



Digital Phase Imaging

Microscopy

Context

Cellular analysis is of major interest in many fields of biomedical research such as drugs testing, and cell pathology for the understanding of biochemical and physical processes of life.

Cell imaging is a challenging task as cells exhibit very weak contrast (low amplitude) due to poor light absorption. Semi-transparent or transparent biological specimens are phase contrast objects where phase shift under transmitted illumination is induced by differences of thickness and refractive index of the cellular components.

Biological specimen exhibiting poor amplitude contrast is usually revealed by labelling biological structures or by using phase optical techniques: microscopy Phase Contrast or Differential Interference Contrast; however, these widely used techniques have inherent limitations.

Labeling processing using fluorescent markers is a time consuming task with undesirable side effects such as photo bleaching and cell toxicity. Phase contrast or Differential interference contrast are mostly qualitative tools due to optical artifacts issues such halo and shading effects, making quantitative measurement and cell content interpretation difficult.

For accurate cellular dynamics analysis, both qualitative and quantitative assessment of morphology changes in living cells under different testing conditions is required. Quantitative phase imaging provides a map of path-length shifts associated with the specimen. This image contains quantitative information of both local thickness and refractive index of the structure and provides a powerful means for cell growth quantification and protein concentration. These techniques now become popular for applications ranging from cell homeostasis to infectious diseases and cancer.

Headquarters

2 Impasse de la Noisette

Hall B3, Suite B311

91370 Verrières Le Buisson - France

Email : contact@phaseview.com Phone > +33 9 54 03 05 43



Technologies Landscape & Current Limitations

Several interferometric quantitative microscopy techniques use the phase properties of coherent light to image a sample. The principal methods for measuring and visualizing phase shifts include various types of holographic microscopy methods. An interference pattern (hologram) is recorded by a camera, and from the recorded interference pattern, the phase shift image is computed. The phase shift can also be measured through a recorded interferogram using Shack-Hartmann based wavefront sensors. Another method, known as Ptychography or Coherent Diffraction Imaging relies on a phase retrieval algorithm to process diffraction patterns formed by the scattered light when passing through the specimen.

Digital holography is achieved using coherent light and is very sensitive to refraction, reflection or changes in the polarization of the light, therefore background noise reduction introduced by optical components in the light path is challenging and requires sophisticated hardware. Coherent diffraction imaging as a lensless technique requires intensive computation to retrieve the phase information from the diffraction patterns and remains an academic research investigation tool. Lateral shearing interferometry and Hartman sensors suffer from systematic aberrations caused by large wavefront curvatures, low photon flux, and from limited resolution due to the microlenses sampling.

Phaseview Digital Wavefront Technology

Digital Wavefront technology is based on recovering phase from the distribution of the energy of light. The essence of this approach is that amplitude and phase distributions are mathematically coupled in defocused images. A straightforward algorithm applied on a set of intensity images around the focus provides the quantitative phase image of the in-focus field.

Digital Wavefront Technology is able to deliver simultaneously and in real time the phase and intensity data, providing high resolution imaging and accurate wavefront map of phase shift induced by samples observed in transmission.

This approach overcomes the limitations of the current technologies as any commercial bright-field microscope equipped with a digital camera can now deliver in a simple manner qualitative and quantitative phase measurement. Thanks to digital Wavefront technology, the phase map resolution equals the camera resolution for efficient cell structure and dynamics analysis.

More information @ www.phaseview.com/technologies

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Value Added In Microscopy Phase Imaging

- No requirement for specialized optics or objectives
- Cells can remain in situ in their growth medium: in flasks, Petri dishes or multi well plates
- No contrast agents required: non-invasiveness, no photo toxicity
- Allows high resolution quantitative phase data for intracellular properties,
- Easy segmentation for counting or volume measurement and time lapse monitoring for cell dynamics and morphological changes studies

Technology Licensing

PhaseView offer licensing agreement opportunities including:

Algorithm for phase extraction from intensity images - [BioPhase software](#)

Standard or custom hardware acquisition system – [BioPhase](#)

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