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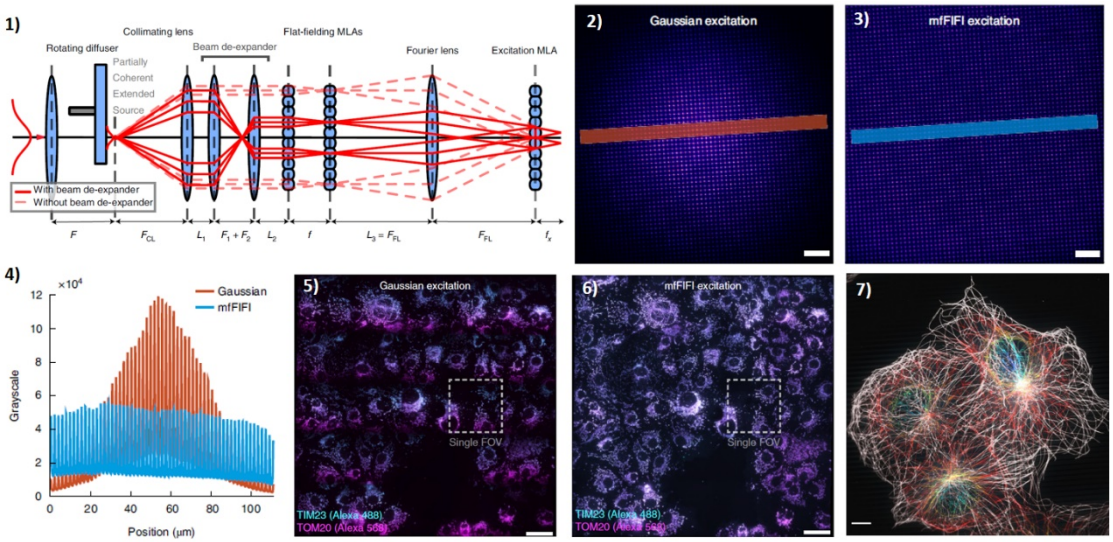
Licensing Opportunity

TTO – Technology Transfer Office

Koehler integrator device for multi-focal confocal microscope



1) Design and implementation of multifocal flat illumination for field-independent imaging, MLA standing for MicroLens Arrays. **2)-3)** Excitation points imaged onto a NaFITC fluorescent dye sample with Gaussian and mfFIFI excitation. Scale bar, 10 um. **4)** Intensity profiles measured along lines in 2) and 3). **5)-6)** iSIM images of Cos-7 cells using Gaussian versus mfFIFI excitation, stitched from 5x5 grid of single FOVs, scale bars 50 um. **7)** Large FOV captured by an iSIM using mfFIFI, showing multiple Cos7 mammalian cells immunolabelled for alpha-tubulin and color-coded for depth. Scale bar: 10 um.

Ref. Nr

6.1906

Keywords

Improved Koehler integrator, homogeneous multifocal flat illumination, multifocal confocal microscopy, high throughput super resolution microscopy.

Intellectual Property

PCT/EP2018/085228

Publications

Nature (2021)
http://dx.doi.org/10.1038/s41586-021-03510-6

Nature Methods (2020)
https://doi.org/10.1038/s41592-020-0859-z

Optics EXPRESS (2020)
https://doi.org/10.1364/OE.395900

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Description

Probing nanoscale cellular structures and dynamics with high imaging throughput was accomplished by improving the illumination design strategy. Multifocal flat illumination for field-independent imaging (mfFIFI) was developed based on an adaptation of the Köhler integrator. The design generates an array of multifocal excitation spots of (1) homogeneous intensity (flat field), (2) constant pitch, (3) diffraction limited size across the FOV.
The multifocal illumination uniformity, the flexible design and the efficient transmission of light enlarge the FOV (e.g. 100 × 100 um2 after magnification). The parallelization of the image acquisition (stitching together adjacent FOVs) further extends the effective FOV for seamless stitching with minimal overlap.
Combining the large mfFIFI FOV with the speed of instant structured illumination microscope (iSIM) imaging allowed stitching together dual-color 3D stacks covering a 500 × 500 × 5 um3 volume within 25 seconds. Overall, mfFIFI can capture multiple mammalian cells or over a thousand bacterial cells within a single FOV at double the diffraction-limited resolution, and parallelized across larger areas to give the larger population context. The method could be used in diagnostic or clinical applications or extended to microfabrication processes.

Advantages

- Homogeneous multifocal excitation.
- Wave optics simulator for optimal resolution performance.
- High-throughput super-resolution imaging.

Applications

- Any multifocal excitation microscope including a spinning disk confocal microscope using a Nipkow disk.
- Parallelized STED and RESOLFT microscopes.
- Controlled patterns: photolithography or micromachining or laser ablation and welding.