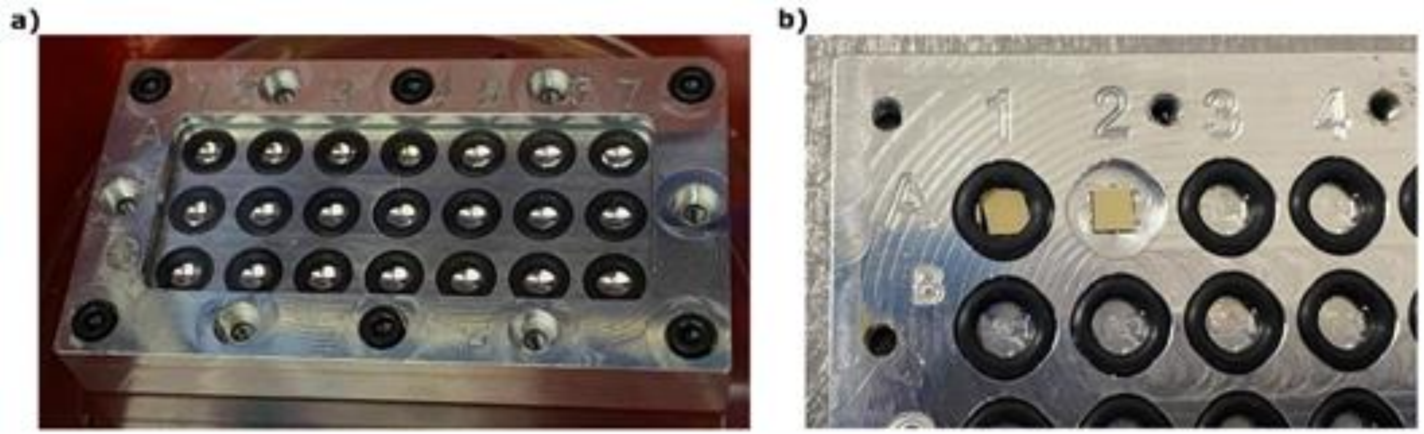


Figure S1. The sealed multi-well platform for hour-long SERS measurements without losing focus. a) Assembled platform. b) placement of the commercial SERS substrates in the platform's wells.

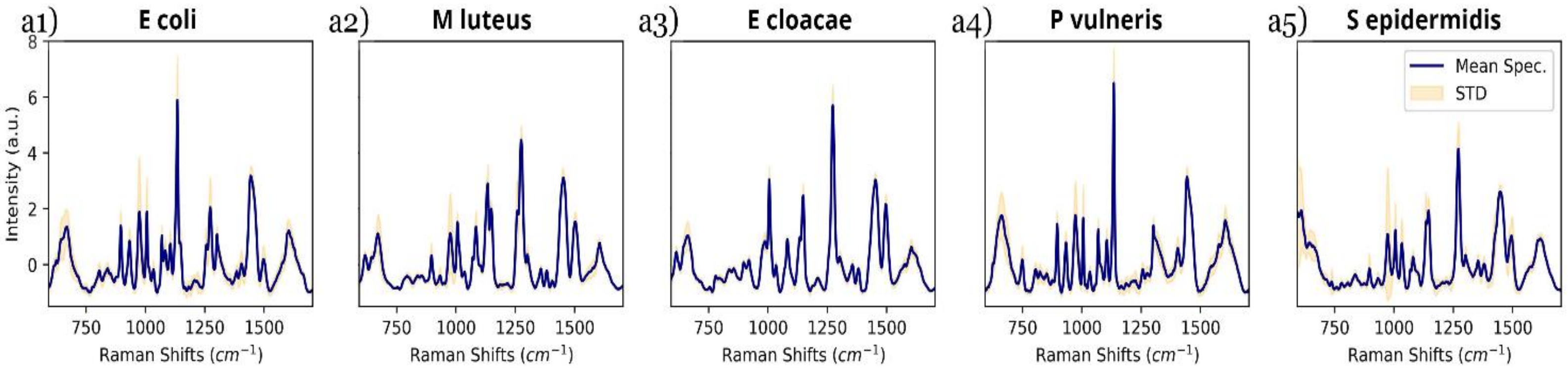
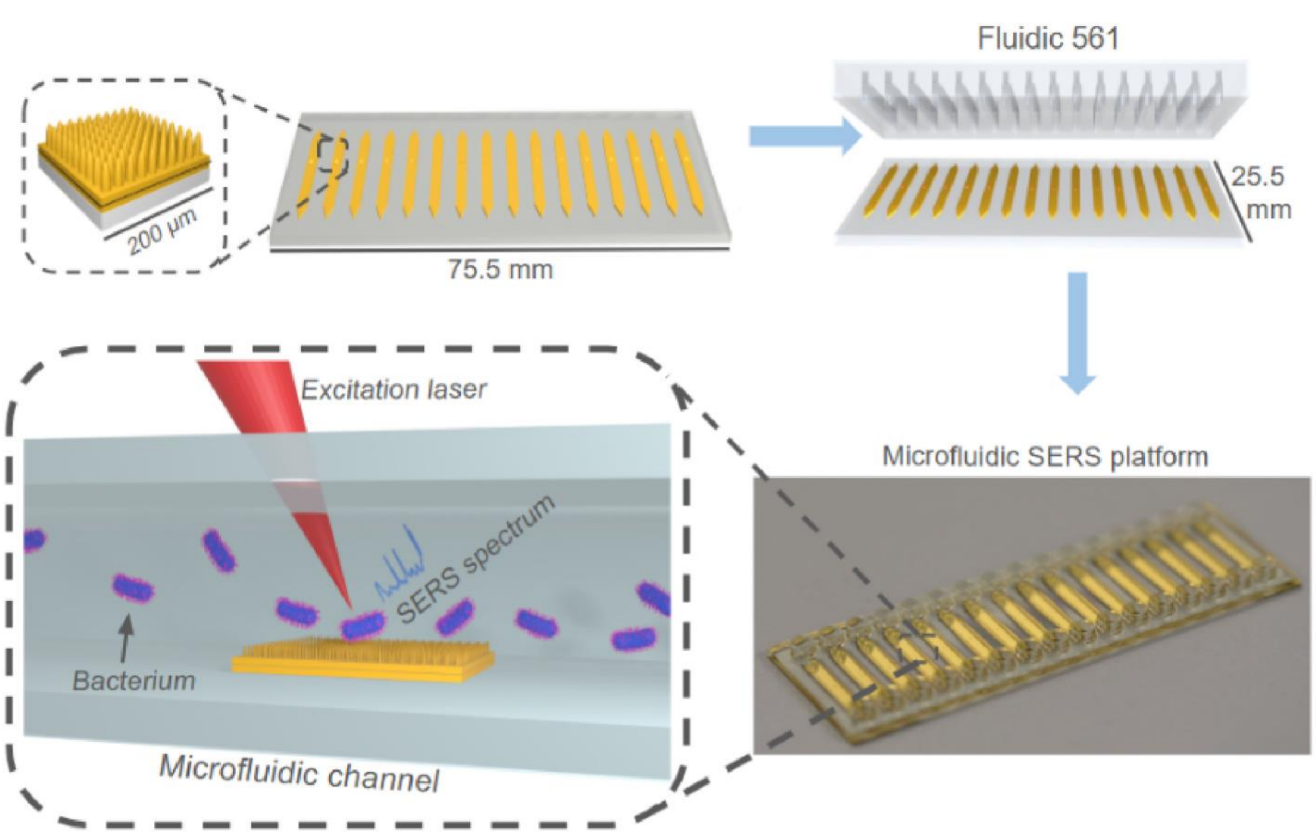
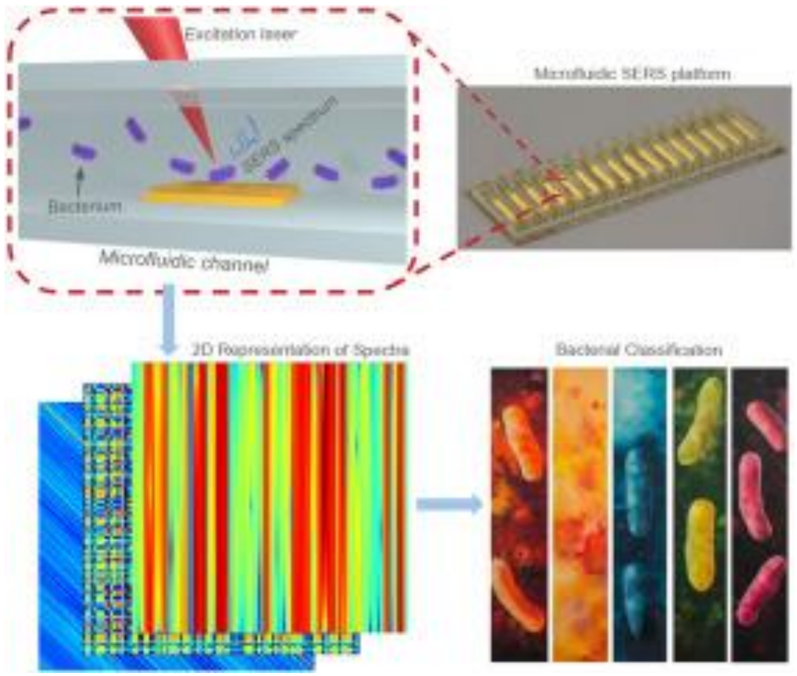


Figure S3. SERS spectra measured in the sealed multi-well platform.

Schematic representation of SERS substrate integration and chip assembly

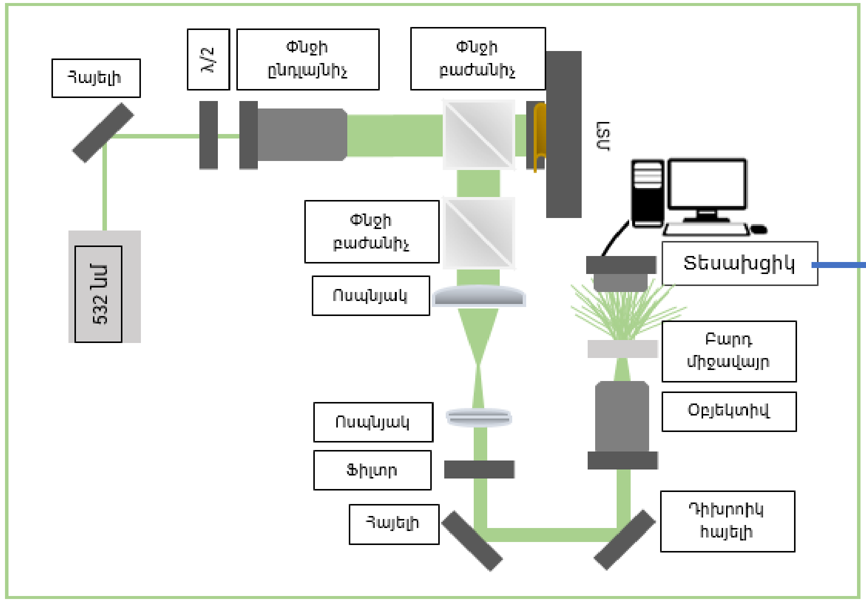


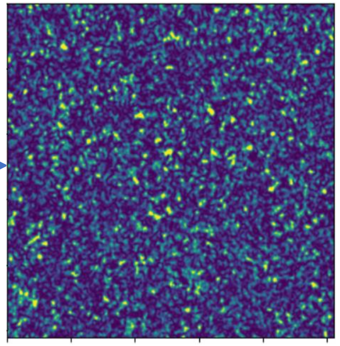


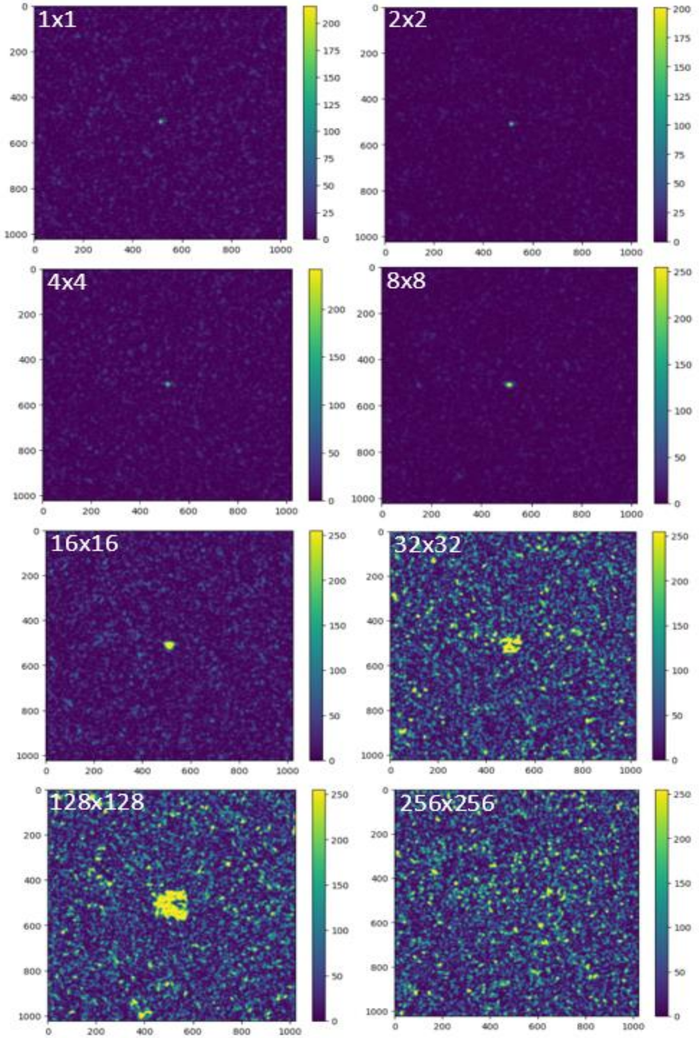
Fluidic 561 is a 16-channel commercial chip

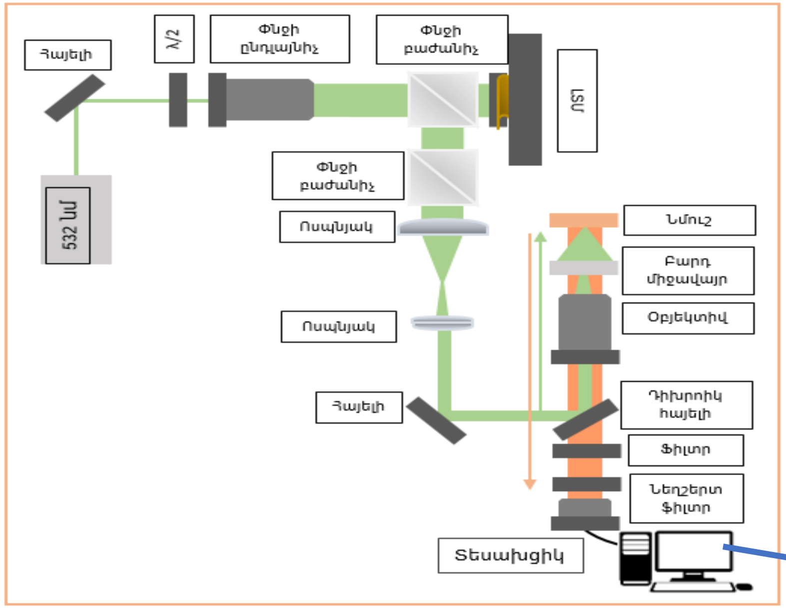
2D Representations:
1. Spectrogram via Short-Time Fourier Transform
2. Pairwise-Distance Plot or Recurrence Plot
3. Autocorrelation Matrix
4. Continuous Wavelet Transform
5. Synchronous Correlation
6.Gramian Angular Field (GAF)
7. Markov Transition Field

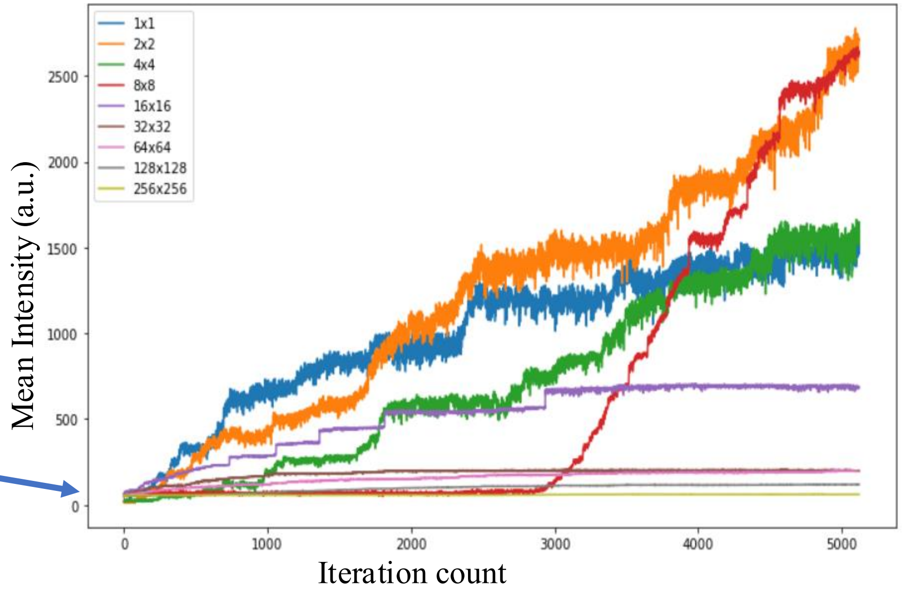
Fluoerescence through complex scattering media



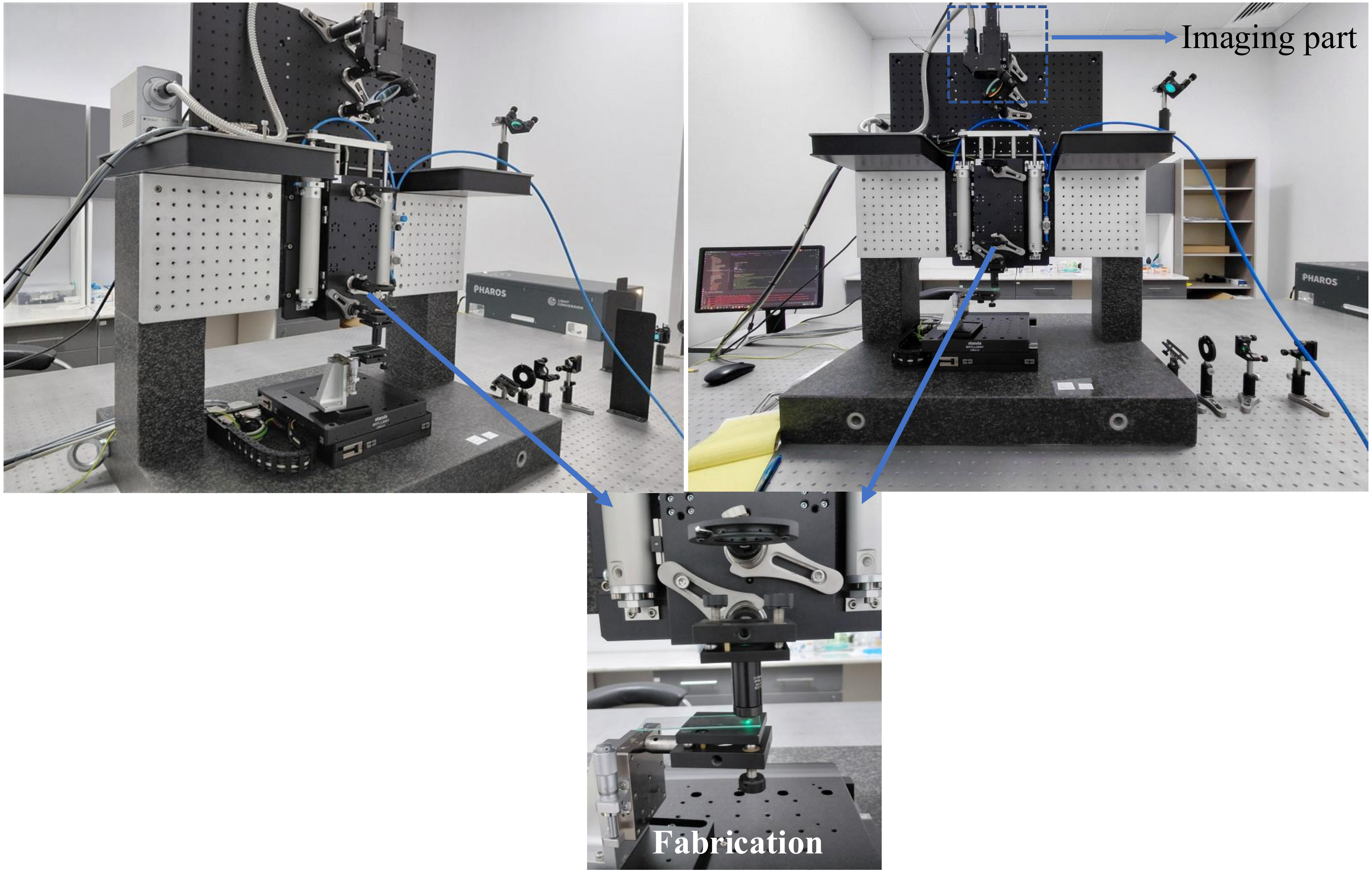




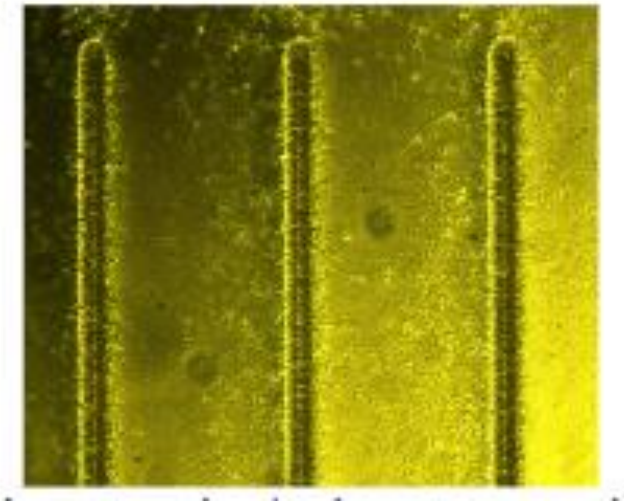




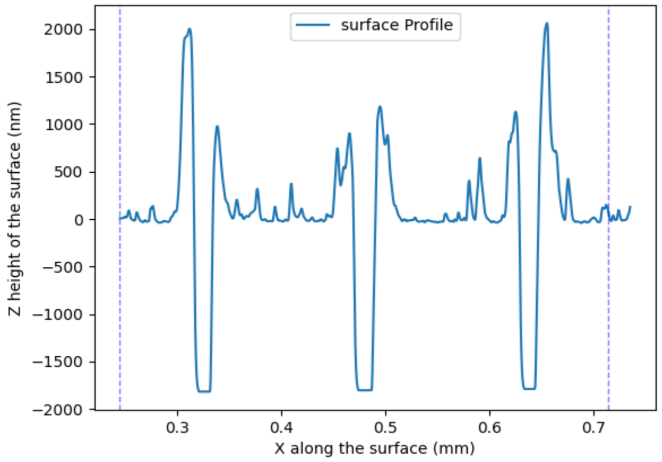
Microfabrication setup



Applications of microfabrication setup

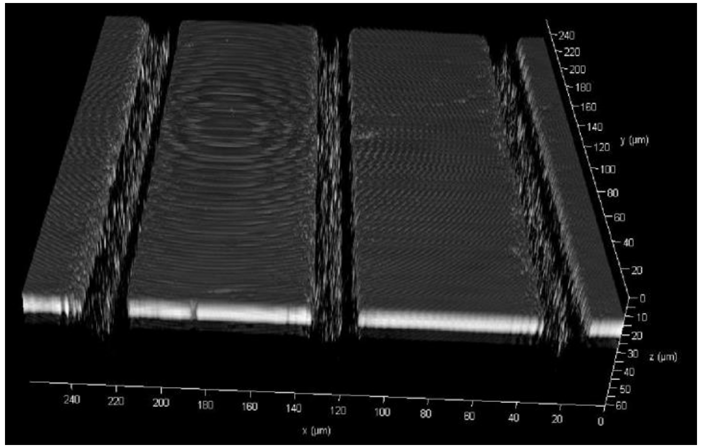


Ablation study (microscope image)



Ablation study (KLA D500 profilometer data)

2pp study, line width is 2.47um.



Z scan image of ablated substrate with Leica confocal microscope

Financial report

Salaries	19.050.000 AMD
Equipments and services	5.390.000 AMD
Total	24.440.000 AMD

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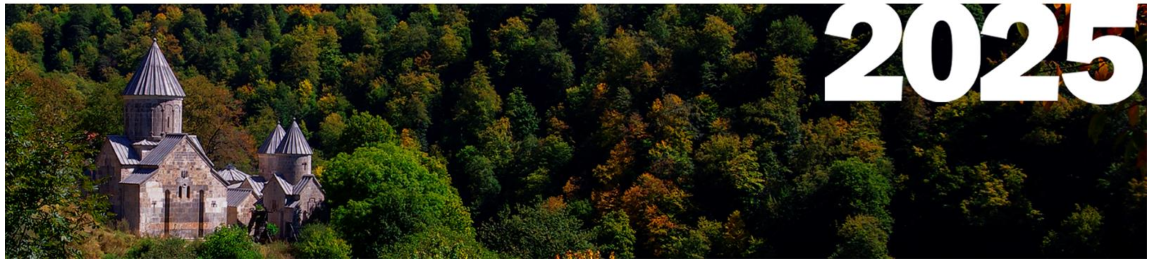

Thank you!

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