Docket #: S15-038

Tetrapod Phase Mask Microscopy

Stanford researchers at the Moerner Lab have designed a family of point spread functions (PSFs), the Tetrapod PSFs, for high precision three-dimensional position measurement of individual particle positions over a large, customizable depth range in optical microscopy. These designs have a tunable depth range up to an unprecedented 20 ?m, which is over 7x larger than current state of the art.

As proof-of-concept, the team performed flow profiling in a microfluidic channel and showed scan-free tracking of single quantum-dot-labeled phospholipid molecules on the surface of living, thick mammalian cells. This invention is primarily aimed at researchers in the life sciences.

Sample +z Microscope Objective Lens Fourier Phase Transform Back focal plane fobi 🗘 Mask Lens f_{4l} Fourier (Pupil) Plane Mirror Intermediate Image Plane Fourier Transform Lens Image Image Sensor Plane

Figure

Phase Mask can be simply implemented with a tilted light-sheet microscope (LSM)

Stage of Research

• **Proof of concept** Demonstrated experimentally the applicability of these Tetrapod PSFs in micro-fluidic flow profiling over a 20um z range, and in tracking under noisy biological conditions.

Applications

- Thick tissue super-resolution microscopy:
 - Sub-wavelength imaging
 - Simultaneous multiple particle tracking
- Microfluidics flow profiling
- Simple, tunable depth of field microscopy
- Bio-film (thick sample) imaging
- Background reduction light sheet microscopy
- Microscope calibration (for depth induced aberrations)

Advantages

- New phase masks with **extremely large depth range up to 20?m** (about 7 times larger than current state of the art)
- Allow simple z range tunability
- Easily tailored and optimized to a required depth range.
- Simple implementation with a tilted light-sheet microscope (LSM)

Publications

- U.S. Published Patent Application 20160301915, <u>"APPARATUSES AND METHODS</u> FOR THREE-DIMENSIONAL IMAGING OF AN OBJECT".
- Shechtman, Yoav, Lucien E. Weiss, Adam S. Backer, Steffen J. Sahl, and W. E. Moerner. <u>"Precise 3D scan-free multiple-particle tracking over large axial</u> <u>ranges with Tetrapod point spread functions.</u>" Nano letters (2015).
- Anna-Karin Gustavsson, Petar N. Petrov, Maurice Y. Lee, Yoav Shechtman, W. E. Moerner. <u>"3D Single-Molecule Super-Resolution Microscopy With A Tilted Light</u> <u>Sheet"</u>. The Preprint Server for Biology.

Patents

- Published Application: 20160301915
- Issued: <u>10,187,626 (USA)</u>
- Issued: <u>10,638,112 (USA)</u>

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