Simultaneous Two and Three Photon Imaging for Personalized Medicine and Real-Time Treatment Optimization

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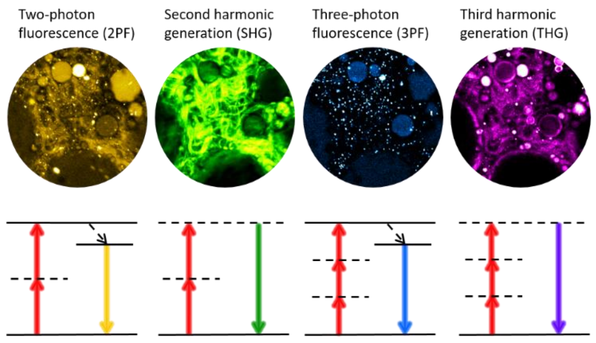
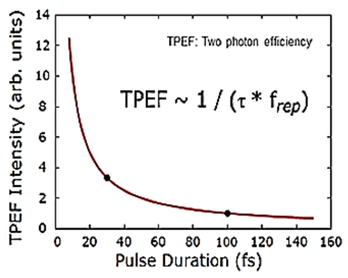
Introduction



Multiphoton microscopy allows for

- Label-free microscopy
- Higher contrast
- Deeper imaging
- 3D imaging
- Low photodamage



*Shorter pulses lead to increased two photon efficiency

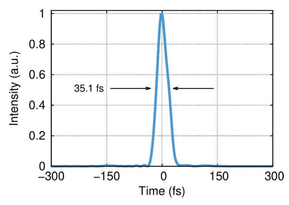
Sub 50 fs Fiber Lasers

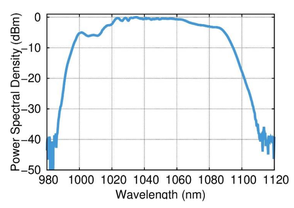
Specifications

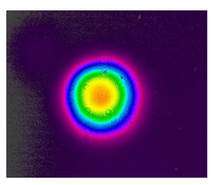
- Pulse duration: < 50 fs (typ. 40 fs)
- Repetition rate: 30 MHz
- Output power: 200 mW (Aalto) / 2 W (Tidal)
- Peak power: 166 kW (Aalto) / 1.6 MW (Tidal)
- Nearly perfect Gaussian beam profile

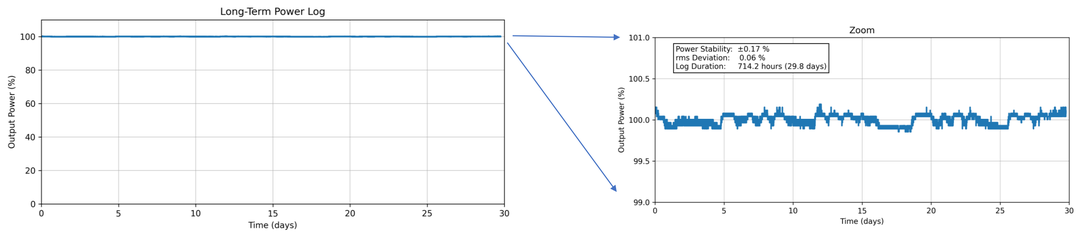
Features

- No water cooling, no fans in laser head
- Dispersion precompensation module integrated
- Remotely controllable
- Active power stabilization - always at optimum
- No training / no manufacturer installation required





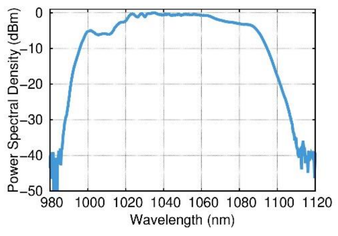


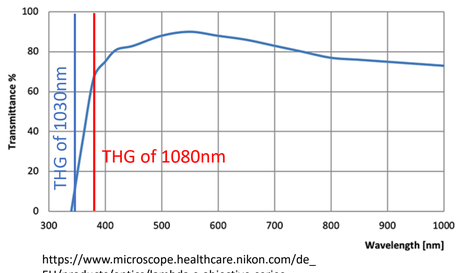


Objective transmission

Most microscope objectives are not transparent for 3rd Harmonic of 1030nm

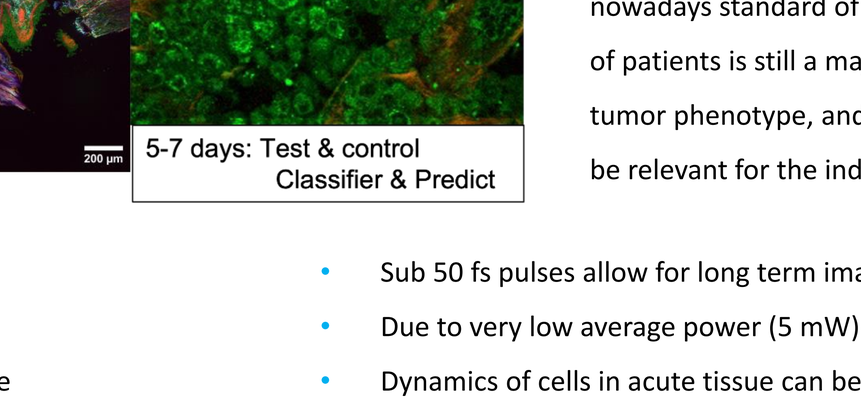
- Sub 50 fs lasers for 2 and 3 photon microscopy
- Wavelength > 1070 nm for THG imaging





https://www.microscope.healthcare.nikon.com/de_EU/products/optics/lambda-s-objective-series

Higher Harmonic Generation Microscopy for Instant Pathology [1]



- SHG and multiphoton fluorescence signals have molecular origin/specificity
- THG is generated at all density variations: 3D phase-contrast microscopy
- HHG microscopy allows for label free and real- time images

Biopsy-based drug testbed for treatment response prediction

Response rates to cancer treatments are still poor, especially in case of lung cancer, where for the most common type of cancer, non-small cell lung cancer (NSCLC), the response rate varies between 9 % and 74 %.

Personalized treatment based on predictive biomarkers is nowadays standard of care. However, over- and undertreatment of patients is still a major problem, as methods do not consider tumor phenotype, and more advanced methods are too slow to be relevant for the individual patient.

- Keep biopsy tissue alive for ~5 days
- Add therapeutic
- Predict patient specific treatment response, based on tissue phenotype
- Sub 50 fs pulses allow for long term imaging over days
- Due to very low average power (5 mW) no heating of the tissue occurs
- Dynamics of cells in acute tissue can be followed over hours and even days

References

[1] L. Van Huizen, J. Daniels, T. Radonic, J. Von Der Thüsen, K. Kalverda, M. L. Groot, J. Annema, "Higher harmonic generation microscopy for instant on-site pathologic feedback of lung biopsies" European Respiratory Journal Sep. 2022, 60 (suppl 66) 3791

[2] M.L. Groot, F. van Mourik, N. Meijns, Y. Ma, O. Prochnow, "Optimization of higher harmonic generation microscopy for acute tissue imaging", Proc. SPIE PC12384, Multiphoton Microscopy in the Biomedical Sciences XXIII, PC123840X (15 March 2023)

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Summary

New class of femtosecond lasers allows for drastically improved results

- Broadband emission spectrum allows for simultaneous two and three photon imaging
- Sub 50 fs pulses allow for long term imaging over days
- Due to very low average power (5 mW) no heating of the tissue occurs
- Dynamics of cells in acute tissue can be followed over hours and even days

Link to White Paper

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