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Lens-free interference microscopy for detection of minute quantity of materials

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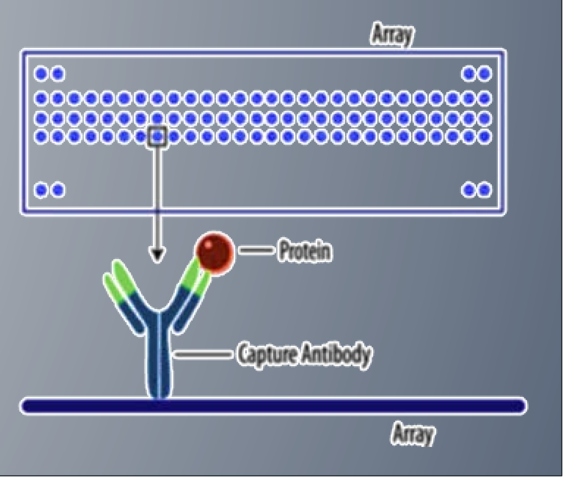
Abstract: Detection of very thin or weakly scattering structures is of high interest in various scientific fields and industrial applications. To achieve this goal, we present novel, compact lens-free microscope with ultra-high *(sub-nanometric)* resolution in the beam direction. This device utilizes birefringence in an unconventional way and offers large *field-of-view* decoupled from spatial resolution. We successfully used the microscope to measure thin transparent objects and microarrays of biomarkers. We were also able to measure changes of the biomarkes after binding events, providing quick and efficient way of analysing fluidic biological samples for multiple specific proteins at once. Furthermore, the performance and portability of the device paves the way towards a rapid analysis of biomedical samples, even in remote areas.

Motivation

- measuring of thin/transparent films
- **medical diagnostics:** *via micro-array technology, in less than 30 minutes with a portable low-cost system.*



Optical setup

- Proposed device utilizes **Savart plates** to divide linearly polarized collimated light into two perpendicularly polarized parallel components.
- These beams **interact** with the sample and are joined again using inversely placed Savart plate.
- Any object-induced phase-shift of one beam then results in **interference**. The resulting interferogram is captured on camera.

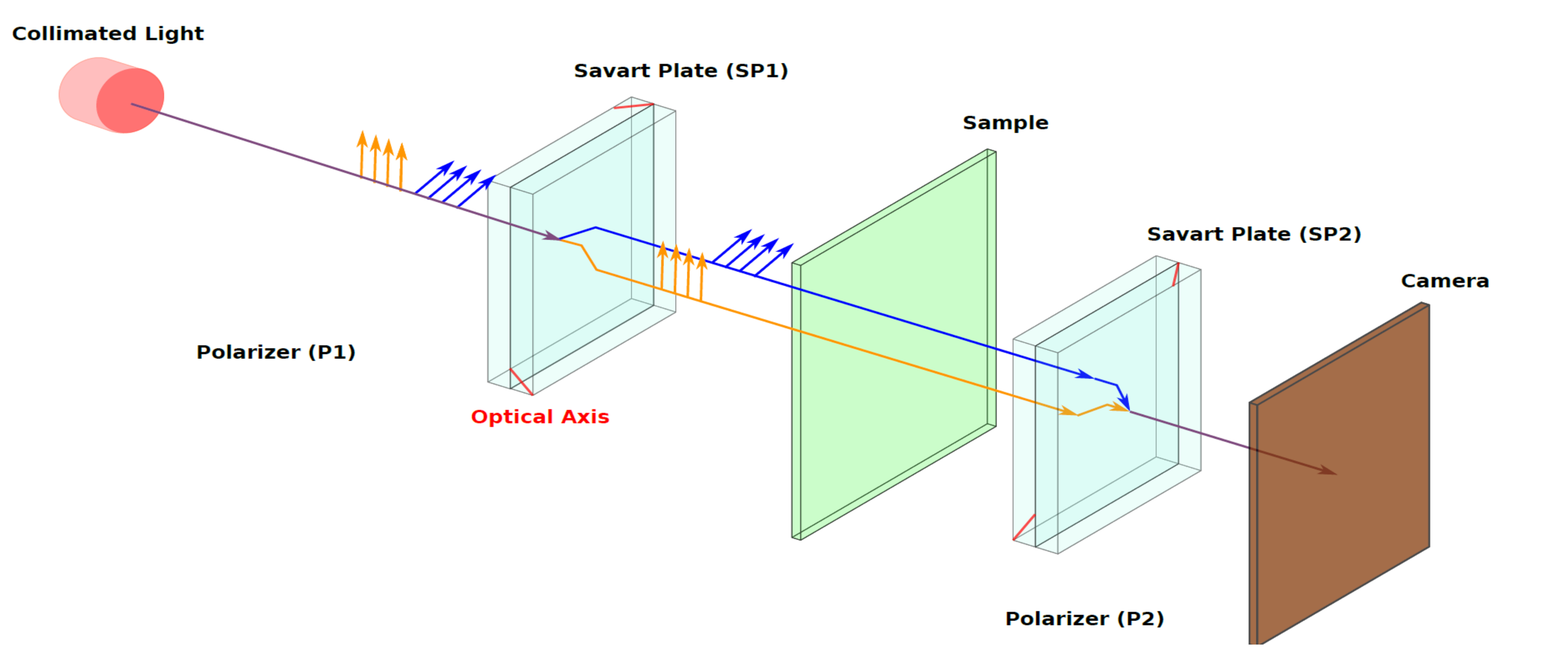


Image 2: Simplified optical setup of the microscope, utilizing two Savart plates.

- **Tilting** of Savart plate is used to induce phase-difference between the two beams. Various tilts under different wavelength illuminations are recorded.

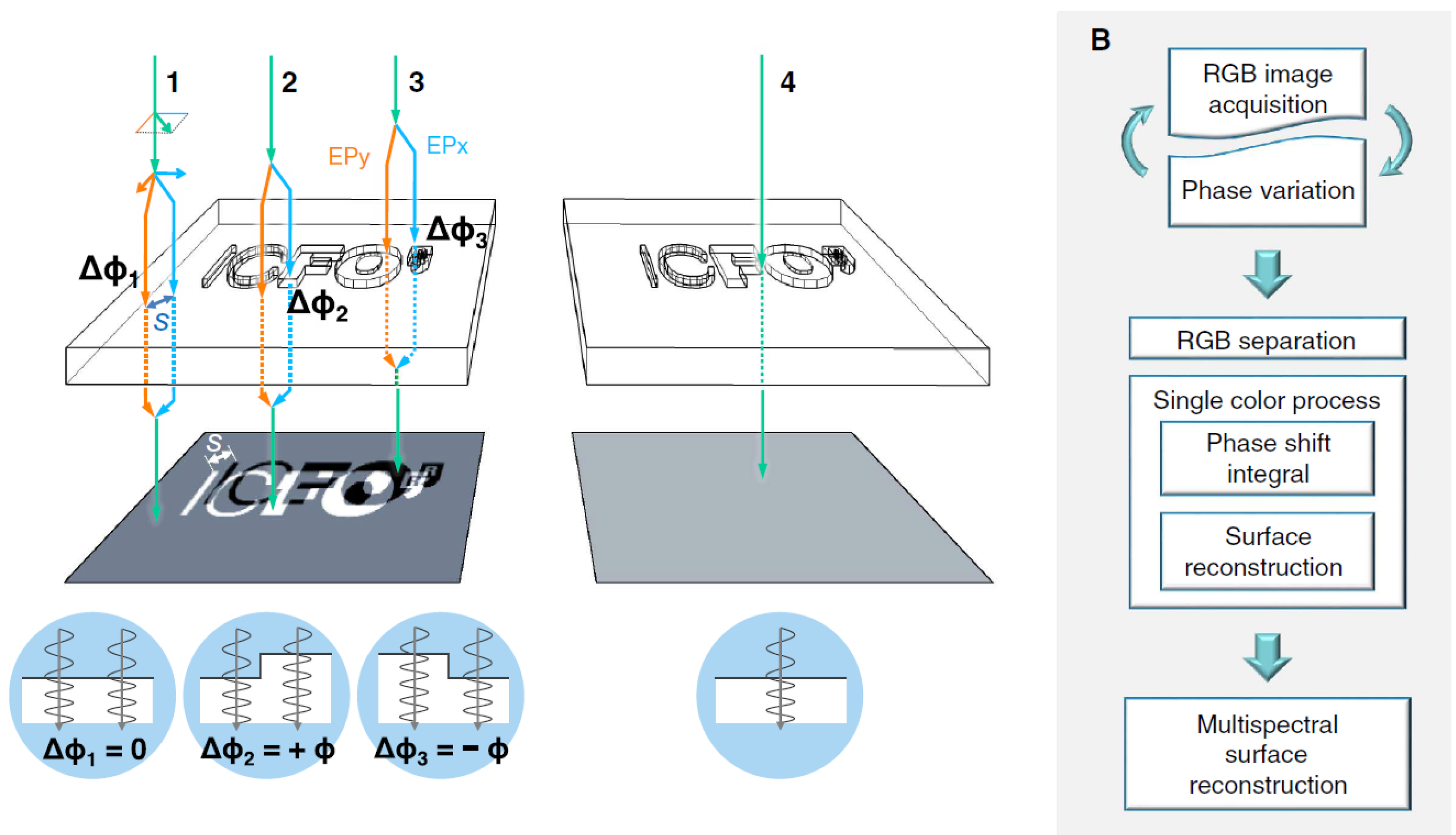


Image 3: Schematics of the beam paths, OPDs and processing workflow. Reproduced from [1]

- Data are processed using novel modified *Phase-shifting digital holography* (PSDH) algorithm, as proposed by Terborg et al [1]. Numerical field back-propagation and surface reconstruction is also applied.

Results

- Thanks to use of unfocused light, field-of-view is limited essentially only by the camera sensor. Currently, we achieved **FoV of 20mm²** with spatial resolution of $\sim 25\ \mu m$ and lateral (OPD) resolution of $< 1\ nm$.
- Various samples were succesfully measured, including: test **USAF** target, microdot arrays of **silica**, microdot arrays of **bovine-serum albumin** (BSA) [2].

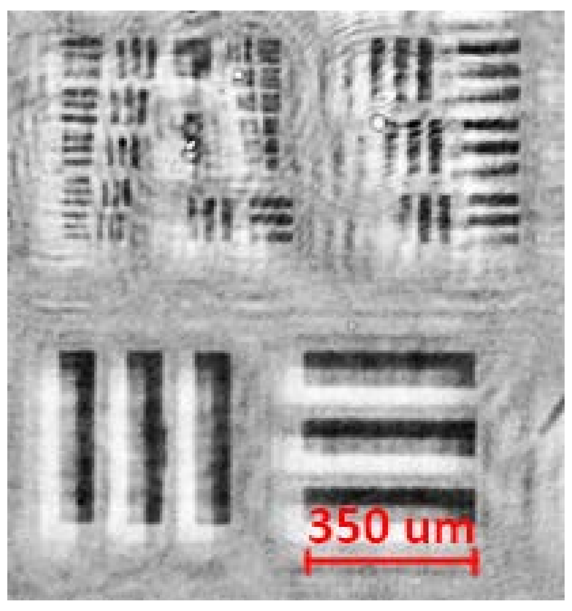


Image 5: USAF spatial resolution test.

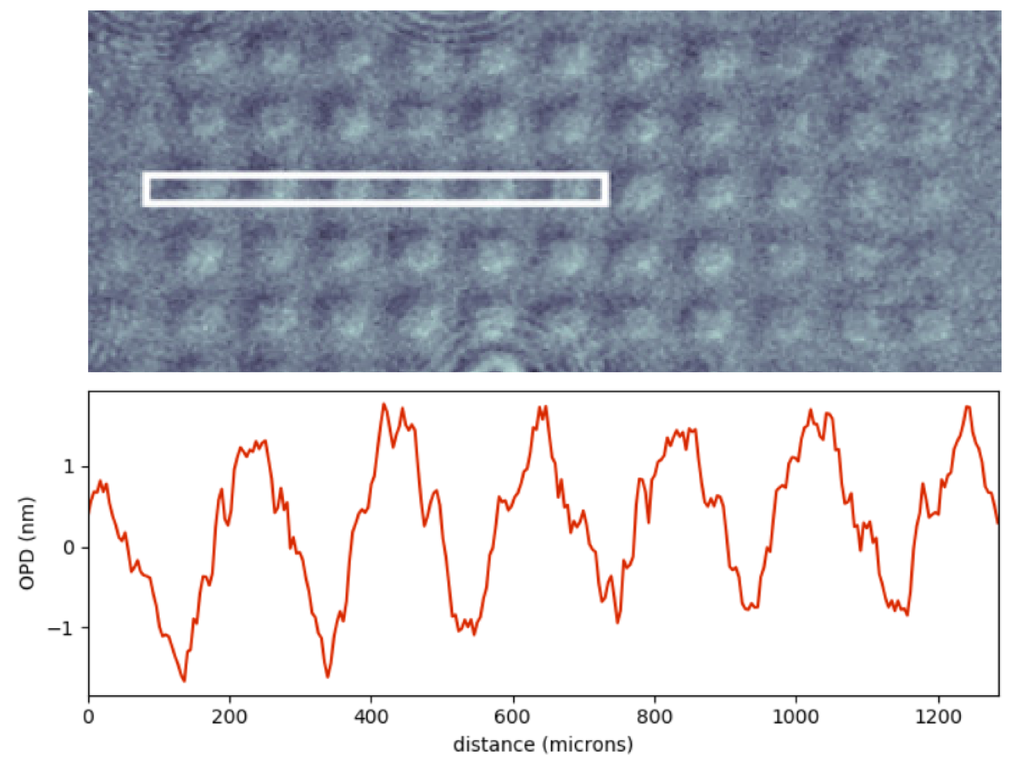


Image 6: OPD profile of 5 nm thick silica dots microarray.

- When **BSA** dots were subject to anti-BSA immunoglobulin G (which selectively binds to BSA), they were converted to bilayers of higher thickness, which were then successfully measured.

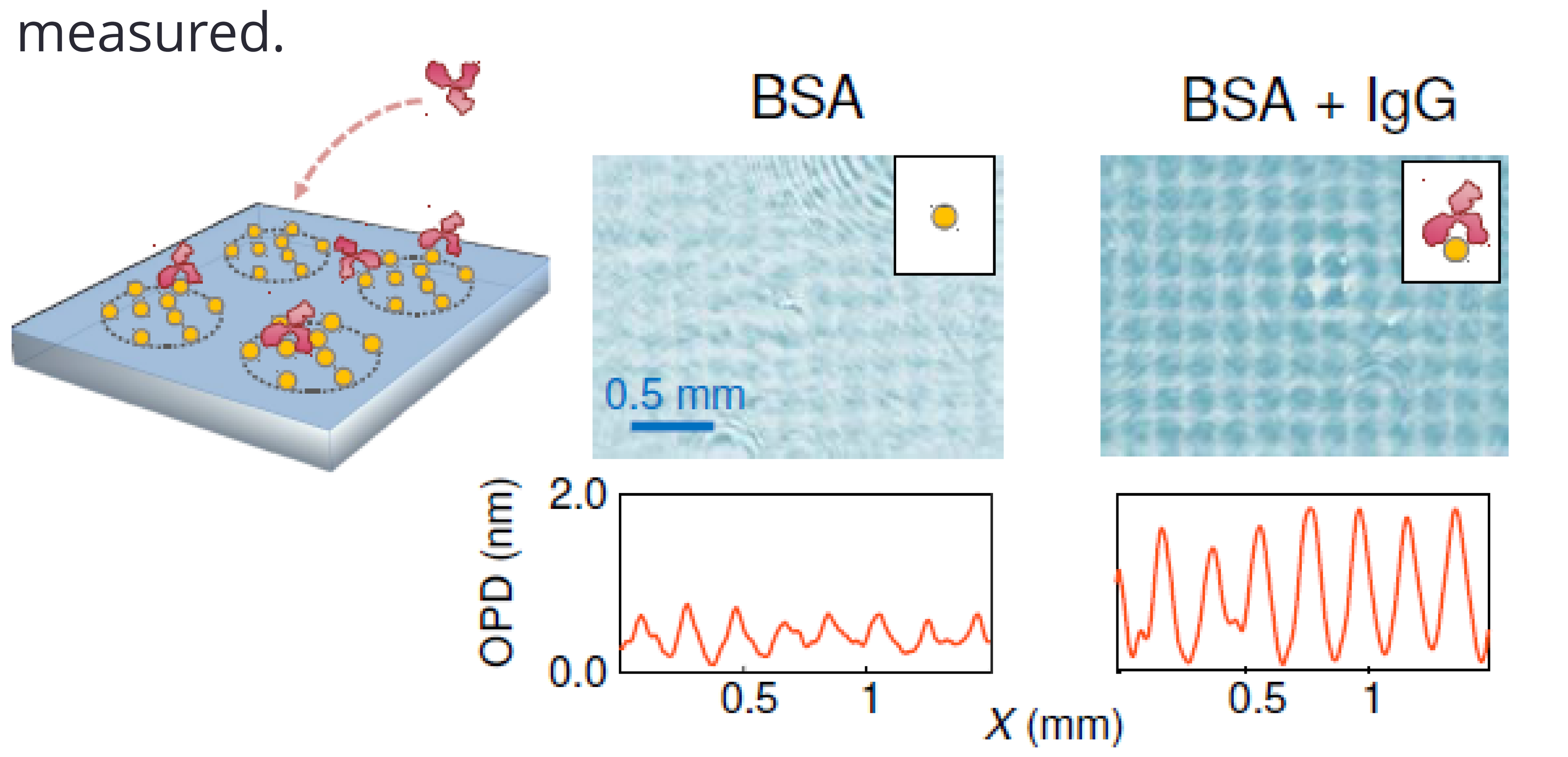


Image 7: OPD images and profiles for BSA and BSA+IgG dot microarrays. BSA+IgG show significantly higher OPD profile.

References:

[1] R. A. Terborg et al., "Ultrasensitive interferometric on-chip microscopy of transparent objects," Science Advances, vol. 2, no. 6, pp. e1600077–e1600077, Jun. 2016.

[2] F. Yesilkoy et al., "Phase-sensitive plasmonic biosensor using a portable and large field-of-view interferometric microarray imager," Light: Science & Applications, vol. 7, no. 2, p. 17152, Feb. 2018.

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