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Advancing Optics and Photonics Worldwide

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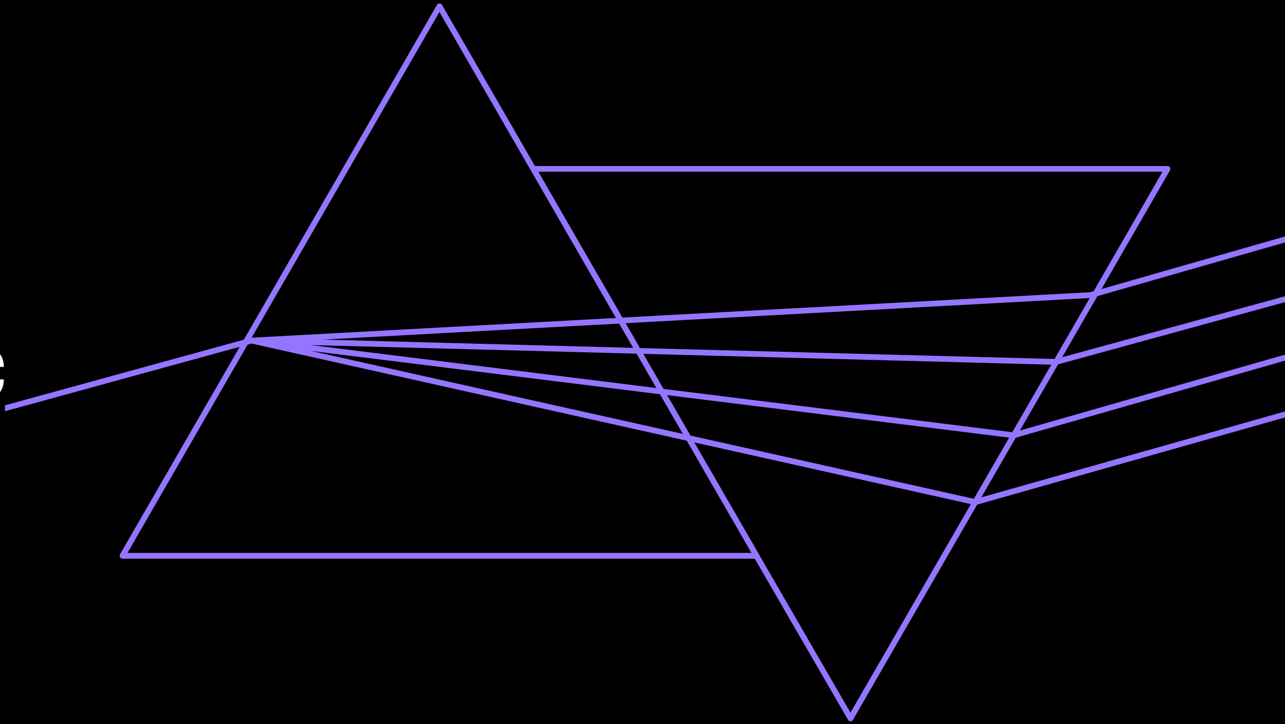
Adaptive Optics for Microscopy and Photonic Engineering



Featuring Martin Booth from the University of Oxford

05 December 2022

A Quick Zoom Tutorial

– Submit a question by clicking on “Q&A”

– Like a question that’s been submitted?
Click the “thumbs up” icon to vote for it.

– Share your feedback in the survey.

OPTICA
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Technical Groups

Create lasting, valuable connections.

Engaging communities
Innovative events
Focused networking
Enriching webinars

optica.org/technicalgroups

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Adaptive Optics for Microscopy and Photonic Engineering

Featuring Martin Booth from University of Oxford
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OPTICA
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Holography and Diffractive Optics

About Our Technical Group

Our technical group focuses on the design and implementation of holographic and diffractive-optic devices and systems for scientific, commercial, and other applications.

We want to connect the 1000+ members of our community through technical events, webinars, networking events, and social media.

Our past activities have included:

- Digital Holographic Microscopy Techniques for Applications in Cytometry and Histology
- Structured Light with Digital Holograms
- Metasurface Holograms
- Real-Time Hologram Rendering from Optically-Acquired Interferograms

Upcoming Networking Events

Optica Holography and Diffractive Optics Technical Group Networking Event

Members of the Technical group are invited to join us for a networking event (date and time to be determined). This event will provide the opportunity to connect with fellow members who share an interest in the of holography and diffractive optics fields of research.

More information will be available in early 2023.

Connect with our Technical Group

Join our online community to stay up to date on our group's activities. You also can share your ideas for technical group events or let us know if you're interested in presenting your research.

Ways to connect with us:

- Our website at www.optica.org/FH
- On LinkedIn at www.linkedin.com/groups/4826728
- On Facebook at www.facebook.com/groups/opticaholography
- Email us at TGactivities@optica.org

Today's Speaker

Prof Martin Booth

University of Oxford, UK

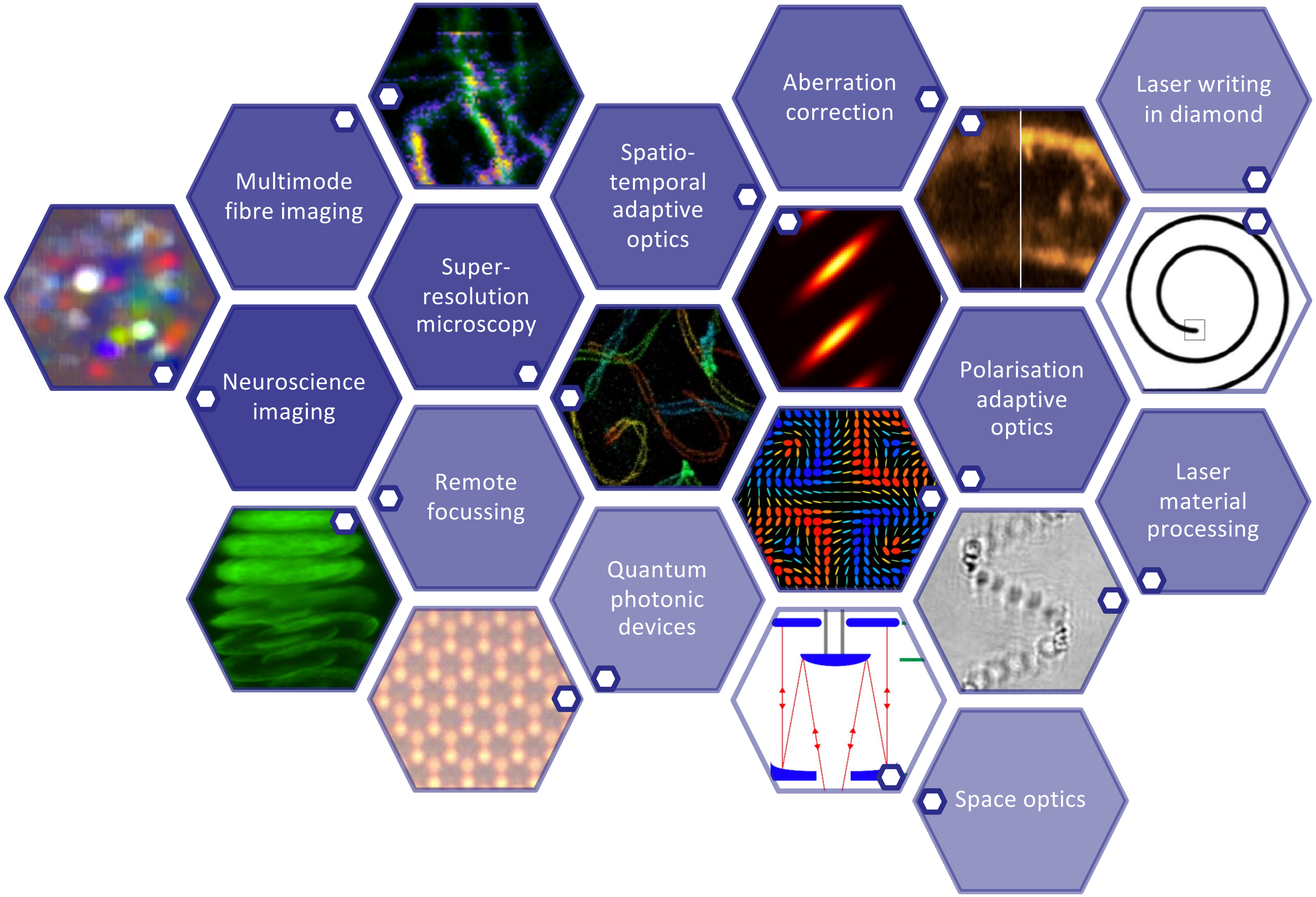
Prof. Booth is Professor of Engineering Science at the University of Oxford. His research involves the development and application of adaptive optical methods in microscopy, laser-based materials processing and biomedical science. He has held Royal Academy of Engineering and EPSRC Research Fellowships and in 2016 received an Advanced Grant from the European Research Council. He was appointed Professor of Engineering Science in 2014. In 2012 Prof Booth was awarded the "Young Researcher Award in Optical Technologies" from the Erlangen School of Advanced Optical Technologies at the University of Erlangen-Nürnberg, Germany, and a visiting professorship at the university. In 2014 he was awarded the International Commission for Optics Prize. He has over 150 publications in peer-reviewed journals, over 25 patents, and has co-founded two spin-off companies Aurox Ltd and Opsydia Ltd.

Adaptive optics for microscopy and photonic engineering: going faster, smaller and deeper

Martin J Booth

Department of Engineering Science
University of Oxford, UK

Dynamic optics and photonics research



Acknowledgements

University of Oxford:

- Dynamic Optics and Photonics group:
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- Department of Engineering Science:
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- Department of Biochemistry
  Ilan Davis, Ian Dobbie, Nick Hall, Richard Parton, Mick Philips, David Pinto, Danail Stoychev
- Department of Pharmacology
  Raphael Turcotte, Nigel Emptage
- Department of Physiology, Anatomy and Genetics
  Adam Packer, Huriye Atiglan
- Atomic and Laser Physics:
  Adrian Menssen, David Felce, Ian Walmsley
- Materials:
  Jason Smith, Yu-Chen Chen, Ben Griffiths, Andrew Kirkpatrick
- WIMM:
  Christian Eggeling, Silvia Galiani, Iztok Urbancic

The World:

- Yale University, USA
- Cambridge University, UK
- Innsbruck Medical University, Austria
- Osaka University, Japan
- SAOT, University of Erlangen-Nürnberg, Germany
- University of Manchester, UK
- CERN
- University of Warwick, UK

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- Biotechnology and Biological Sciences Research Council
- Wellcome Trust
- Leverhulme Trust
- European Research Council
- Medical Research Council
- University of Oxford OUP John Fell Fund
- Jesus College, Oxford
- SAOT, Erlangen

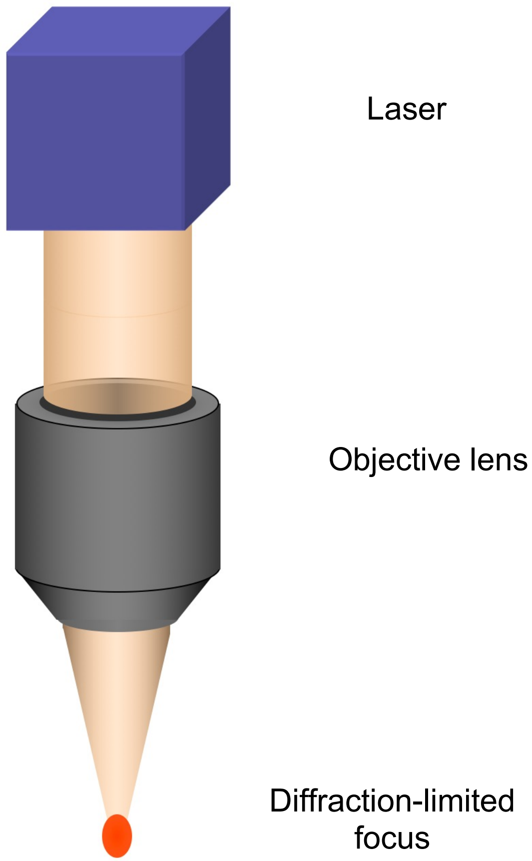
Website: http://www.eng.ox.ac.uk/dop/ Email: martin.booth@eng.ox.ac.uk

High resolution photonic engineering

- Focus size/resolution of system
  - Wavelength
  - Numerical aperture (NA) of objective
  - 3D resolution
  - ~250nm lateral, ~500nm axial

$$\Delta x \approx \frac{\lambda}{2NA} \qquad \Delta z \approx \frac{n\lambda}{NA^2}$$

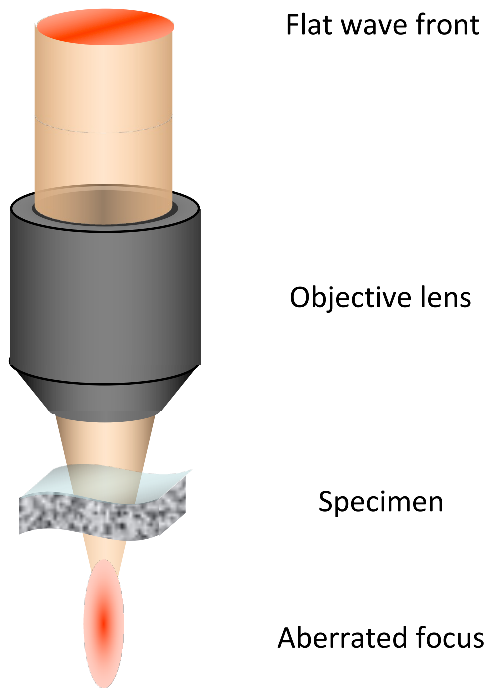
- Applications
  - Observation: microscopy
  - Modification: micro/nano fabrication
  - Manipulation: optical tweezers
  - Stimulation: biology



Aberrations in microscopes

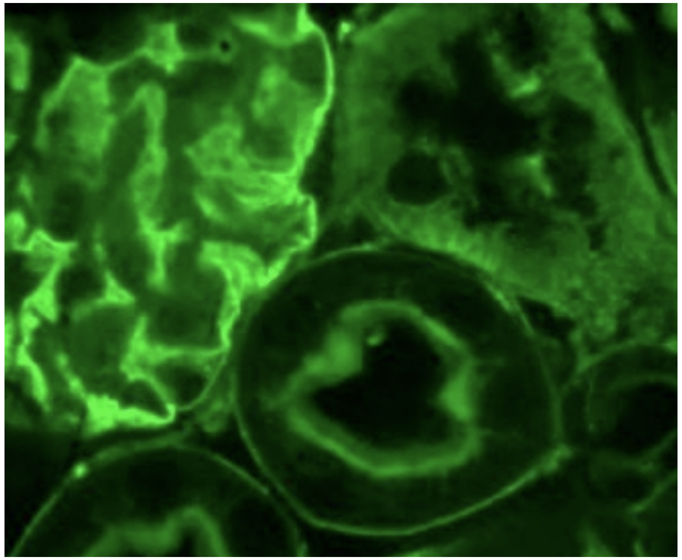
- Sources of aberrations
  - Optical system
  - Specimen
  - Refractive index mismatch

- Effects of aberrations
  - Enlarged focal spot
  - Loss of resolution
  - Decrease in image quality and contrast

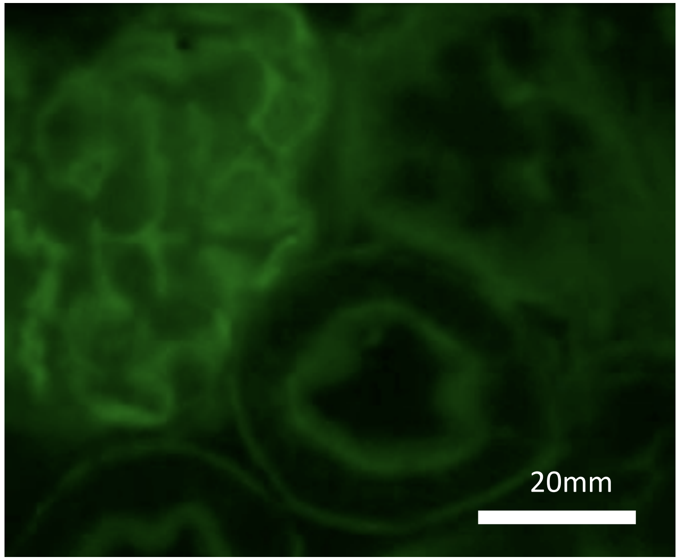


Aberrations in microscopes

Without system aberrations



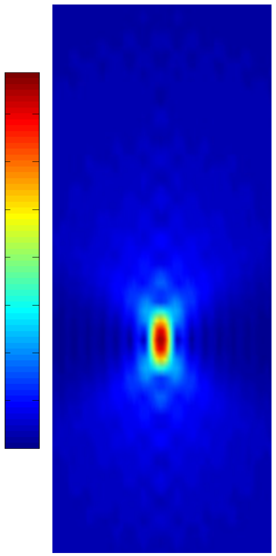
With system aberrations

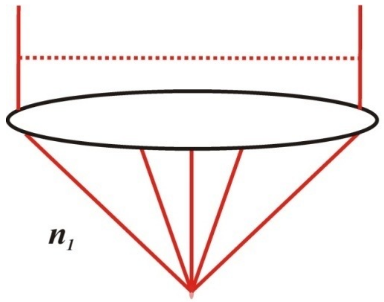


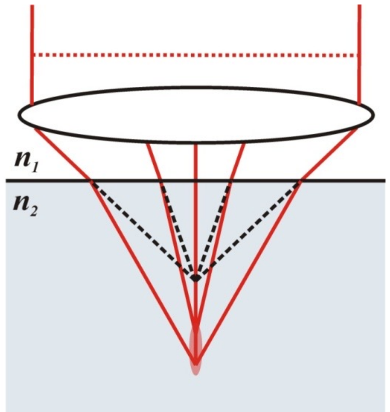
Confocal fluorescence images of labelled mouse kidney section

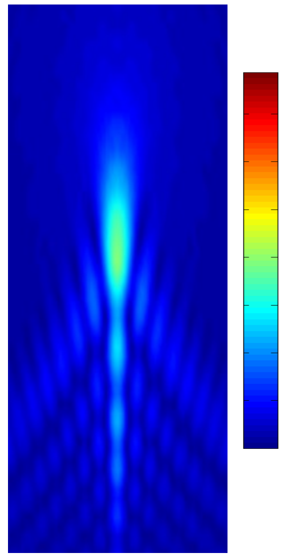
Aberrations from index mismatch

- Depth dependent spherical aberration when focussed through a refractive index mismatch (e.g. immersion/mounting medium)
- Aberrations increase with depth, numerical aperture and magnitude of refractive index mismatch







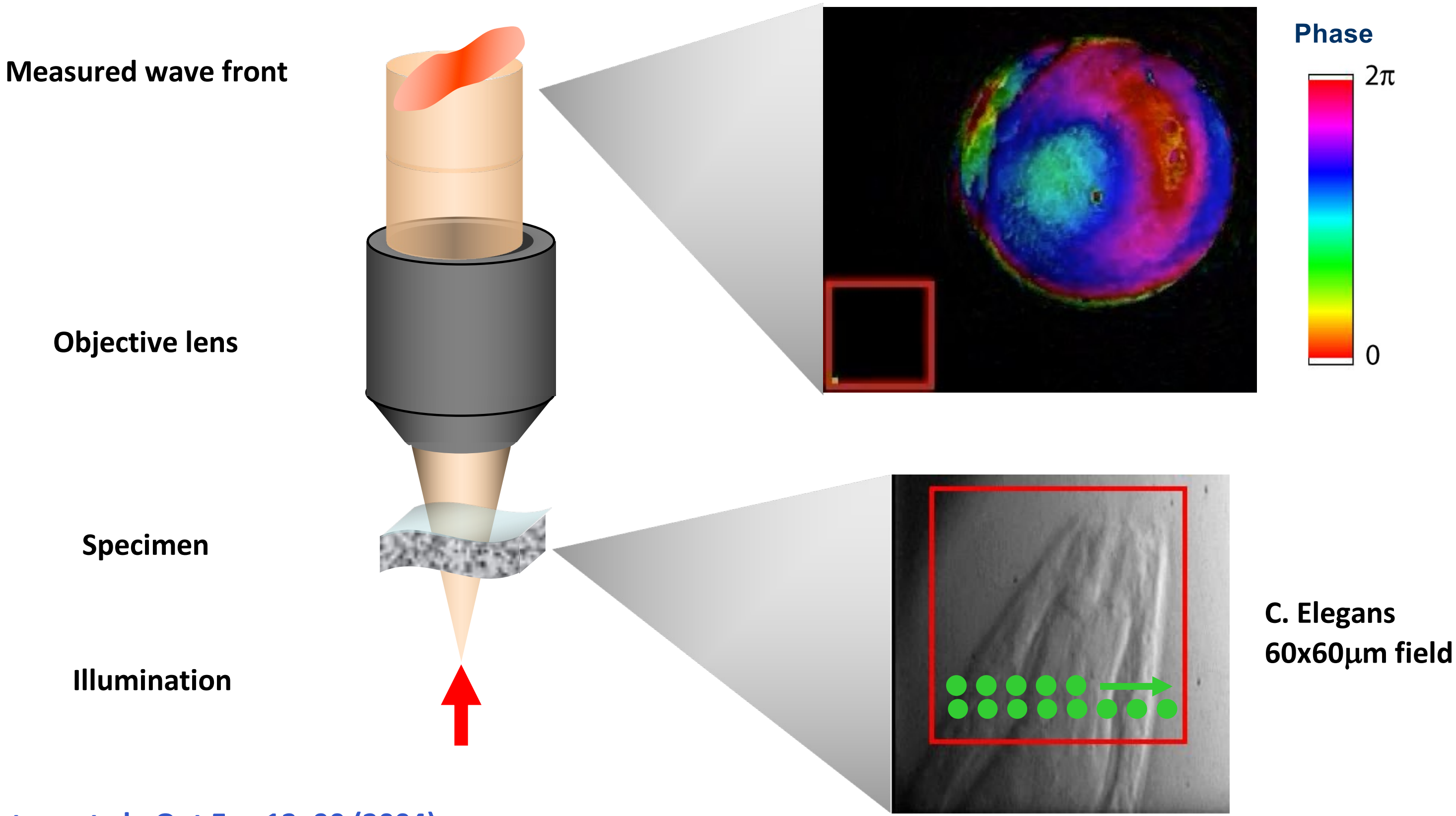


Effects of aberrations

- Enlarged focal spot
- Loss of resolution
- Decrease in contrast

Specimen-induced aberrations

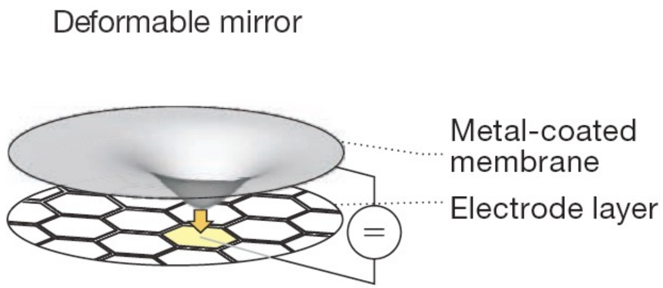
- Variations of refractive index throughout specimen structure
- Measurement of phase aberrations through interferometry at λ = 633nm

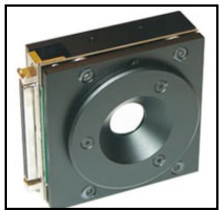


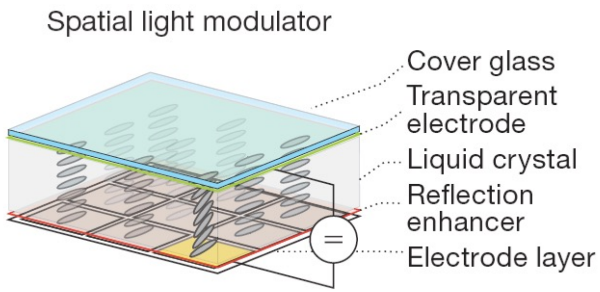
Schwertner et al., Opt Exp 12, 90 (2004)

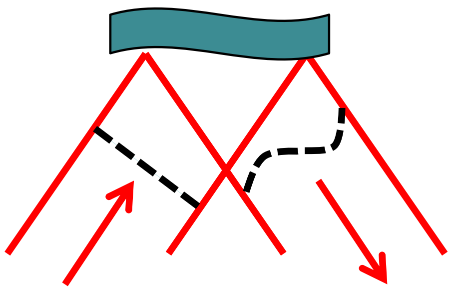
Dynamic elements for correction of optical aberrations

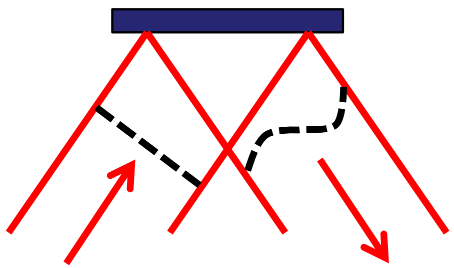
- Introduce an equal but opposite (conjugate) aberration
- Use a dynamic optical element – adaptive optics



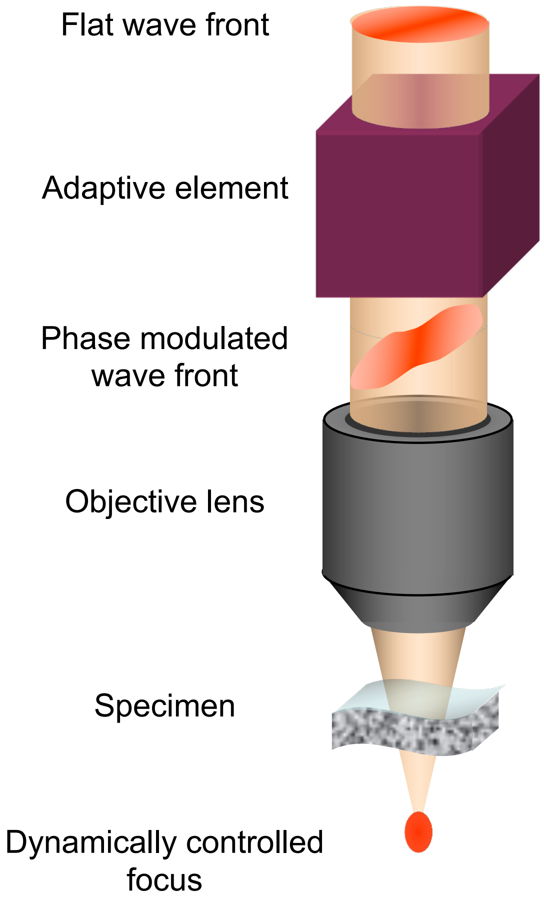




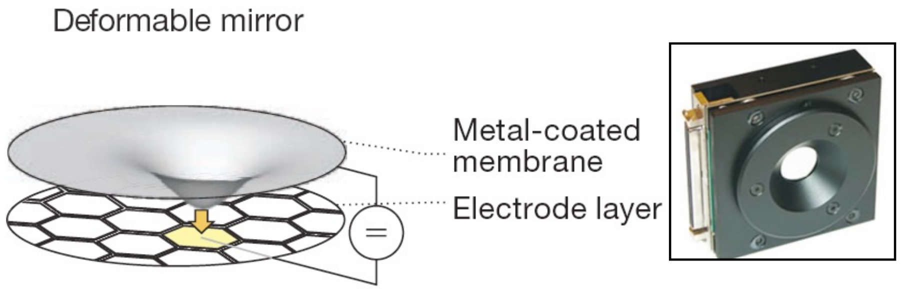


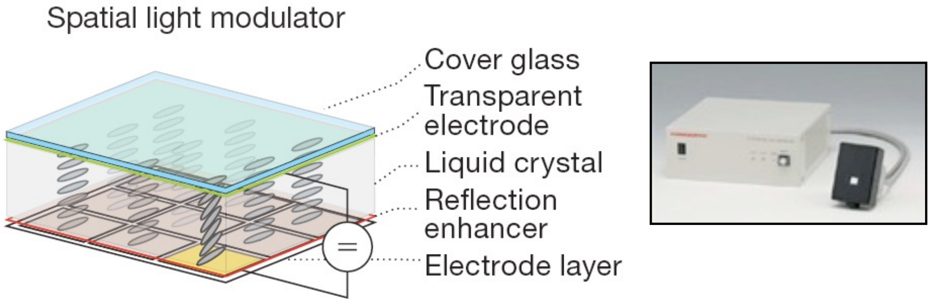


Adaptive optics for microscopy and photonic engineering



- Control phase of light using an adaptive element – a deformable mirror or SLM





Talk outline

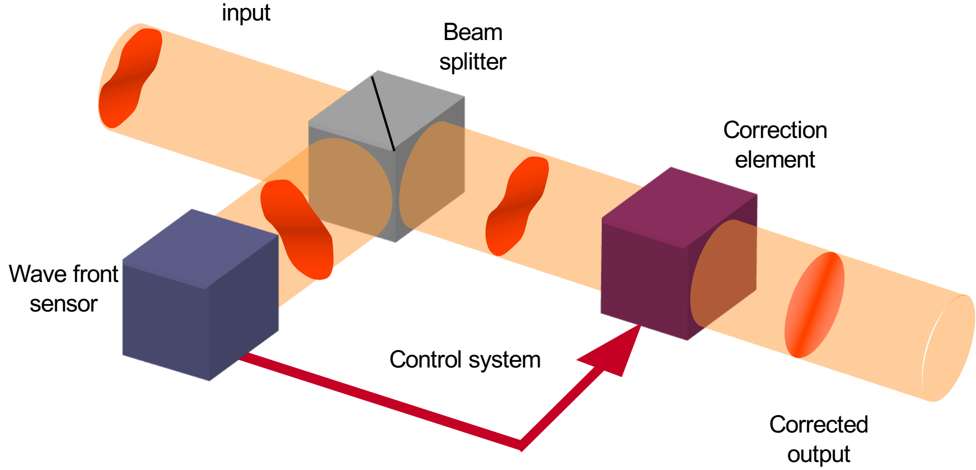
- Adaptive optics in microscopy for going:
  - Deeper
  - Faster
  - Smaller
- Adaptive optics for laser fabrication of photonic devices

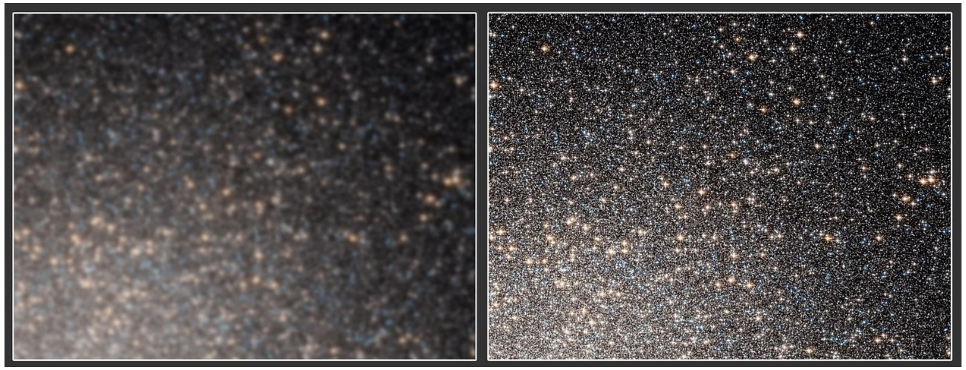
Adaptive optics for going

DEEPER

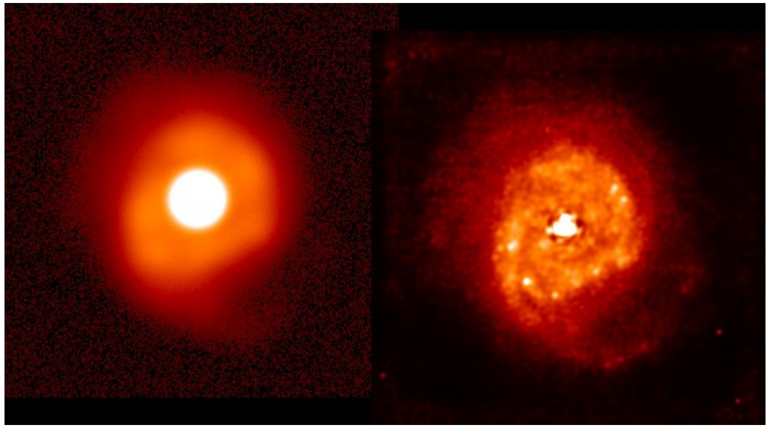
Adaptive optics

Using deformable mirror technology to improve images by removing optical aberrations

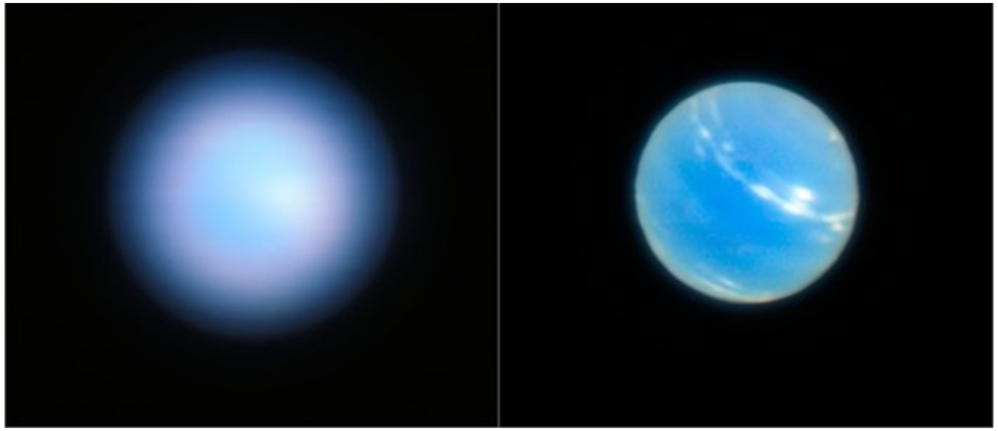




Global cluster before and after AO correction [Credit: ESO]



NGC7469 – Canada France Hawaii Telescope



Neptune - MUSE/GALACSI instrument [Credit: ESO/P. Weilbacher (AIP)]

Image based, wavefront sensor-less adaptive optics

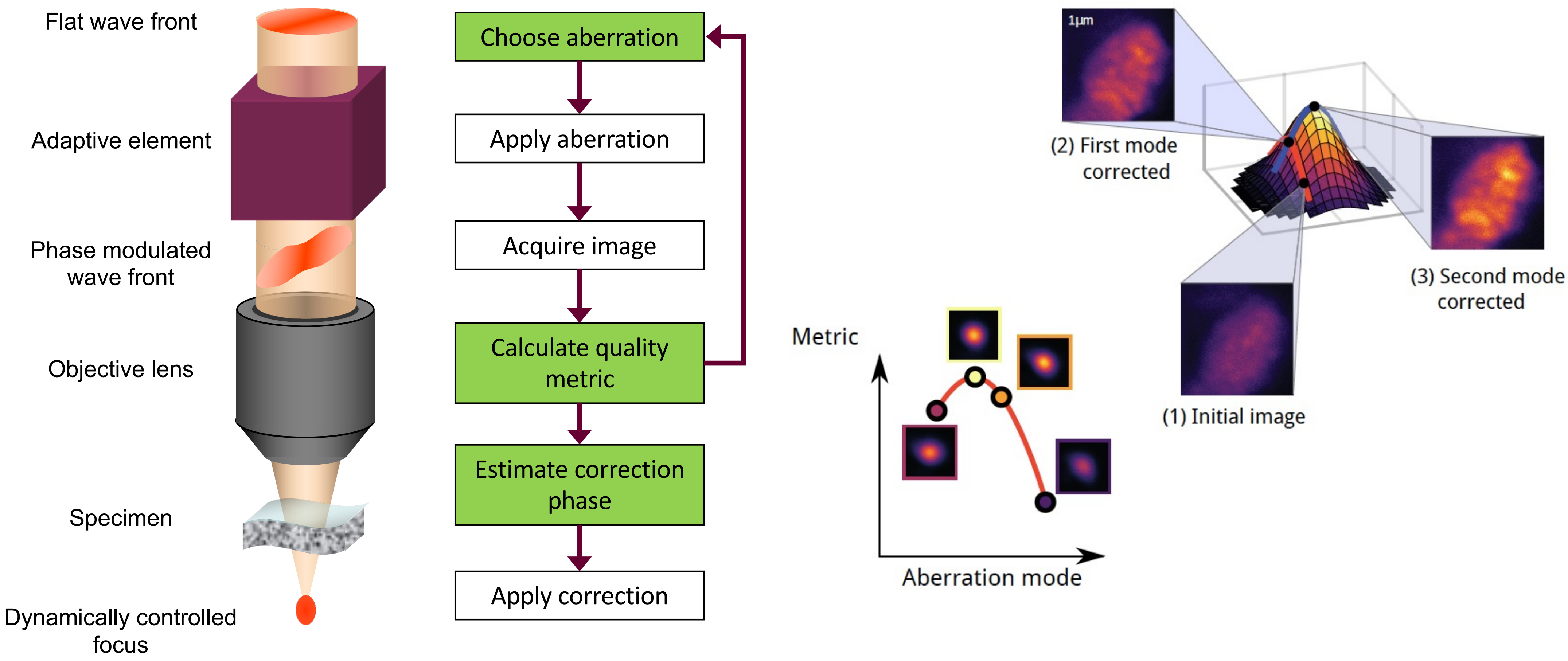


Image based adaptive optics

- Example: Correction of a single aberration mode (astigmatism) in transmission microscope
- Acquire three images with different applied aberrations
- Infer optimum correction using system model

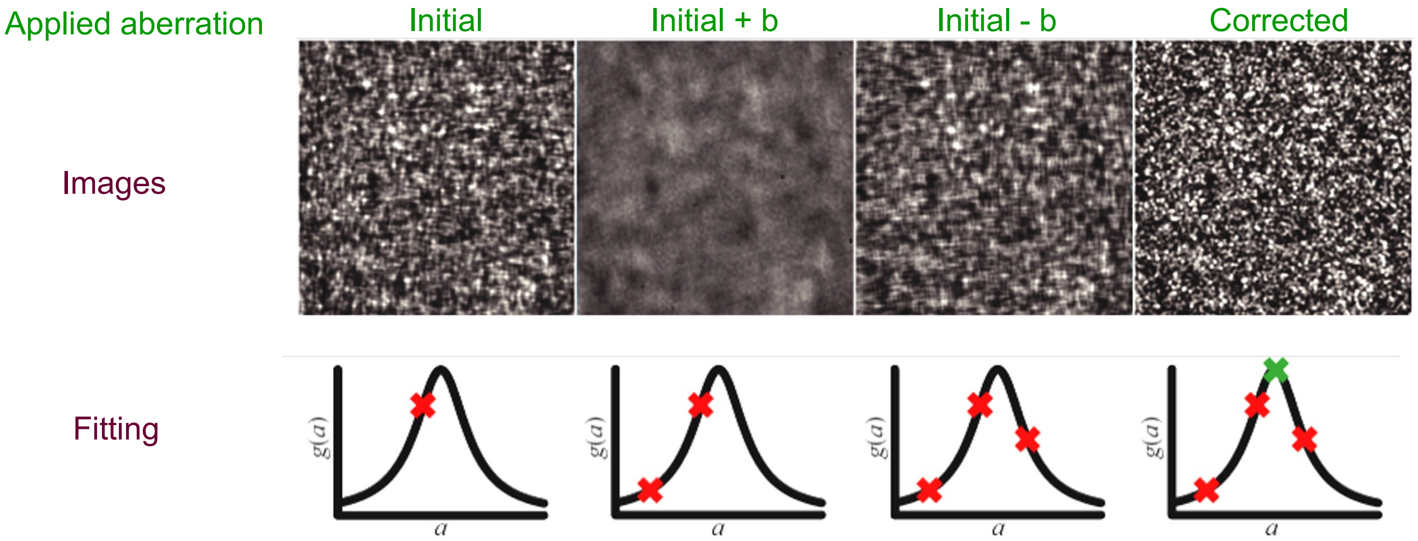
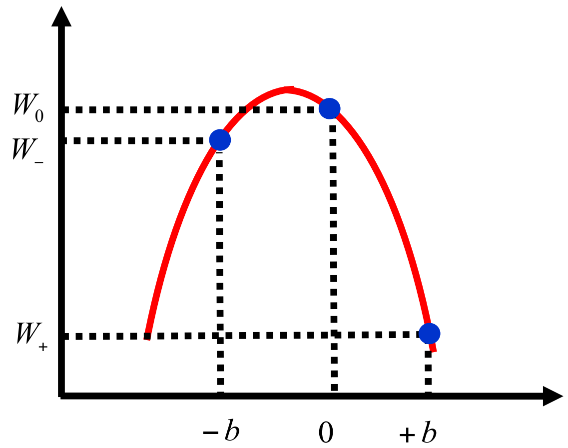


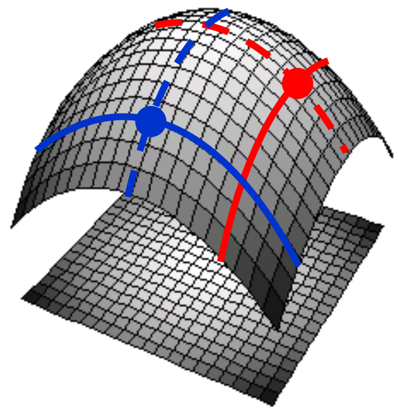
Image based adaptive optics

- Find a mathematical representation with suitable optimisation metric
- Correct individual mode with variable parabolic maximisation
- Image structure – extra degree of freedom, so three measurements required



$$a_{corr} = -\frac{b}{2}\frac{(W_+ - W_-)}{(W_+ - 2W_0 + W_-)}$$

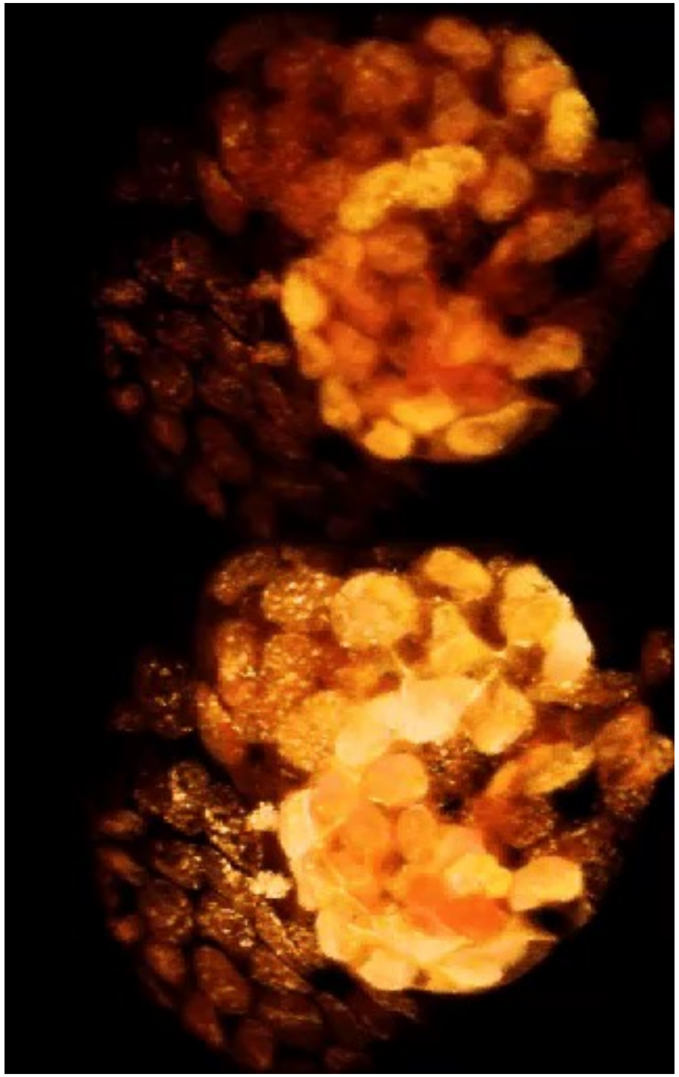
- Take three measurements per mode
- Multi-variable parabolic maximisation – separable maximisation in each variable
- 2N+1 measurements for N modes



Adaptive optics in two-photon microscopy

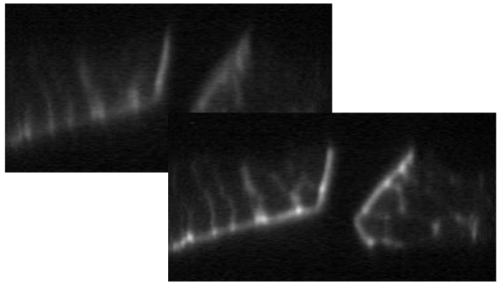
Correction of specimen induced aberrations in 3D imaging of a fluorescently labelled mouse embryo using a two-photon laser scanning microscope.

Original - Top
Corrected - Bottom

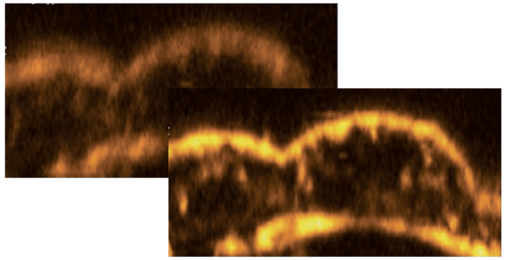


Debarre et al., Opt Lett 34, 2495 (2009)

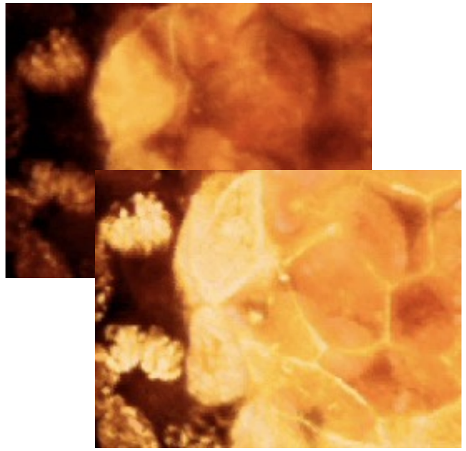
Demonstrations of adaptive optics in microscopy



Confocal fluorescence microscopy
Booth et al., PNAS 99, 5788 (2002)



Third harmonic microscopy
Jesacher et al., Opt Lett 34, 3154 (2009)



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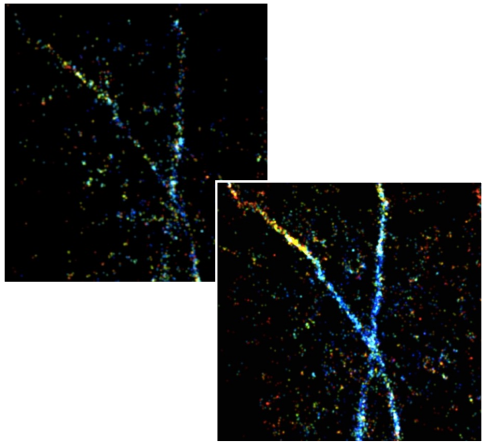
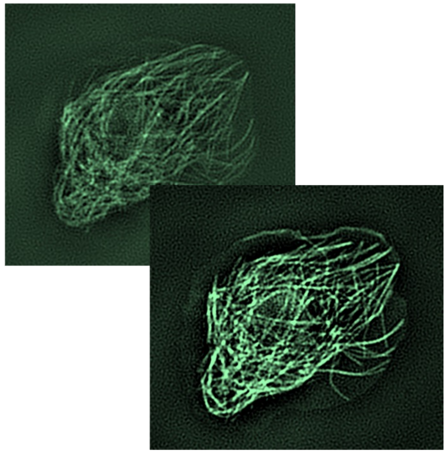
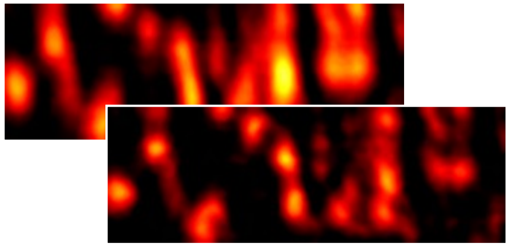


STORM nanoscopy
Burke et al., Optica 2, 177 (2015)



Structured illumination nanoscopy
Zurauskas et al., Optica 6, 370-379 (2019)

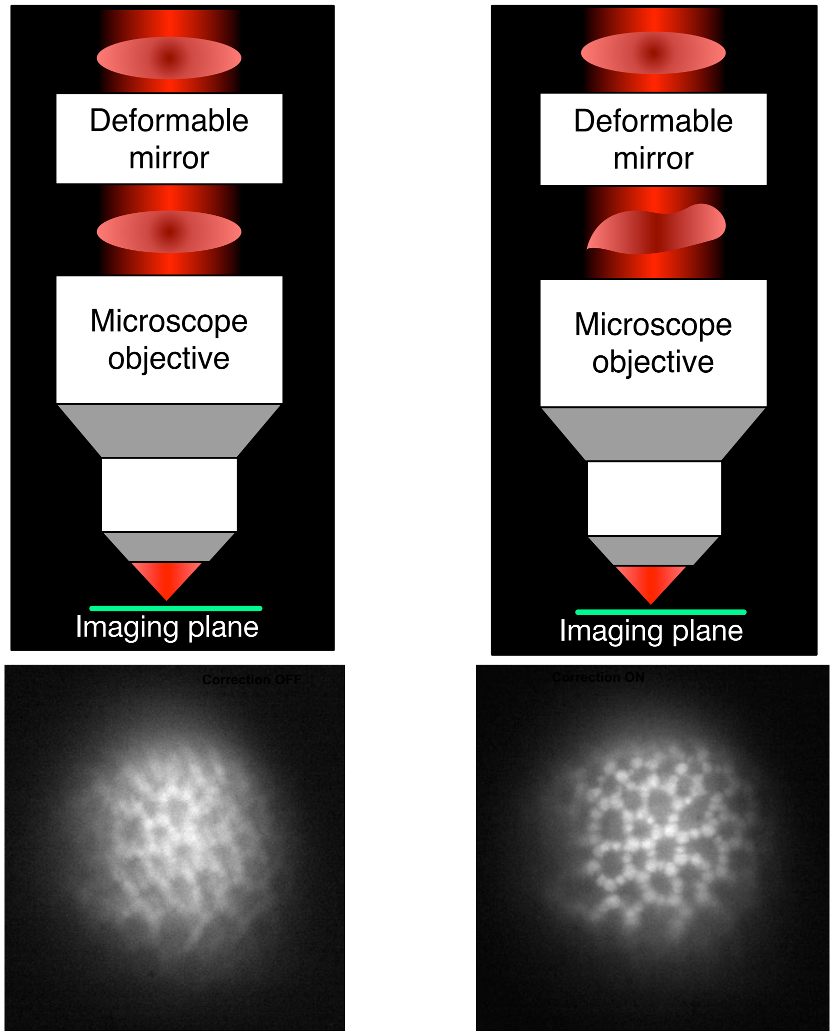


STED nanoscopy
Patton et al., Opt Expr (2016)

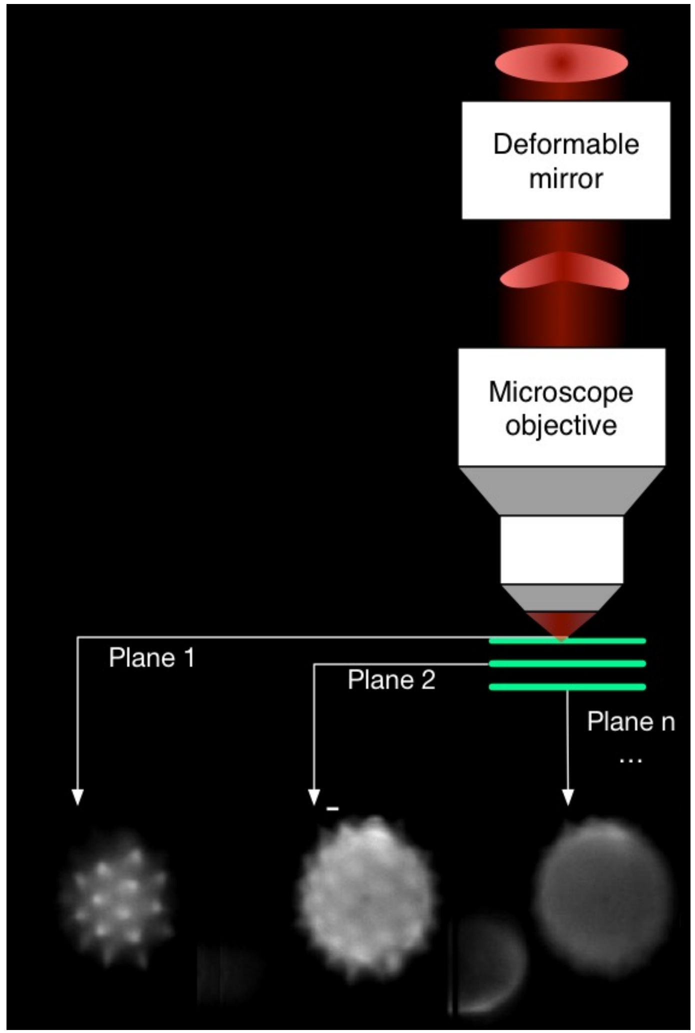
Adaptive optics for going

FASTER

Adaptive optics for fast remote focusing

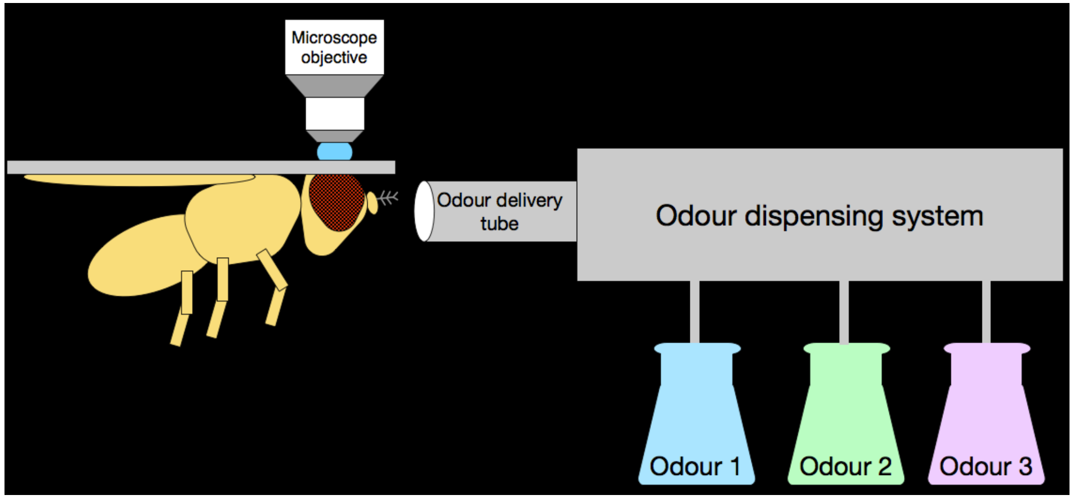


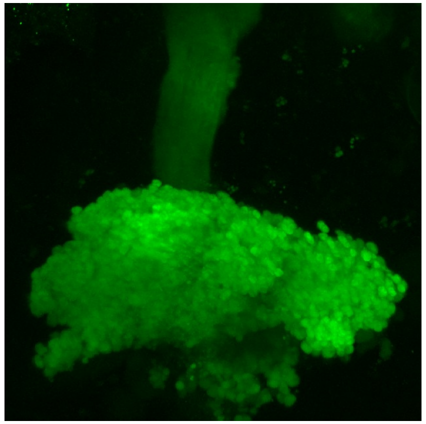
AO for aberration correction



AO for remote focusing

Imaging live Drosophila fruit fly brains



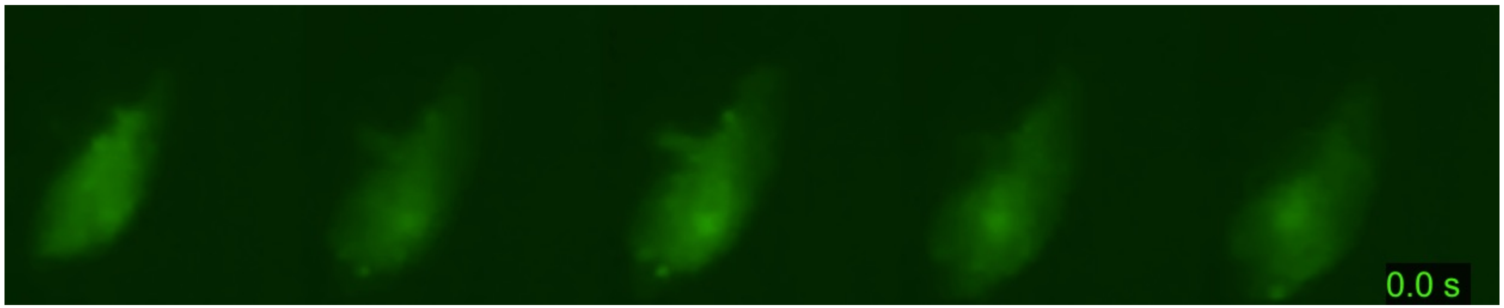


- Imaging of Ca ion fluorescence labels (GCaMP)
- Spatio-temporal focusing two-photon fluorescence microscope
- High speed (>10Hz) across large volumes (>100μm)
- High sensitivity
- Cope with specimen motion
- At least cell body level resolution (~5μm)

Parallel two-photon microscopy for neural imaging

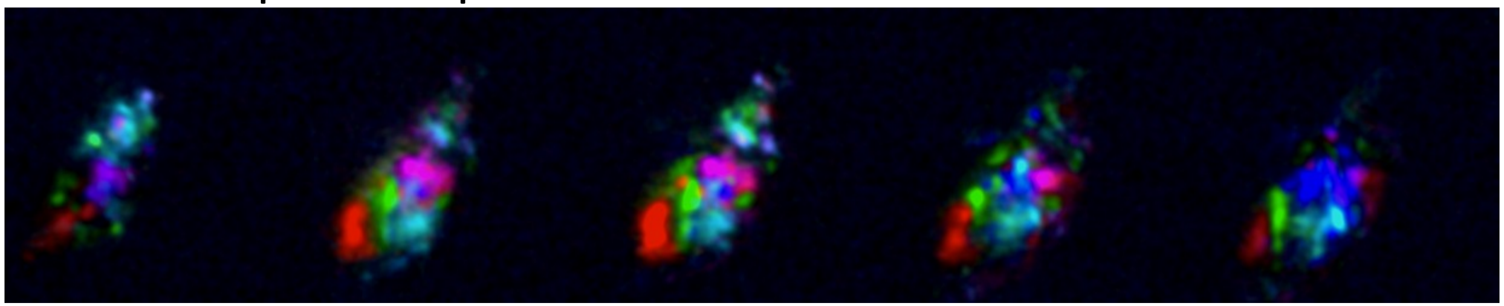
Axial position

-10 µm **-5 µm** **0 µm** **+5 µm** **+10 µm**



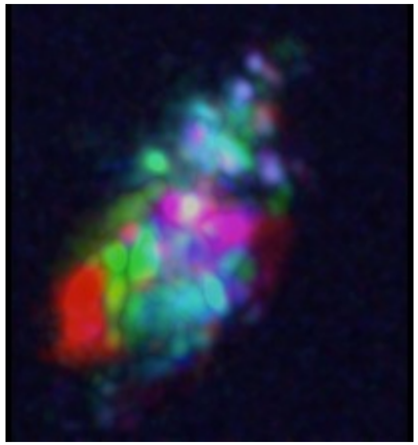
10 µm

Colour coded independent components



Extracted signals from Kenyon Cells in Drosophila brain mushroom body

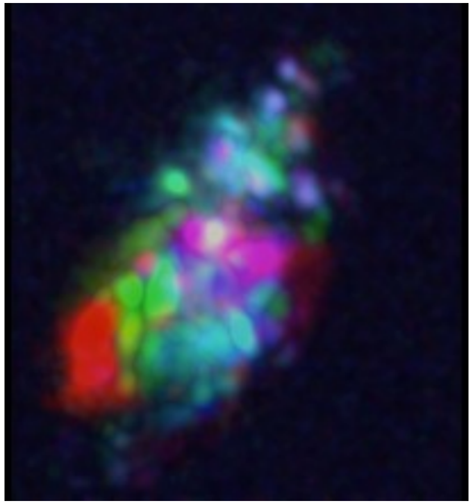
Response to three different odours (IAA, MCH, OCT)



Zurauskas et al., Biomed. Opt. Exp. 8, pp. 4369-4379 (2017)

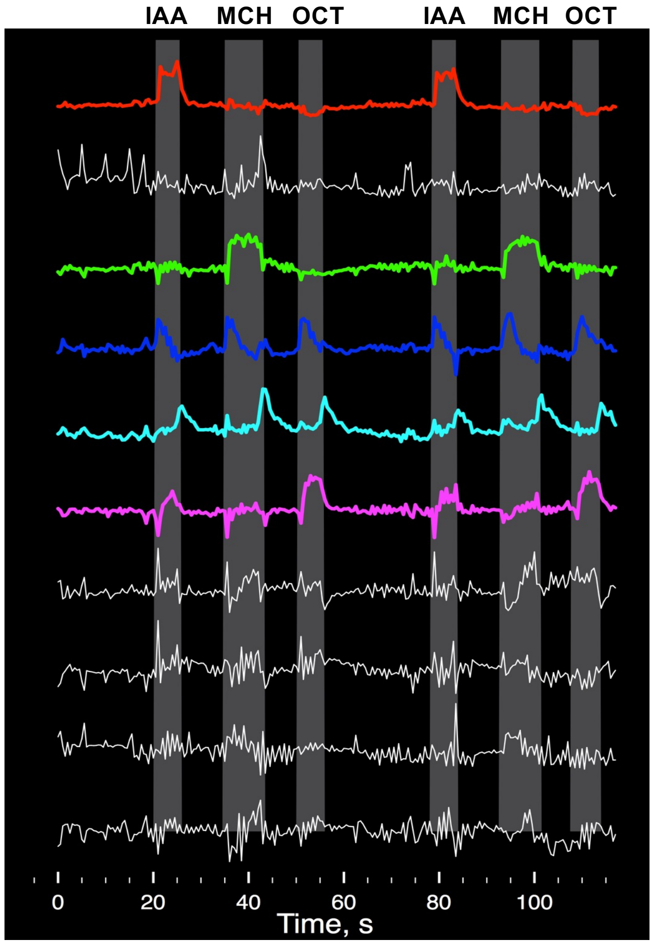
Parallel two-photon microscopy for neural imaging

Extracted signals from Kenyon Cells in mushroom body in response to three different odours (IAA, MCH, OCT)



← Left:
Volumetric rendering of independent components in calyx

Right →:
ΔF/F traces for independent components

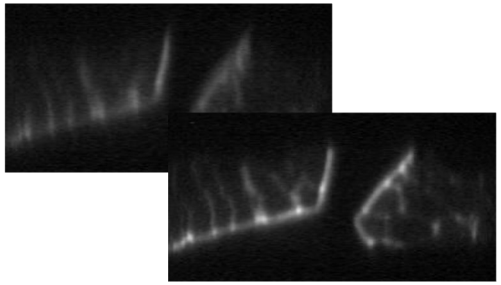


Zurauskas et al., Biomed. Opt. Exp. 8, pp. 4369-4379 (2017)

Adaptive optics for going

SMALLER

Demonstrations of adaptive optics in microscopy



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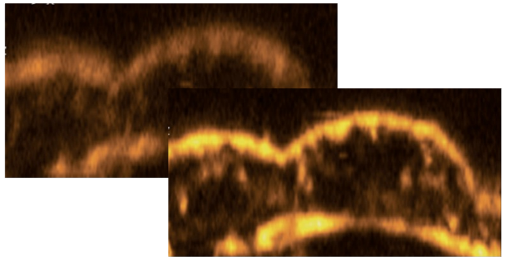

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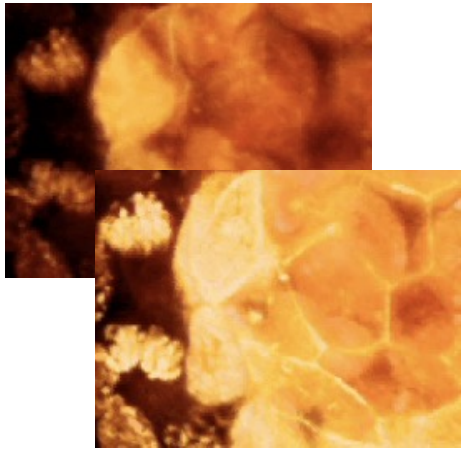

Two-photon microscopy
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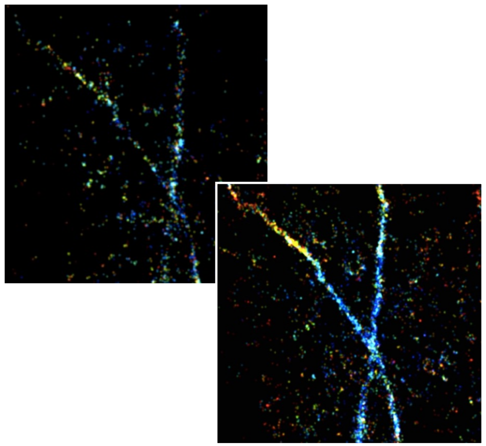

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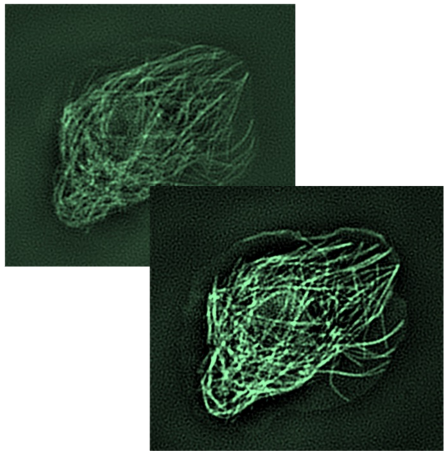
Burke et al., Optica 2, 177 (2015)



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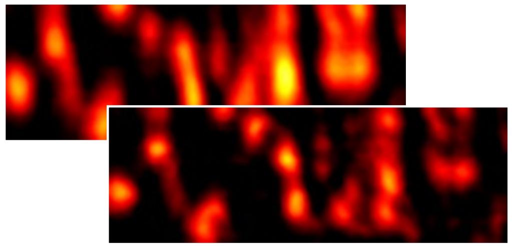
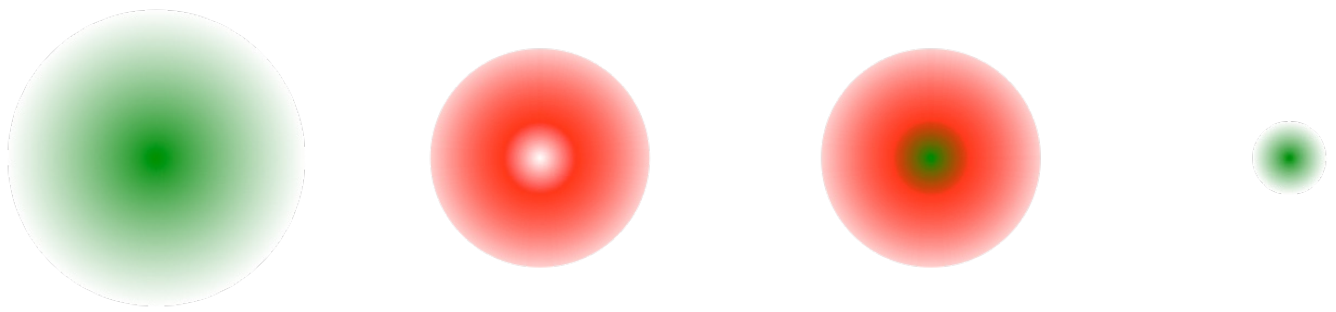
Zurauskas et al., Optica 6, 370-379 (2019)



STED nanoscopy
Patton et al., Opt Expr (2016)

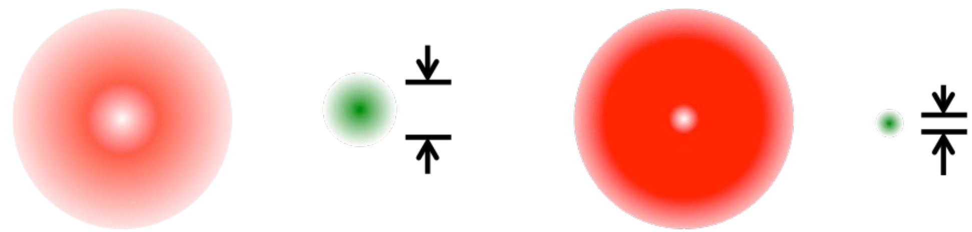
Stimulated emission depletion (STED) nanoscopy

Excited fluorescence | Depletion beam with intensity zero | Stimulated emission depletion | Resulting fluorescence



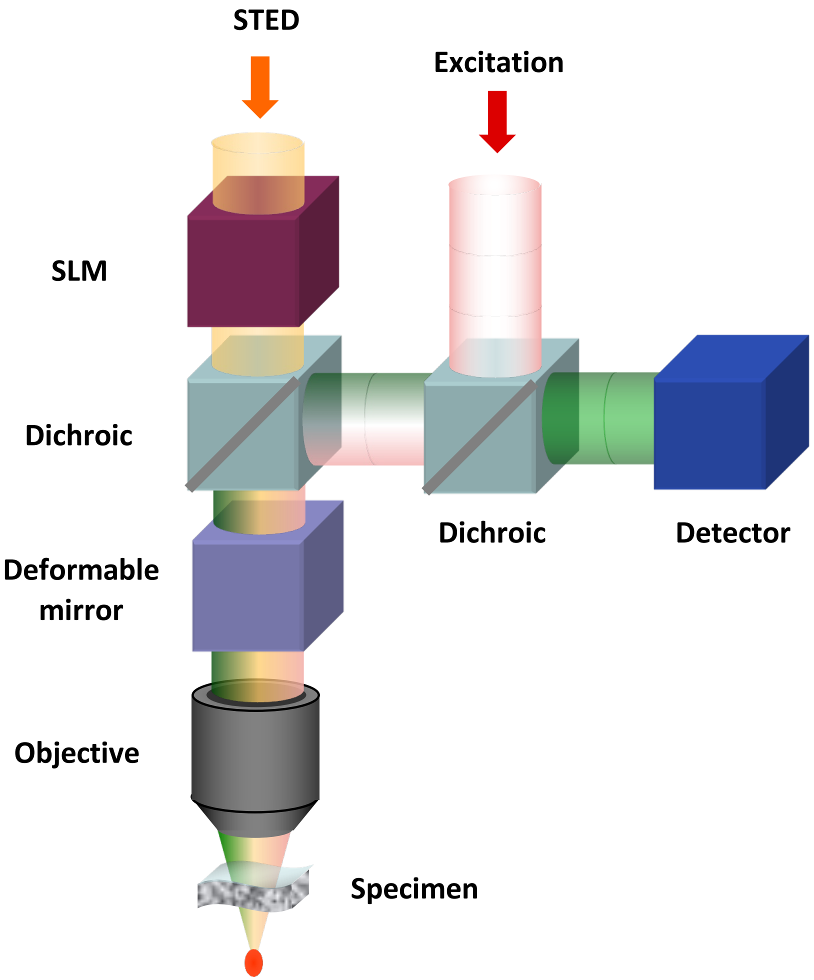
Depletion beam intensity: Low High

Saturation of stimulated emission effect leads to super-resolution



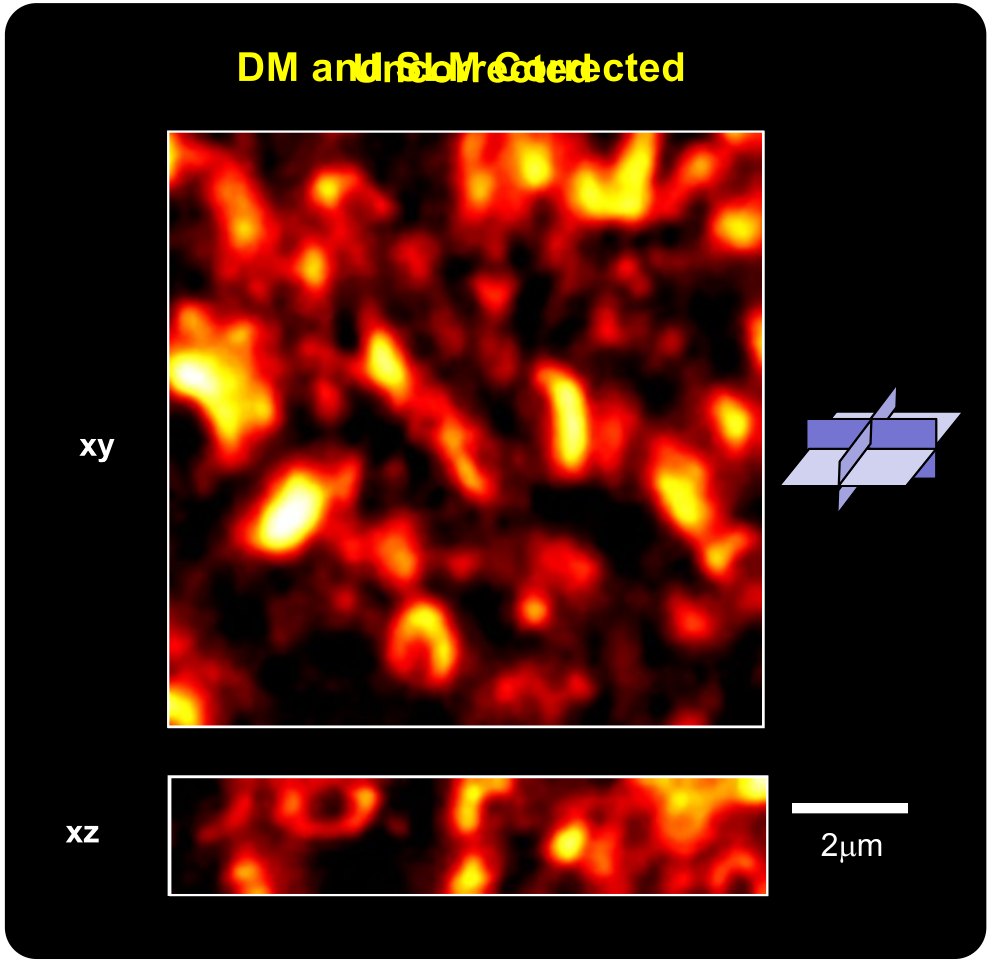
Hell and Wichmann, Opt Lett 19, 780-782 (1994)

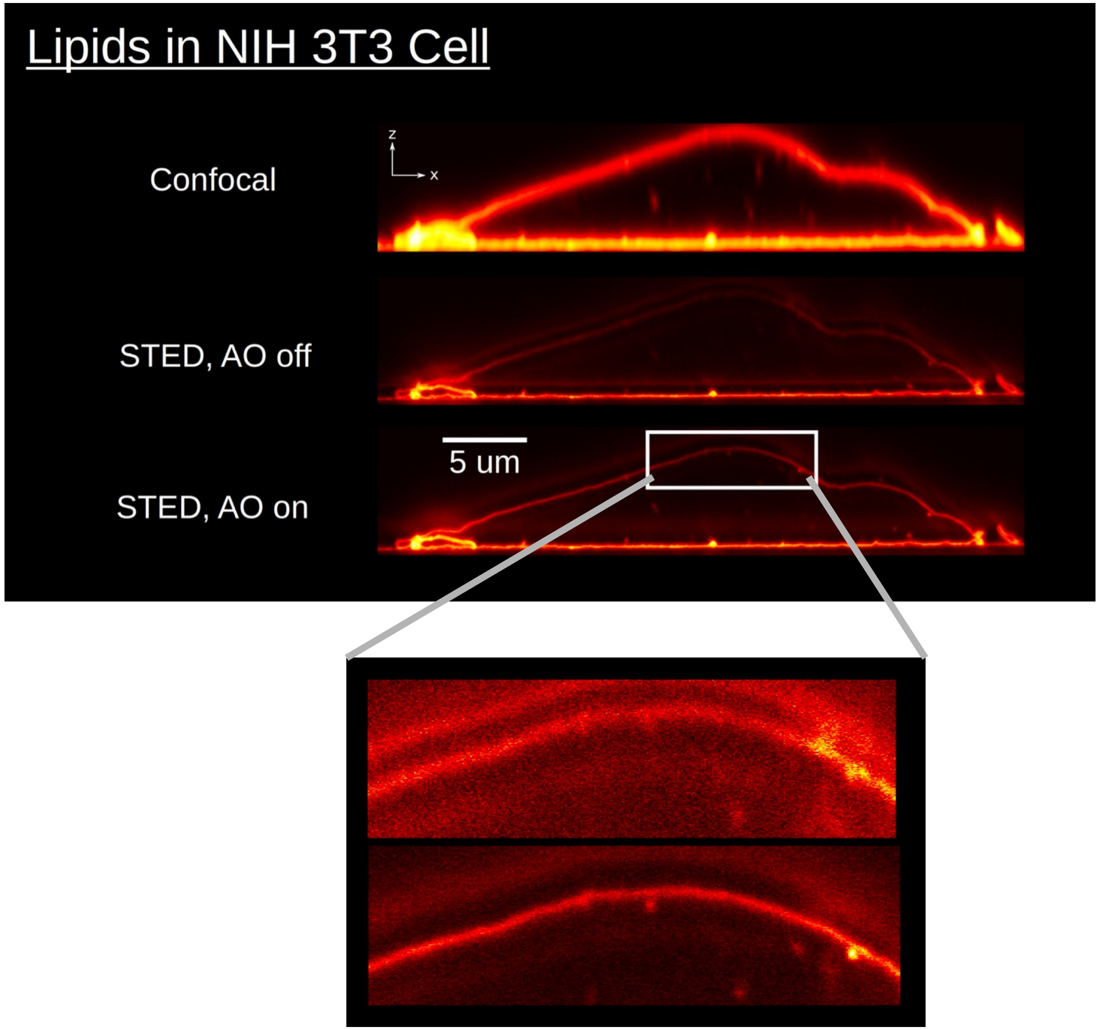
Dual adaptive optics system for STED



- Scheme for correction of aberrations with complex specimen structures
- Spatial light modulator (SLM) providing phase mask for 3D STED imaging
- Deformable mirror (DM) providing common correction of all paths
- SLM providing additional correction of STED beam path

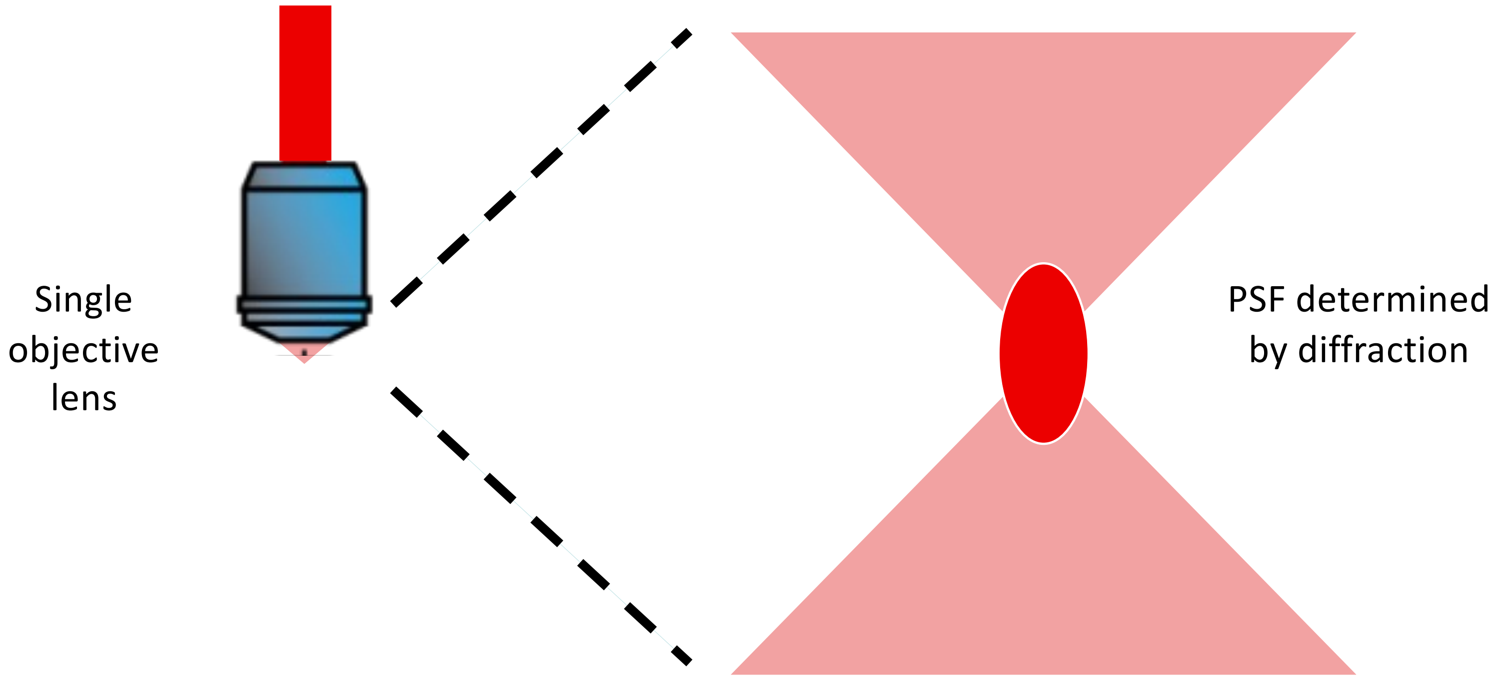
3D STED Imaging in cells and thick tissue



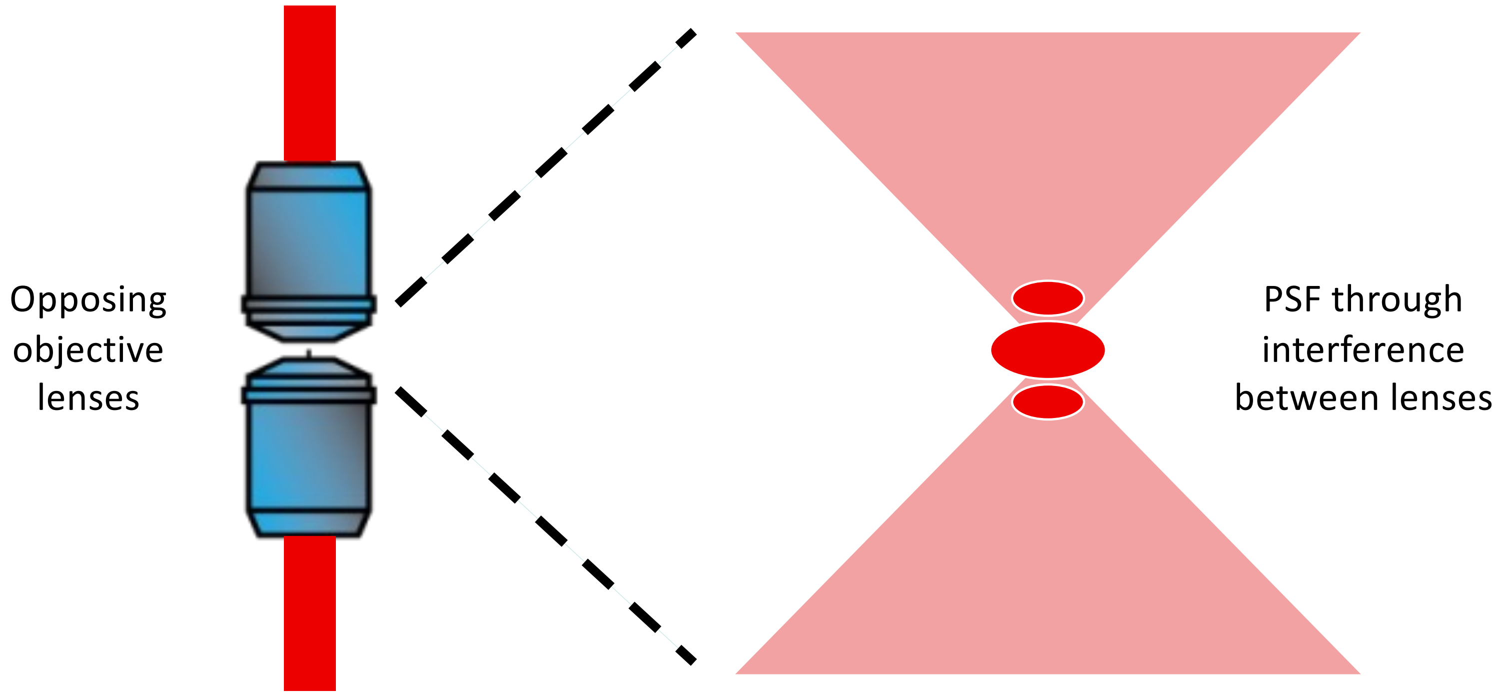


Patton et al., Opt Express 24, 8862 (2016)

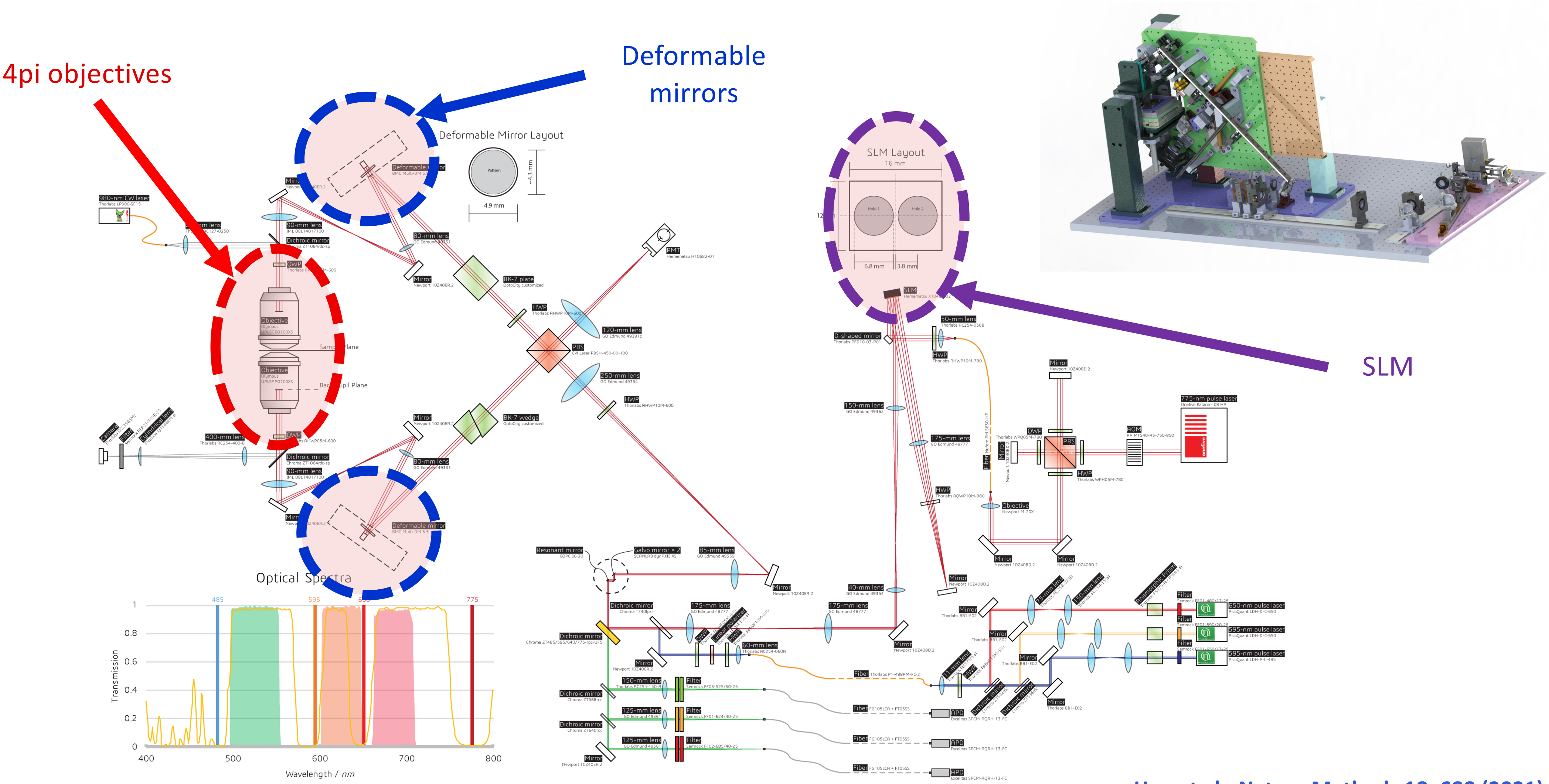
4pi microscope configuration



4pi microscope configuration

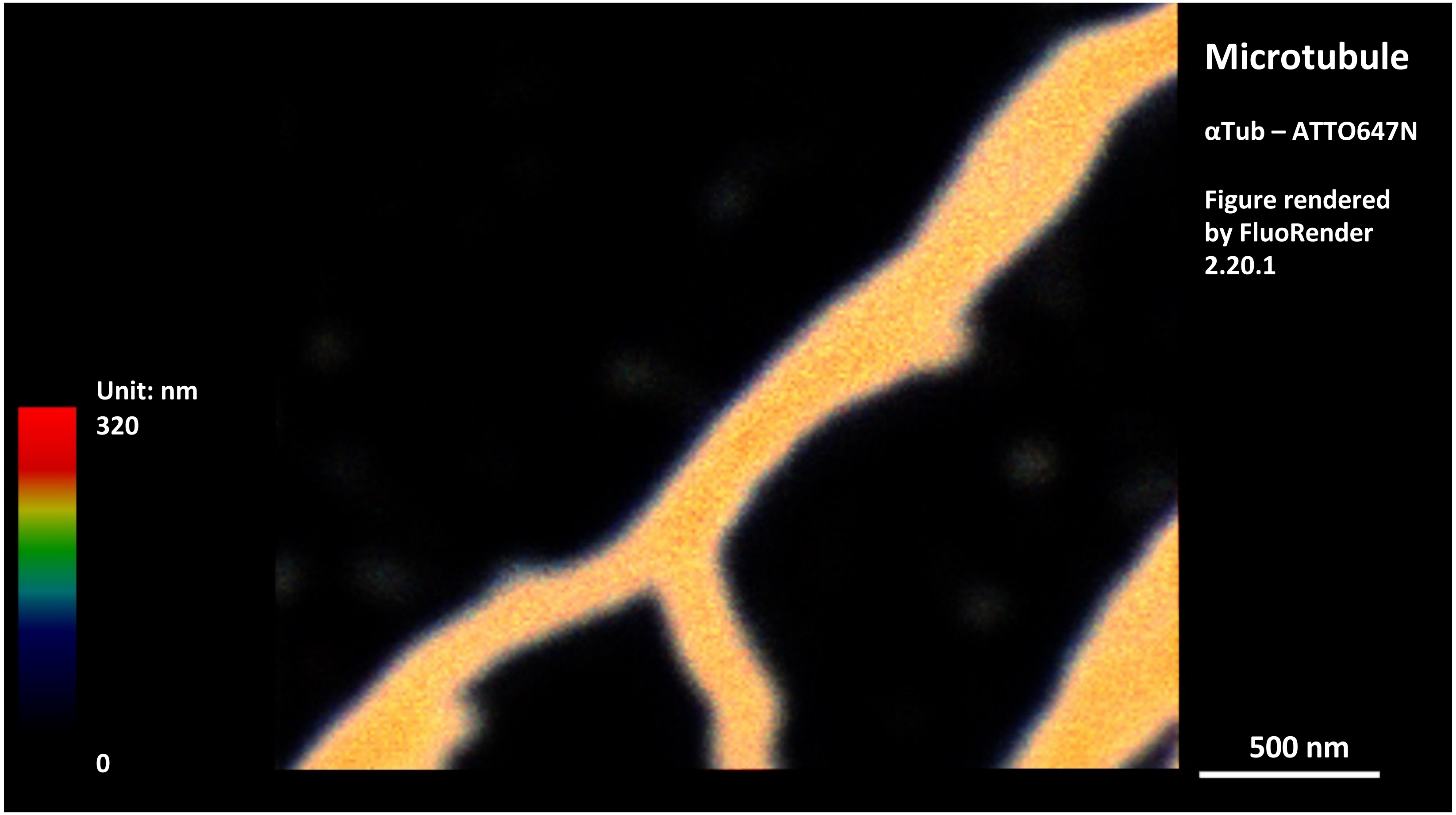


AO-IsoSTED (4pi STED) Optical Layout



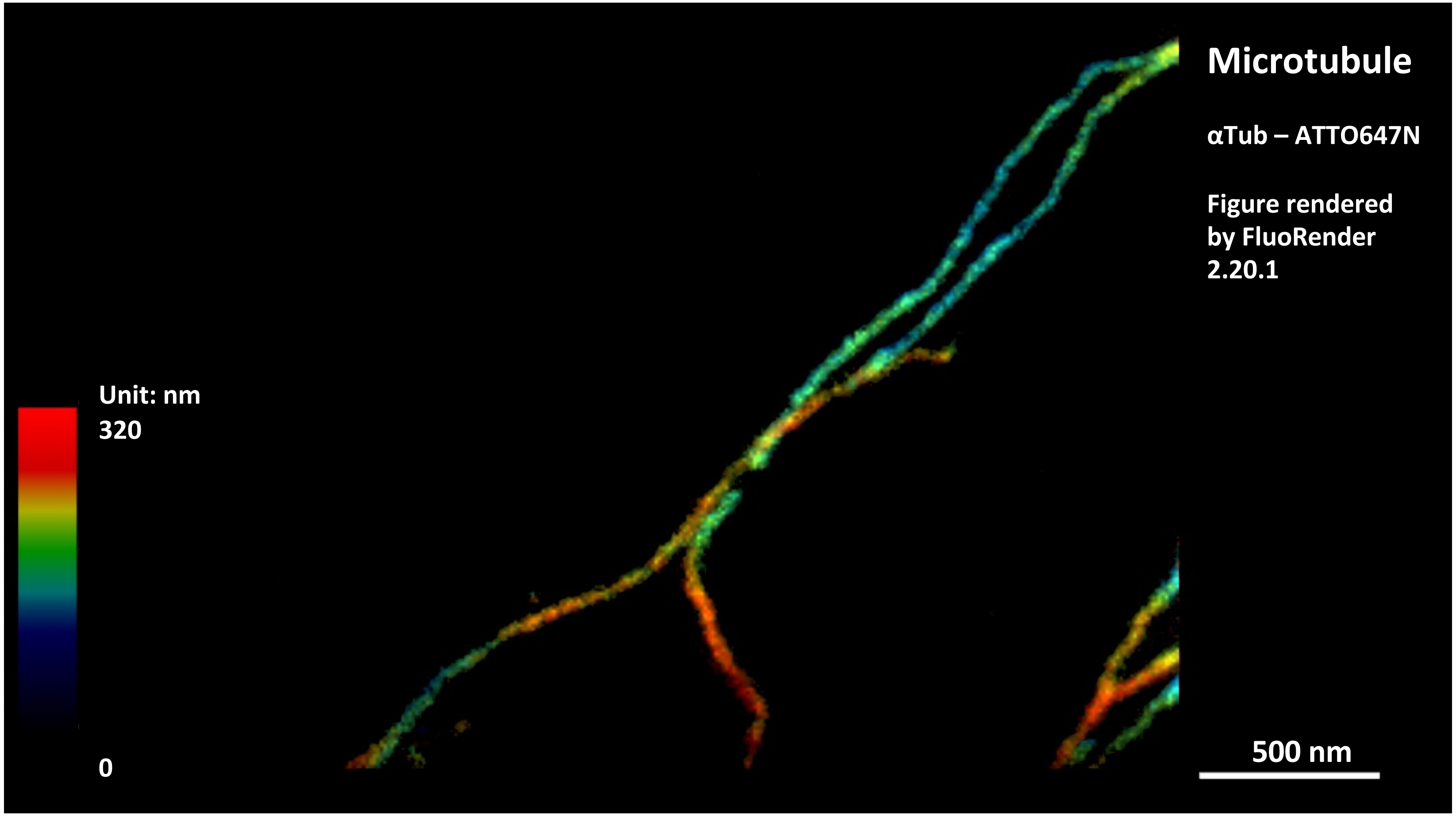
Hao et al., Nature Methods 18, 688 (2021)

Resolution Comparison - Confocal



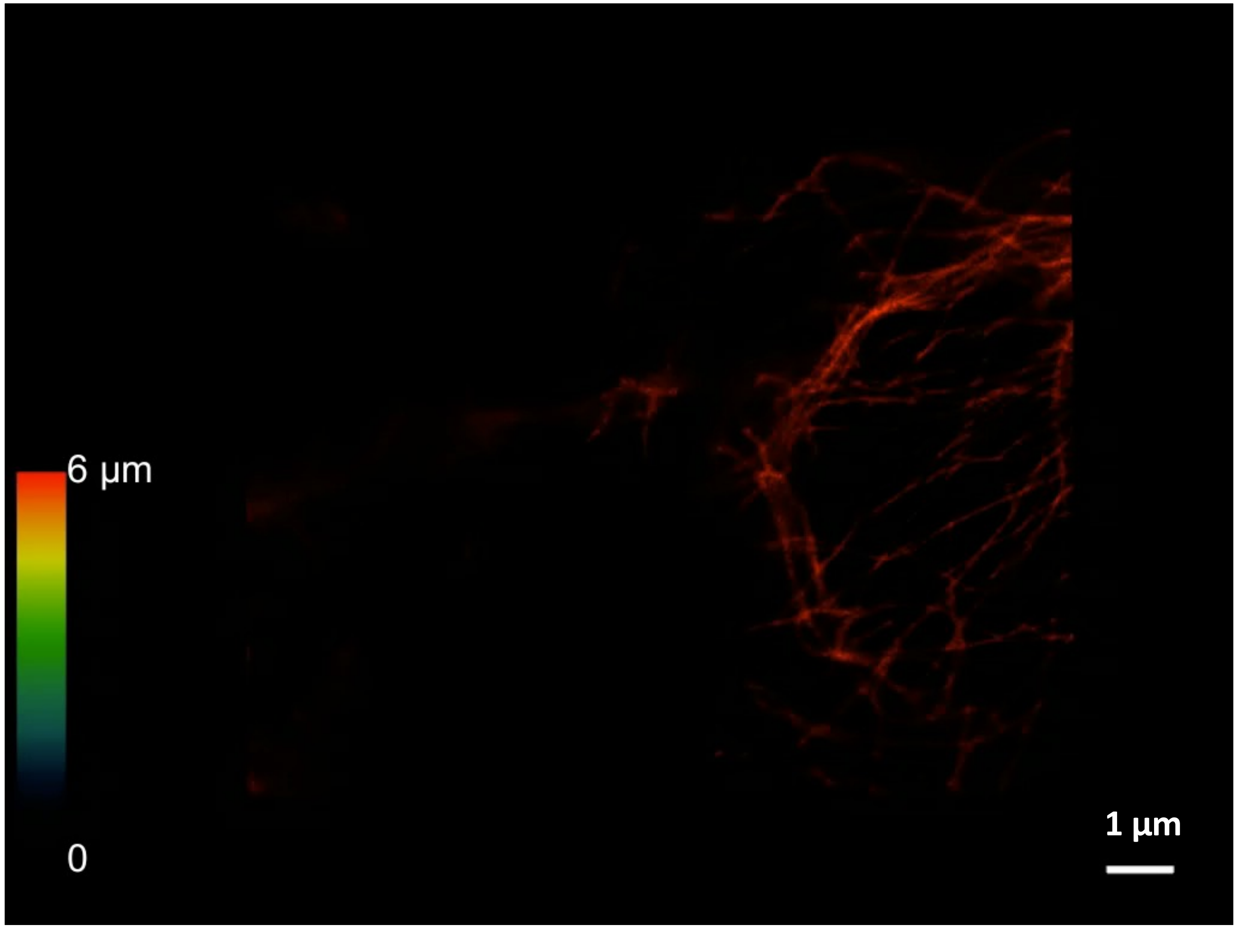
Hao et al., Nature Methods 18, 688 (2021)

Resolution Comparison - isoSTED



Hao et al., Nature Methods 18, 688 (2021)

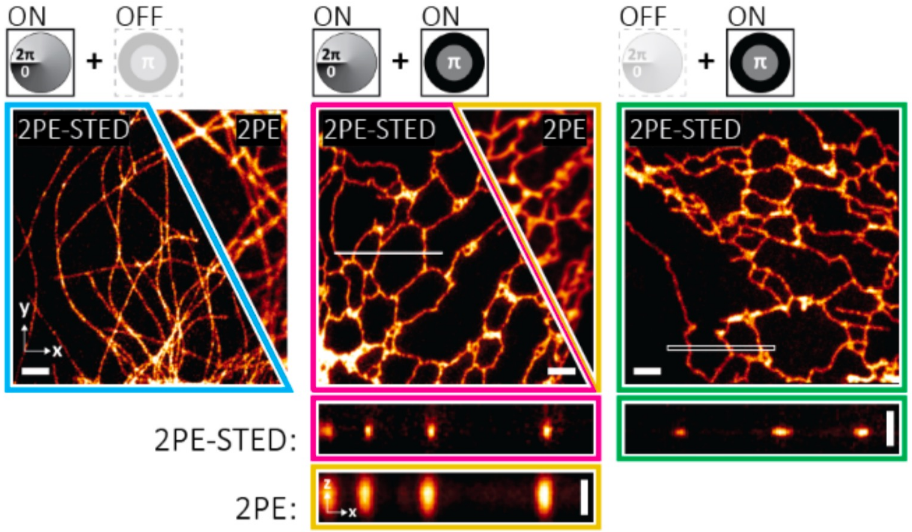
Whole-Cell AO-isoSTED Imaging

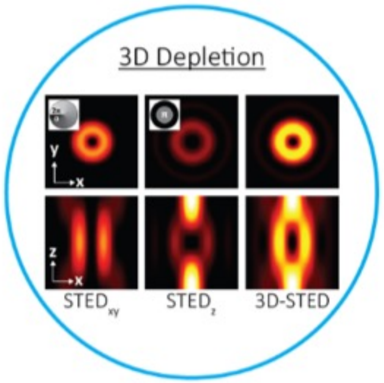


Microtubules, αTub – ATTO647N
Figure rendered by FluoRender 2.20.1

Hao et al., Nature Methods 18, 688 (2021)

Super-resolution – two-photon AO STED microscopy

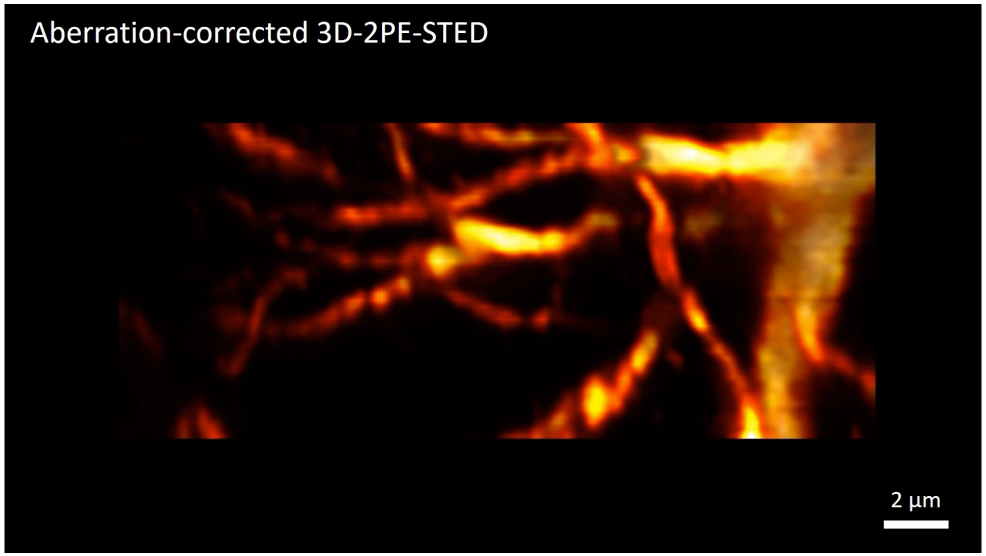




Two-photon 2D and 3D STED microscopy in fixed and living tissues

– enabled by Shack Hartman based adaptive optics

Aberration-corrected 2PE-STED microscopy
~200μm into fixed mouse brain tissue

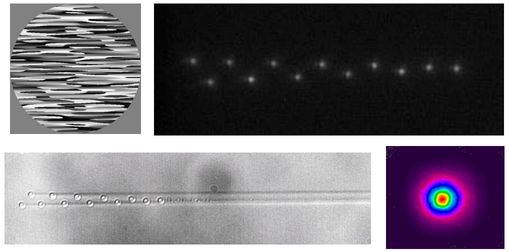


Valasco et al., Optica 8 (4) p442, (2021) Adaptive optics for

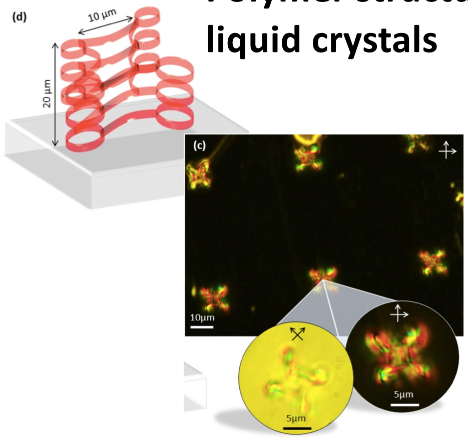
PHOTONIC FABRICATION

Adaptive optics for photonic fabrication

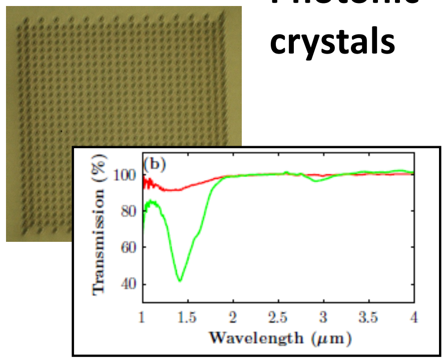
Waveguide circuits

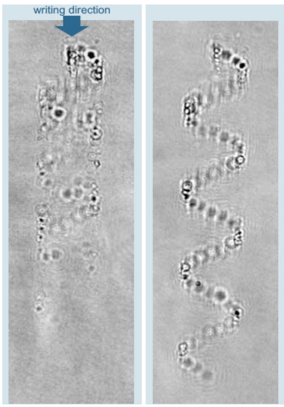


Polymer structured liquid crystals

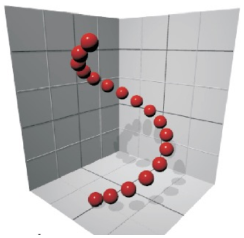


Photonic crystals

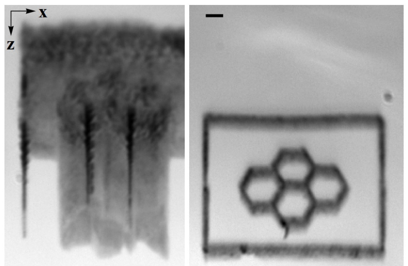




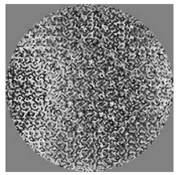
Parallel 3D laser fabrication

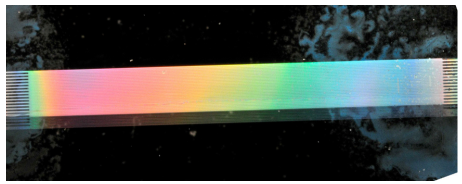


Laser fabrication in diamond



Holographic volume optics

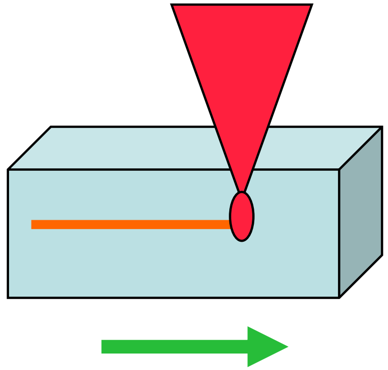




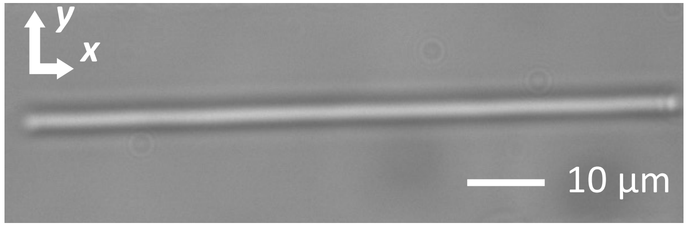
Laser fabrication with femtosecond lasers

- Ultrashort pulsed laser oscillators or amplifiers
  - Typically ~100 fs pulse length
  - Repetition rates 1 kHz – 80 MHz
  - Wavelengths 800-1100 nm
  - Average powers 1-10 W

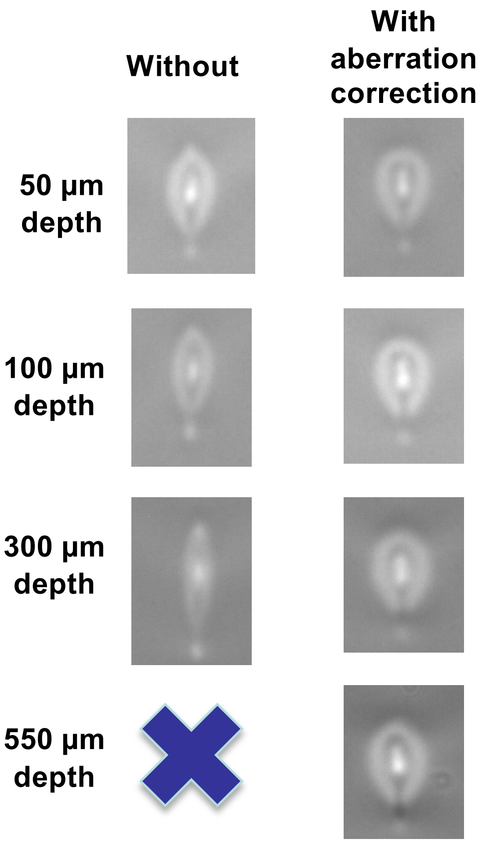
- Non-linear effects confined in 3D to laser focus
  - Multi-photon absorption processes
  - Avalanche ionisation
  - Heating, melting
  - Ablation, void creation
  - Phase changes, etc.



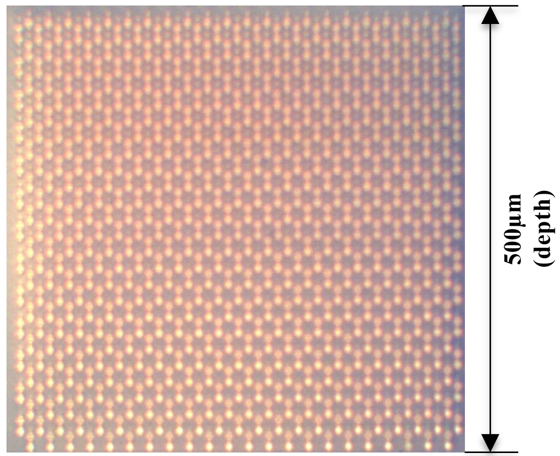
DIC microscope image of laser written waveguide

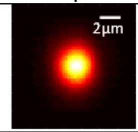
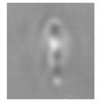
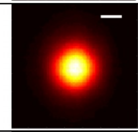
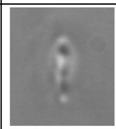
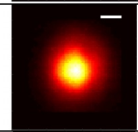
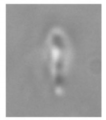
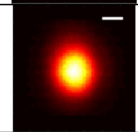
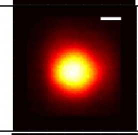
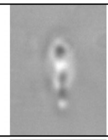
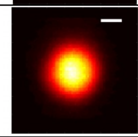
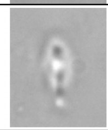
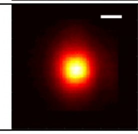


Adaptive correction for large waveguide arrays



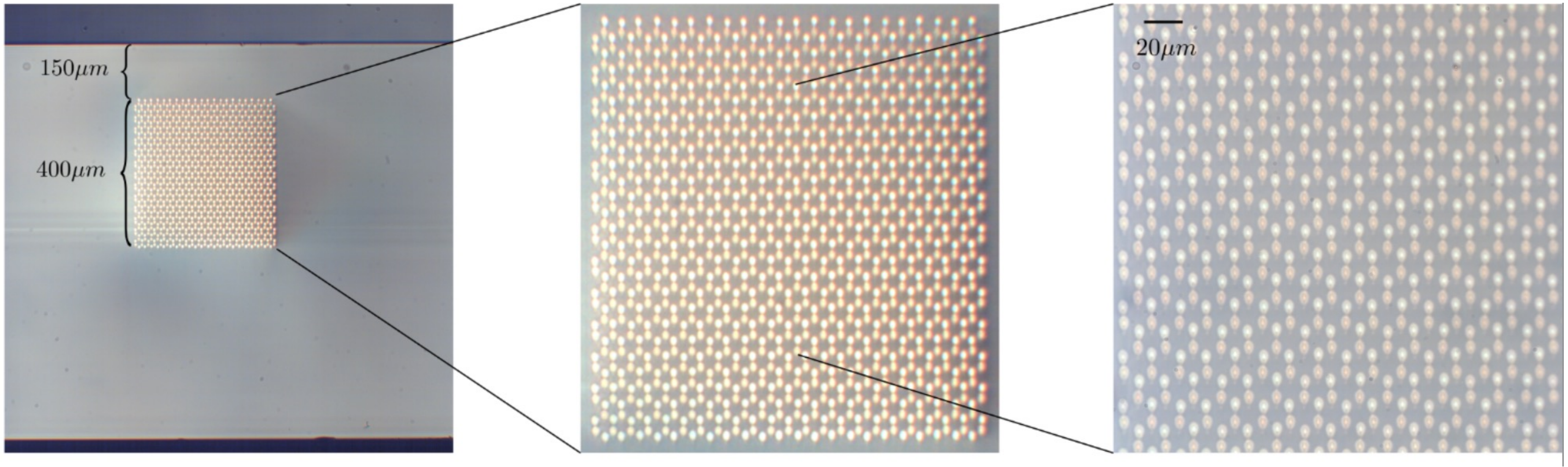
Uniform waveguide lattice (End- on image)

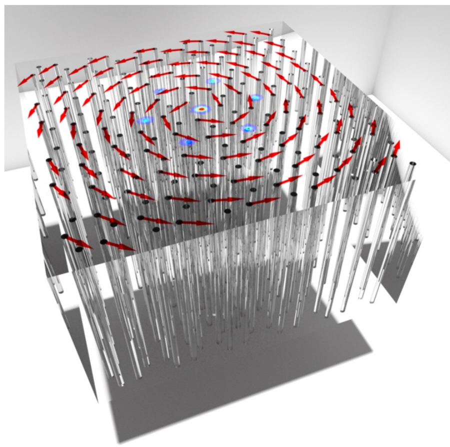


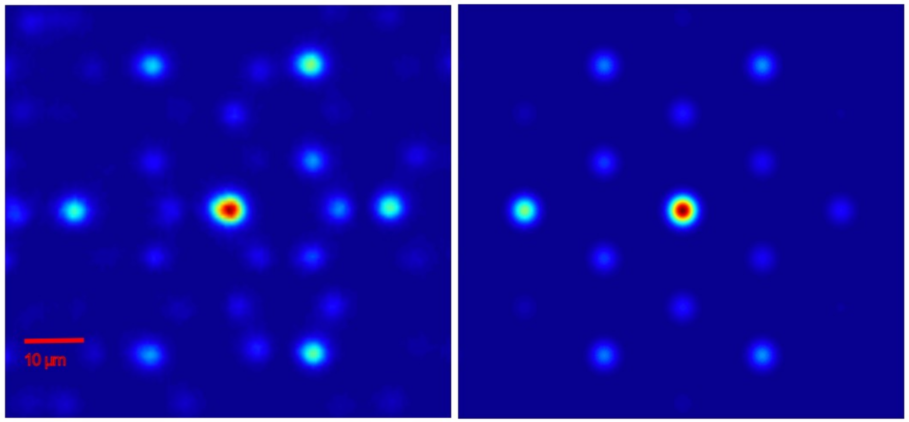
Depth (μm)	End-on image	Near field mode profile	Throughput
170			89.4%
250			92.4%
350			90.5%
450			92.2%
650			86.4%
850			86.7%
1000			87.4%

Eagle 2000 glass.
Writing Laser: Pharos, 532nm, 1 MHz, 70nJ, 2mm/s. Chip length 12mm. Testing laser: 777nm

Photonic quantum simulators



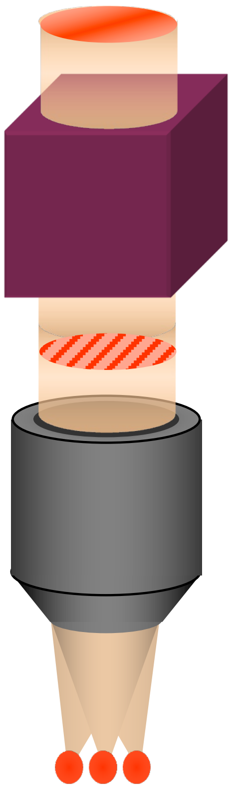




Experimental Theoretical

Menssen, *et al*. PRL 125 (2020)

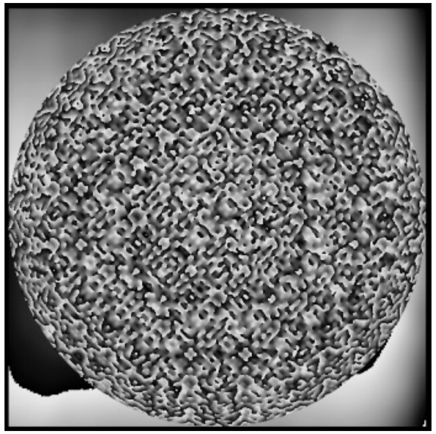
Parallel optical fabrication

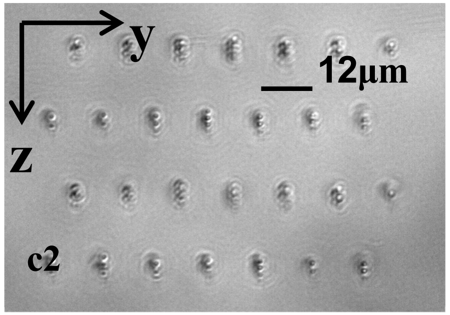


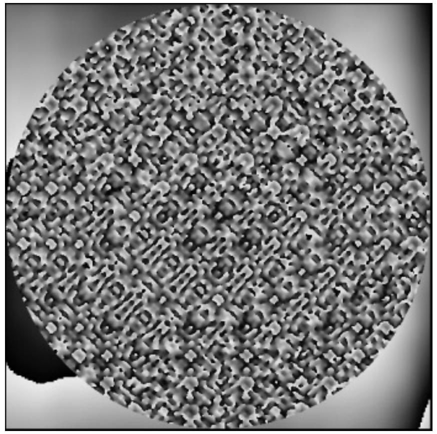
- Use high resolution adaptive element (e.g. liquid crystal spatial light modulator)
- Generate diffraction grating (hologram) that creates multiple focal spots
- Device reconfigured to control spots indepedendently
- Parallelisation to over 100 foci considerably increases fabrication speed.

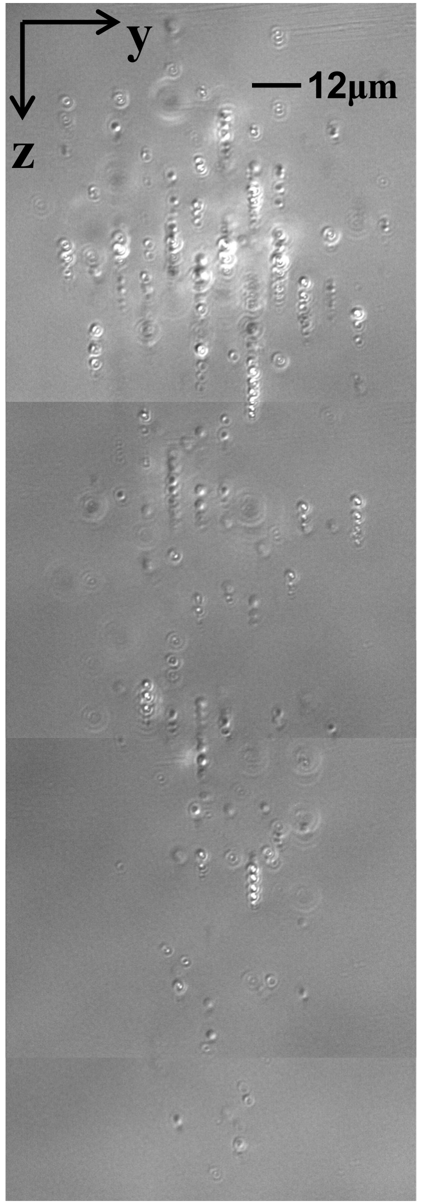
Hamamatsu LCOS-SLM

Parallel optical fabrication









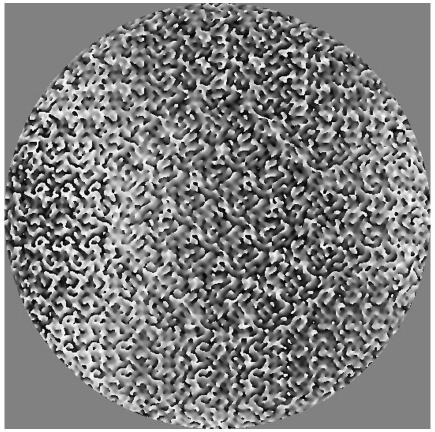
0.5 NA objective lens, 196 parallel foci arranged in three dimensions

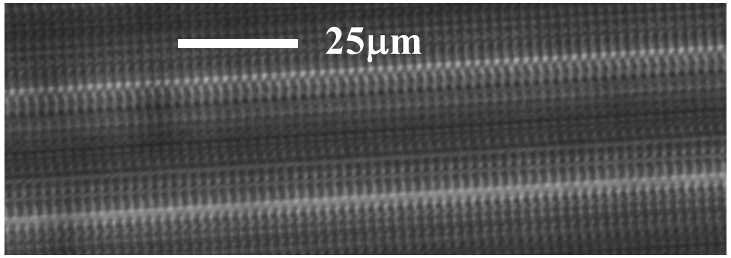
Aberration correction (left) essential for reliable fabrication

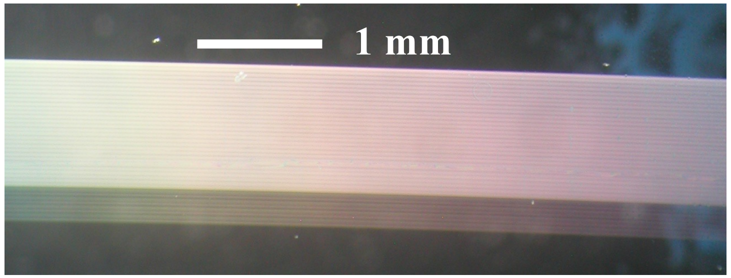
Salter et al, Opt Exp 22, p17644 (2014)

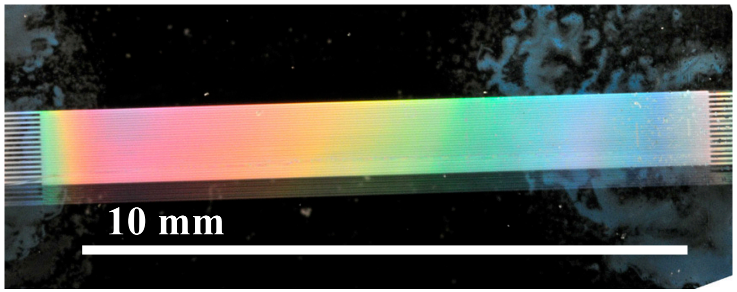
Parallel 3D fabrication

SLM hologram





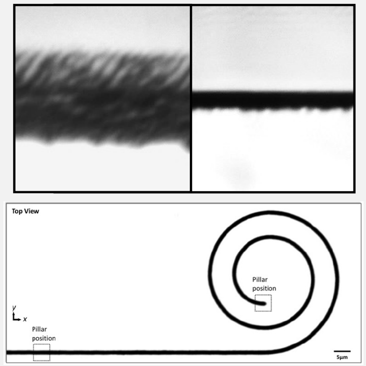




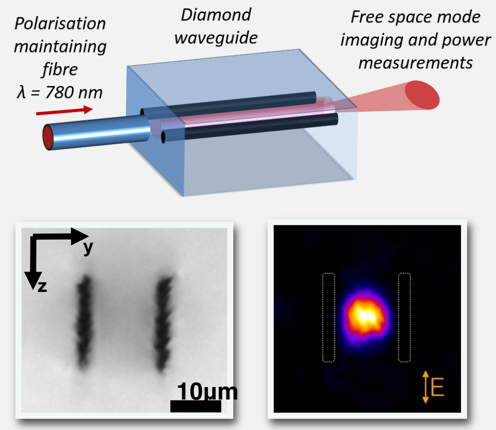
- Voids in fused silica
- 196 foci per laser pulse (7x7x4 FCC block)
- Stage translation 2.25mm/s synchronised with laser pulse train
- 28000 foci per second, $1mm^3$ volume structure (10 x 1 x 0.13 mm, $40x10^6$ foci) in 40 min
- Potential to achieve 10x speed improvement for 1kHz repetition rate laser

3D femtosecond laser adaptive writing in diamond

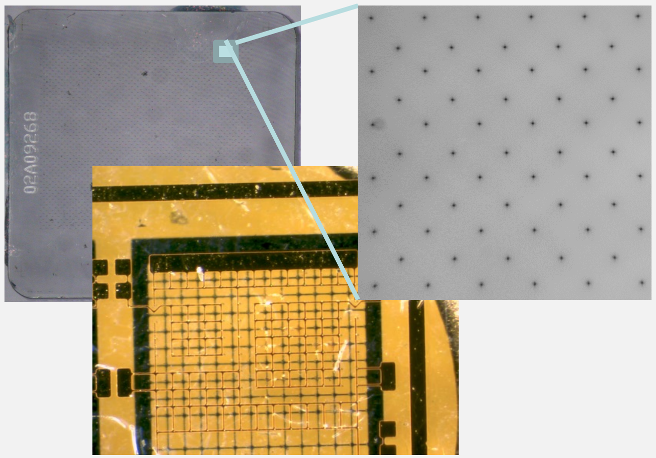
Ultrafast laser writing with adaptive aberration correction



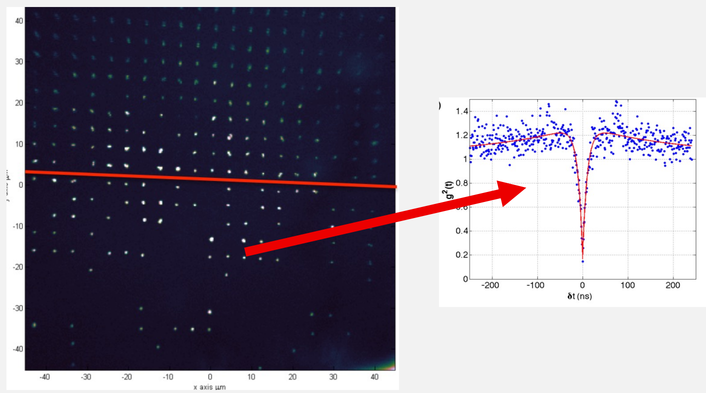
Laser written 3D graphitic conductors



Waveguides in diamond



Diamond radiation detector arrays

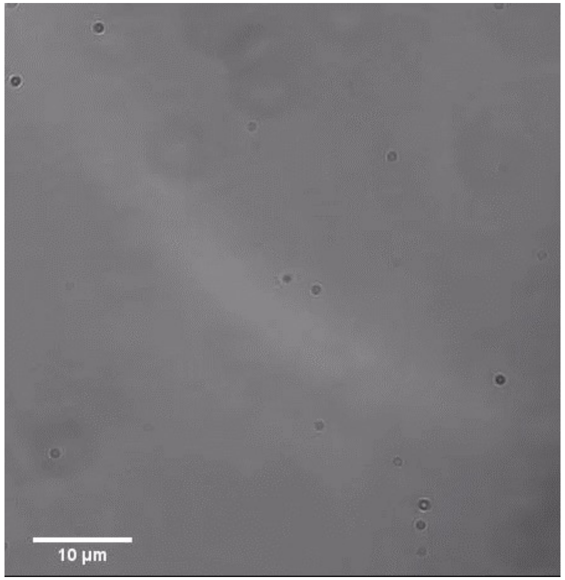


Laser writing of single nitrogen vacancy colour centres

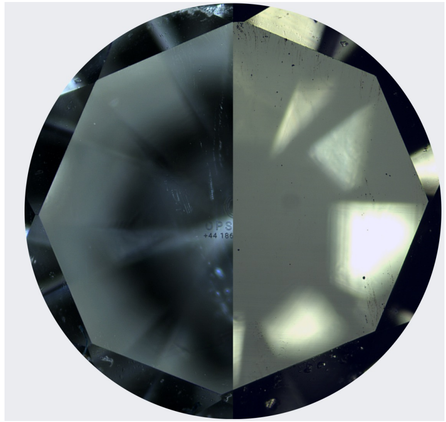
Industrial application of adaptive laser writing

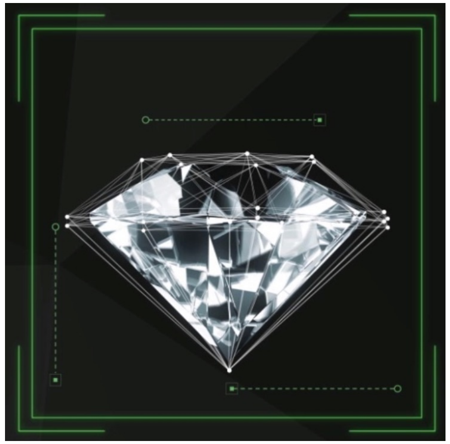
OPSYDIA

http://opsydia.com



Subsurface security marking for gemstones

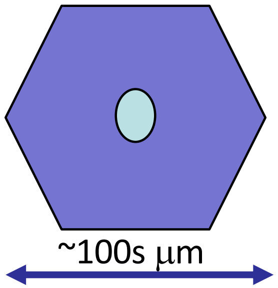


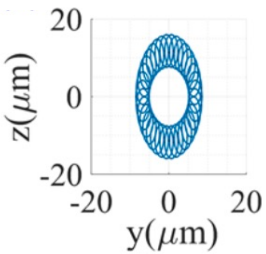


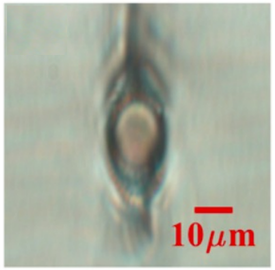
The author declares a significant interest in Opsydia Ltd.

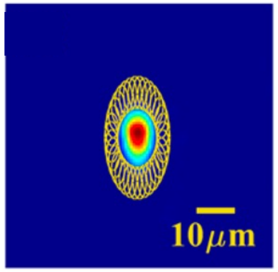
Sapphire fibre waveguides through adaptive laser writing

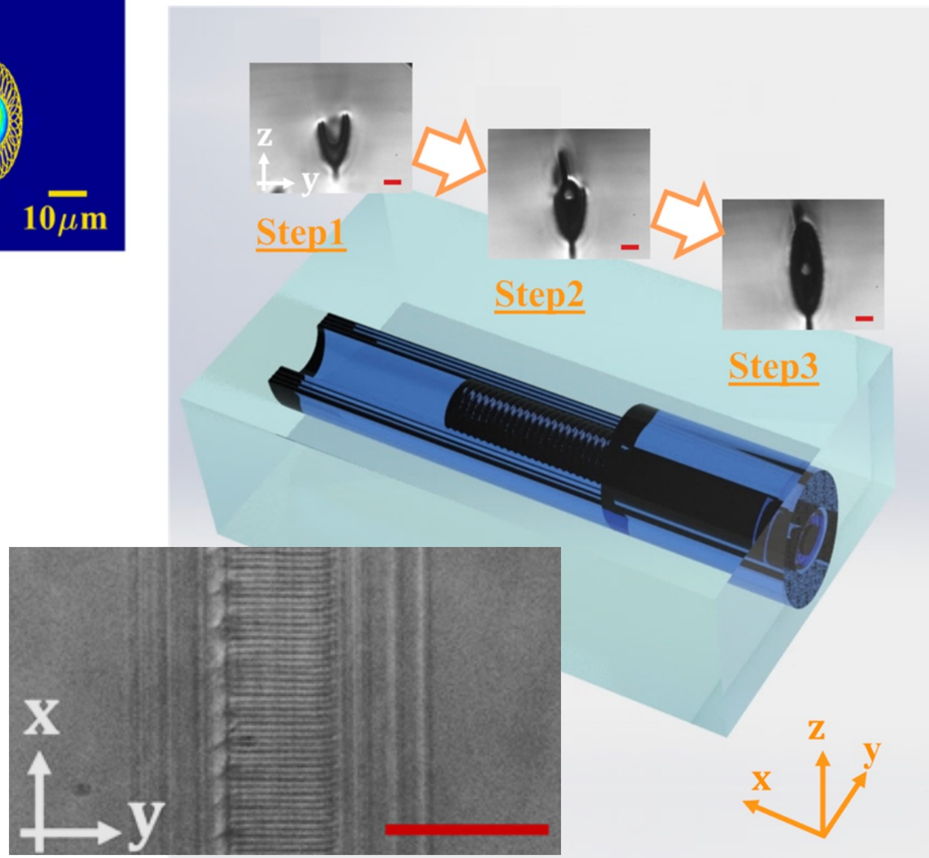
Single mode fibre Bragg grating waveguide in sapphire optical fibres – high temperature operation

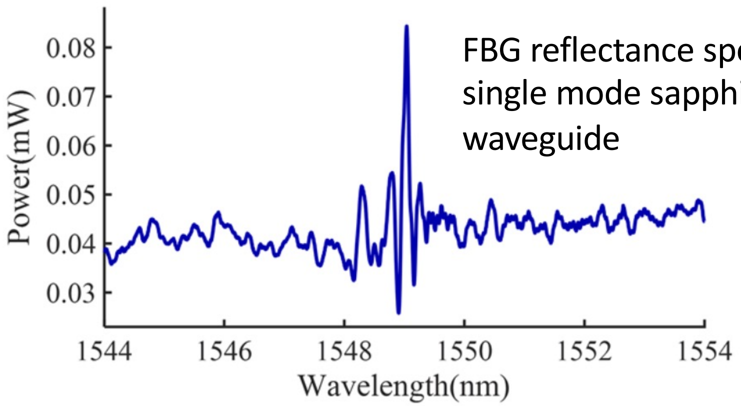












FBG reflectance spectrum in single mode sapphire fibre waveguide

Wang et al., Opt Expr 30 (9), 15482 (2022)

Future developments in adaptive optics

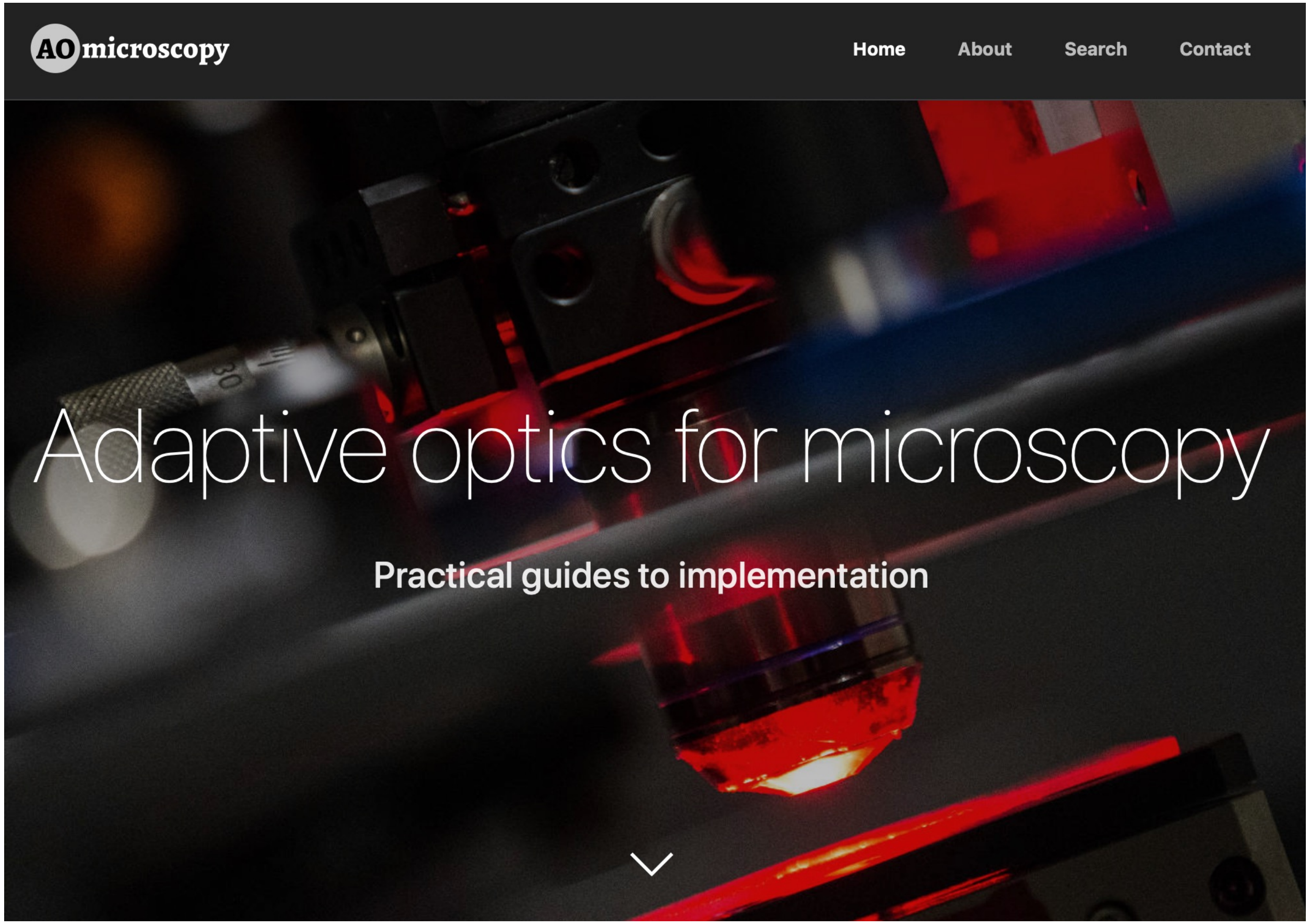
- Pushing limits of depth, speed and precision

- Applications:
  - Microscopy, Laser material processing
  - Other areas, Ophthalmology, Clinical, …

- New frontiers for adaptive optics:
  - Spatio-temporal, Spectral, Polarisation, Coherence

- Enhancements in usability and applicability
  - Toolkit of methods to enable wider adoption of adaptive optics in microscopes

aomicroscopy.org



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Advancing Optics and Photonics Worldwide

Technical Groups

Question & Answer