Quantitative differential interference contrast (DIC) microscopy based on structured aperture interference

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Background:

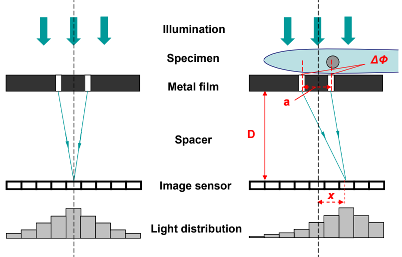
DIC microscopy renders excellent contrast for optically transparent biological samples without the need to introduce any exogenous contrast agents into the samples. Due to this noninvasive nature, DIC microscopes are widely used in biology laboratories. However, standard DIC techniques have several limitations. They are inherently qualitative as a consequence of nonlinear differential phase response and entanglement of amplitude and phase information. In addition, images of birefringent samples typically suffer from artifacts because the standard DIC technique depends on polarized light.

Objective:

To create a simple, quantitative and artifact-free DIC microscopy method for agent-free biological imaging by using our newly developed wavefront sensor based on structured aperture interference.

Structured aperture interference:

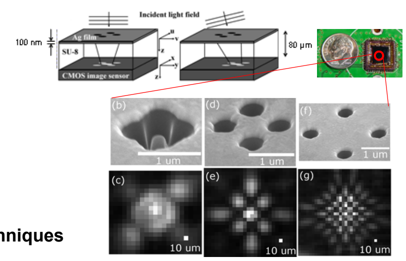
The basic concept is similar to a Young's double-slit experiment. However, we have generalized the experiment to utilize varieties of 2D structured apertures, e.g. four holes, rose-shaped, or even a single hole (under certain conditions).



Phase $\Delta\phi \approx \frac{2\pi}{\lambda}\frac{a}{D}x$ **Young's interference**

Amplitude The signal of the pixels

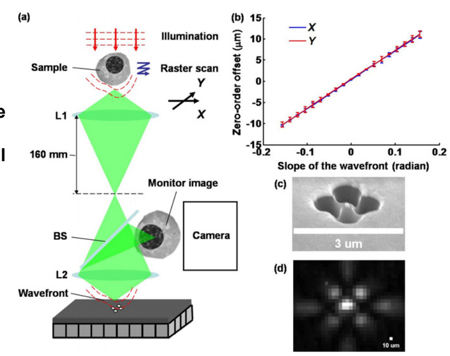
Advantages:
- **High lateral resolution (determined by the aperture size)**
- **Quantitative (calibration free), linear phase response**
- **Unentangled amplitude and phase information**
- **Simple to fabricate using standard microfabrication techniques**



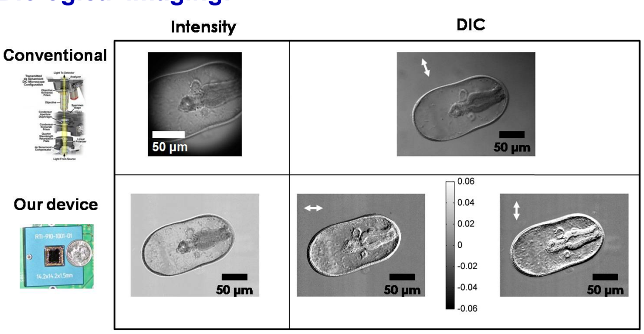
Novel quantitative DIC microscopy method:

- **Two back-to-back objective lenses form a 1:1 optical relay system.**
- **The wavefront containing the absorption and refraction properties of the sample is well-preserved at the image plane by this simple microscope system.**
- **Our on-chip wavefront sensor at the image plane can quantitatively measure the amplitude and the local slope of the wavefront.**
- **By raster-scanning the sample in the X-Y plane, we obtain complete knowledge of the wavefront.**

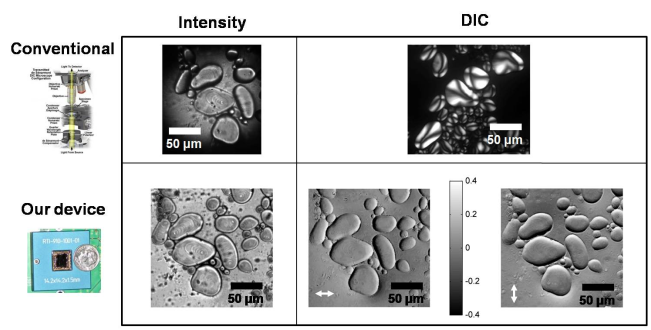
Advantages:
- **Quantitative DIC imaging**
- **Simple aberration-free optics**
- **Unpolarized white light: Artifact-free images of birefringent samples**



Biological imaging:



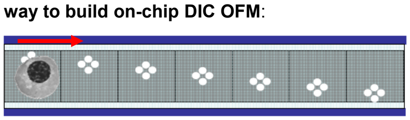
- **DIC images offer enhanced contrast**
- **Similar resolution as conventional techniques**
- **Quantitative DIC images**
- **DIC information measured in both orthogonal directions**



- **Birefringence produces "Maltese cross" artifact in traditional DIC image**
- **Amplitude and phase information of the sample is separated in our method**

Future directions:

A way to build on-chip DIC OFM:



References:

1. Xiquan Cui, Matthew Lew, Guoan Zheng and Changhuei Yang. 'Quantitative differential interference contrast (DIC) microscopy based on structured aperture interference,' preparing.
2. Matthew Lew, Xiquan Cui, Xin Heng, and Changhuei Yang. 'Interference of a four-hole aperture for on-chip quantitative two-dimensional differential phase imaging,' Optics Letters 32, October 2007.