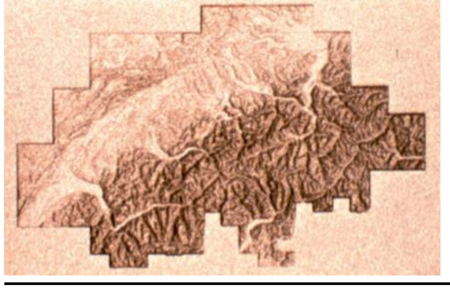
SWISSLASER NET

Lasers to see, cut, and move

Biomedical Photonics Workshop

Bern, Switzerland

26 November 2009



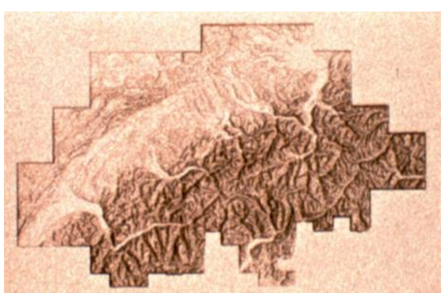
Dr. Kurt Weingarten

kw@time-bandwidth.com

Time-Bandwidth® Products

Ultrafast lasers

to see, cut, and move



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Outline

- **Short introduction**
  - **Time-Bandwidth Products**
  - **Fast-Dot EU Project**
  - **The goal - could we do all of this with one laser?**
- **Moving – Optical Tweezers**
- **Imaging – Nonlinear (2-photon) Microscopy**
- **Cutting – Cellular Micro- to Nanosurgery**

TBP product range

OEM & Customized
Pico- & Femtosecond **Lasers**

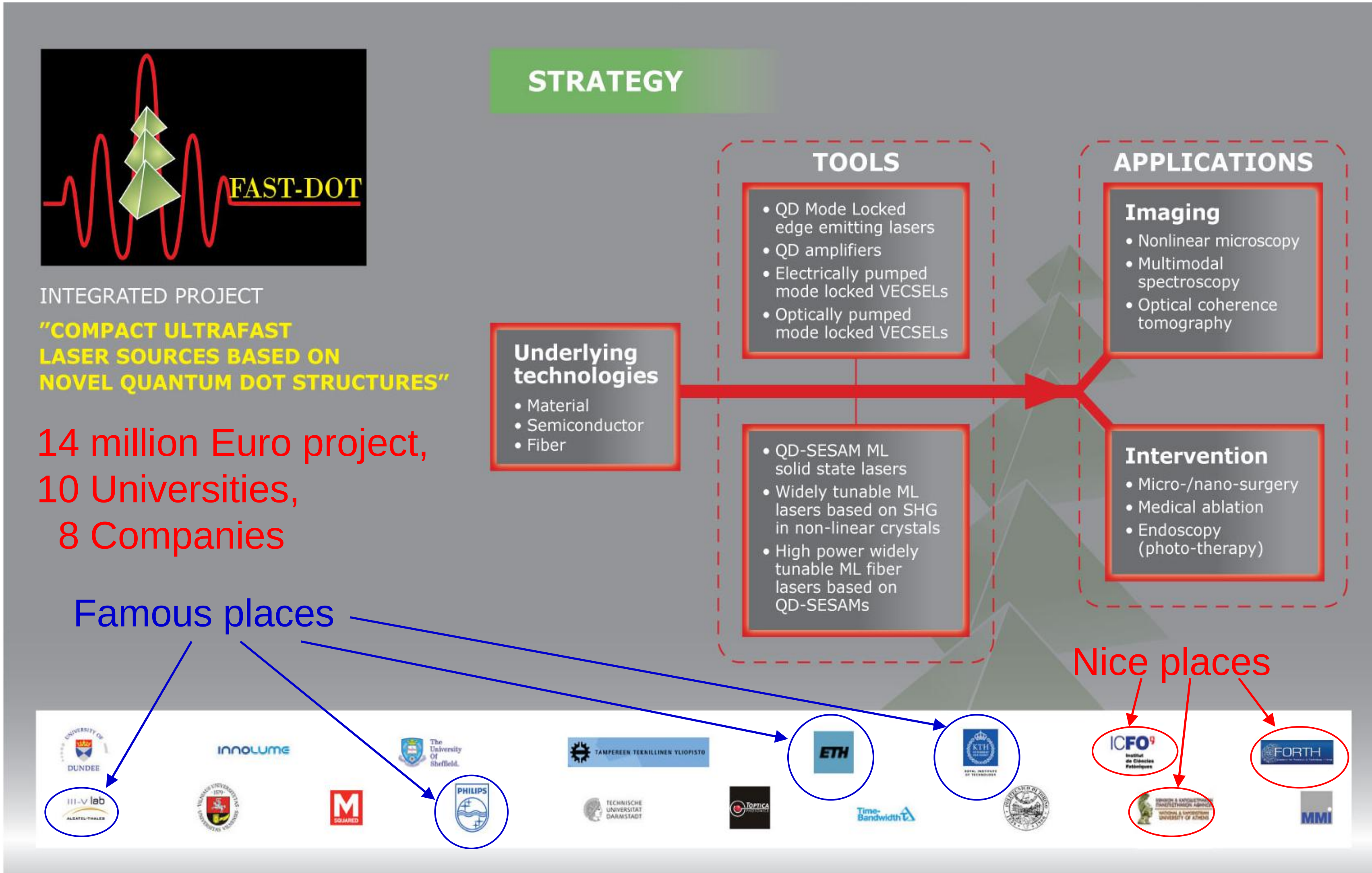
Flexible, modular set of product platforms

Customizable for scientific or industrial applications

Broad set of performance parameters

Pulse durations	**<50 fs to >500 ps**
Wavelengths	**260 nm – 1550 nm**
Output power	**<1 W to >50 W**
Pulse energies	**up to 1 mJ**
Repetition rates	**single shot to >10 GHz**

Fast-Dot project www.fast-dot.eu



MMI Company Details

- Established: 1998
- Headquarters: Glattbrugg, Zürich, Switzerland
- Branches: MMI GmbH, Germany
  MMI Inc., USA
- Represented in more than 65 Countries

Vision:

To be the preferred provider for unlimited micromanipulation solutions and lead the way in single and rare cell applications

Special thanks to Dr. Stefan Niehren

niehren@molecular-machines.com

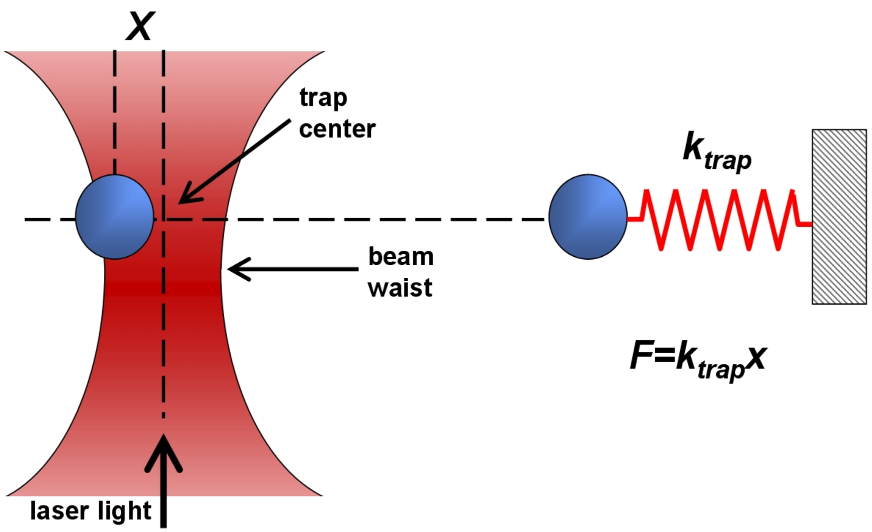
Molecular Machines & Industries

Moving:

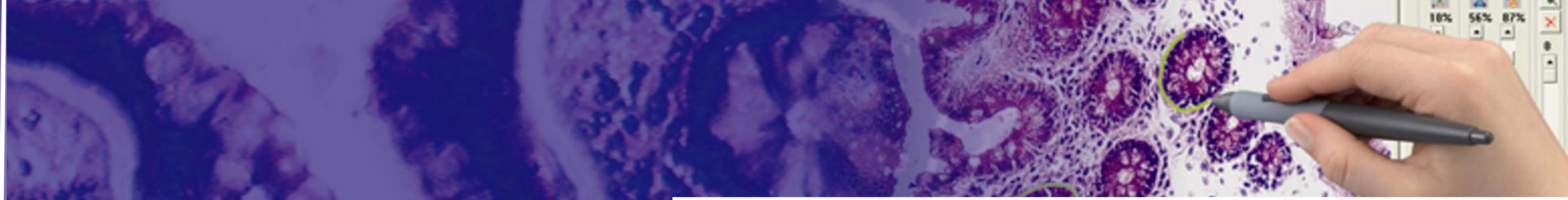
optical tweezers

What is an optical trap or optical tweezer?

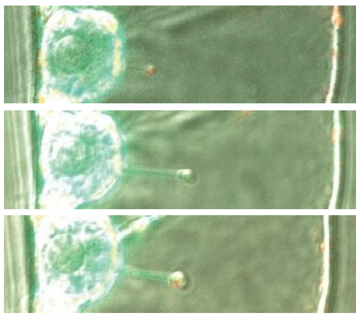
- **A tightly focused laser beam provides an attractive or repulsive force (typically on the order of piconewtons)**
  - **Objects are attracted to the center of the beam, slightly above the beam waist. The force applied on the object depends linearly on its displacement from the trap center - just as with a simple spring system.**

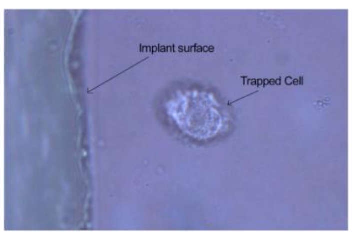


source: en.wikipedia.org/wiki/Optical_tweezers



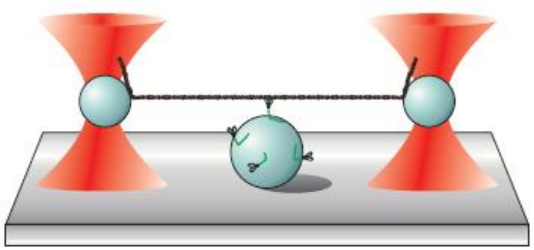
Biological Applications





Cell-based Studies
- Cell fusions and cell-to-cell interactions
- Implant studies
- Intracellular manipulations
- Study of neuronal networks
- Drug effects on cells
- Ca2+-channel studies

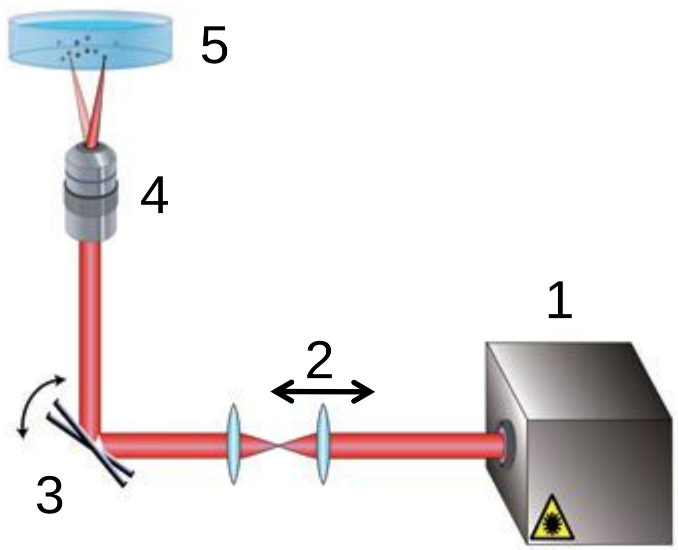
Measurements of Binding Forces
- DNA studies
- Viscosity measurements
- Antibody, antigen binding forces
- Bacterial adhesion studies
- Virus to cell adhesion studies



Molecular Motor Studies
- Actin, Myosin interactions
- Kinesin Motors
- Dynein Motors

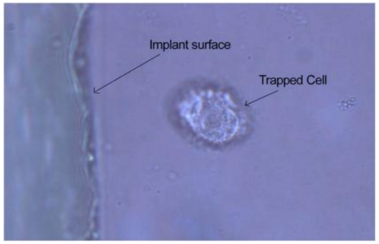
How optical tweezers work:
Optical setup of MMI CellManipulator

1 Laser 1064 nm, 8 Watt
2 Focusing lens
3 Galvo scanners 2 kHz
4 Objective with high NA
5 Cells, particles in solution

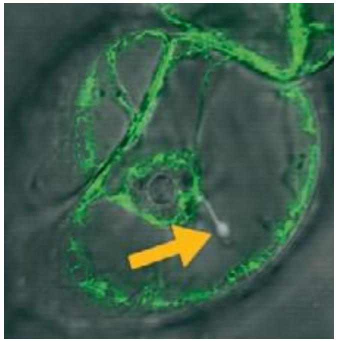


What objects I can trap?

- Polystyrene beads (p. ex.: Polysciences: Polybead®Microspheres 4.50µm)
- Silica beads
- Biological cells



- Intracellular vacuoles
- Others ...



mmi CellManipulator Movie

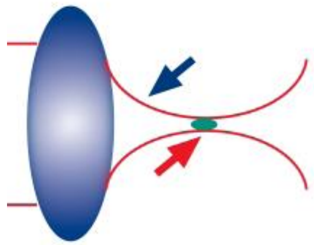
Seeing:

two-photon microscopy

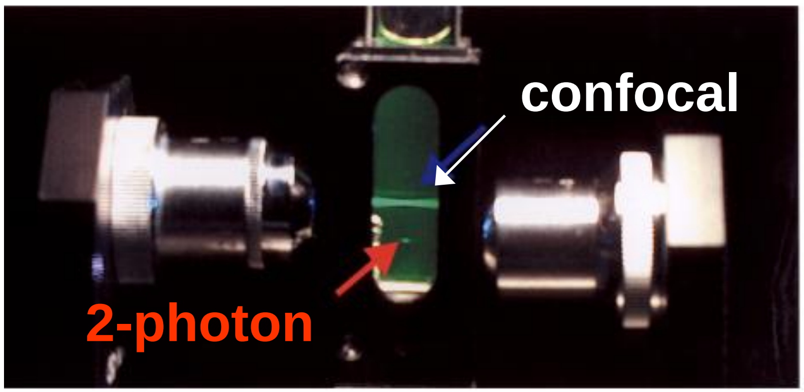
Two-Photon Microscopy (nonlinear imaging)

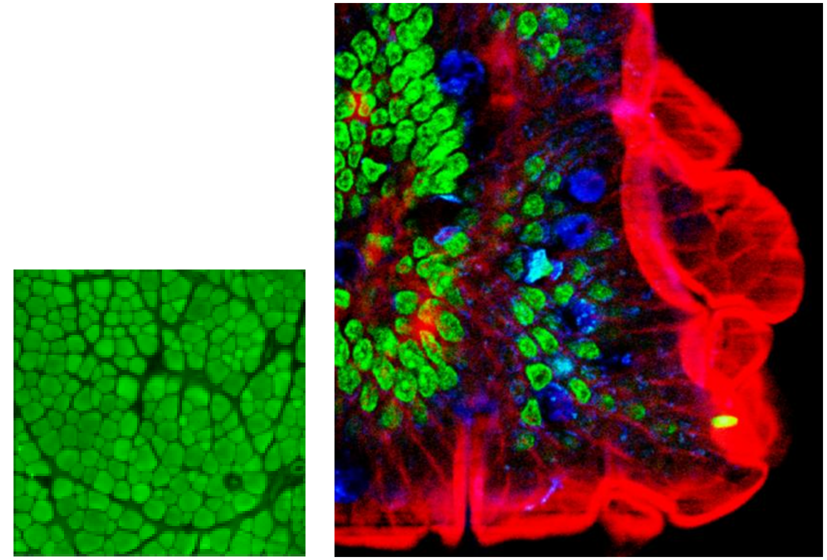
- **Two photons of "long-wavelength" light (typically near infrared) are absorbed to create one fluorescent signal photon at visible wavelengths (half the wavelength of the excitation photons)**
- **Using infrared light minimizes scattering in the tissue**
- **The background signal is strongly suppressed compared to confocal microscopy**
- **These effects lead to an increased penetration depth**
- **Re-constructing multiple scanned imaging planes can give high-resolution 3-D images**
- **Two-photon excitation can better imaging than confocal microscopy due to its deeper tissue penetration, efficient light detection and reduced phototoxicity.**

Two-Photon Microscopy Images



Excited signal confined to focus point (peak in time and intensity)



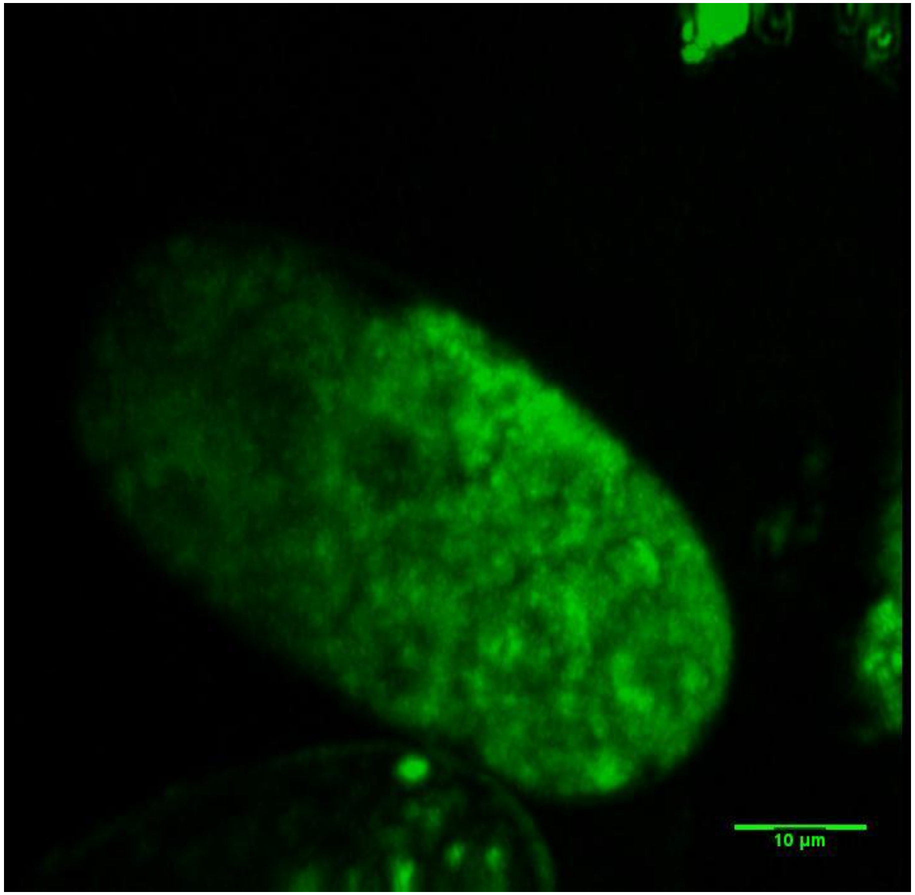


examples of 2-photon images

FOM ~ Signal ~ Peak Power * Average Power

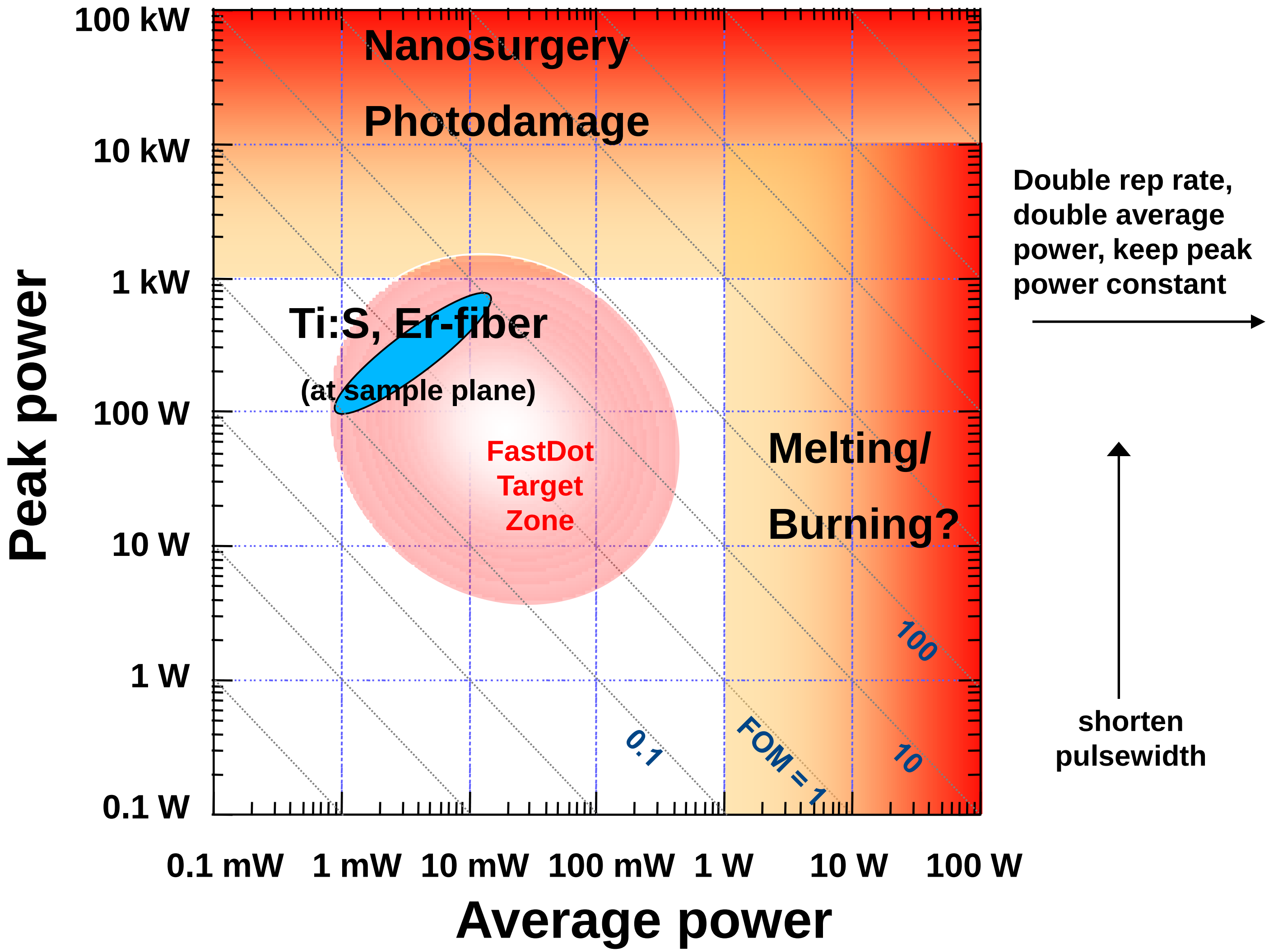
This Figure of Merit allows us to better map out lasers for biophotonics imaging, as parameters such as repetition rate and pulse width are implicitly including in this value

3D image reconstruction



C. elegans embryo 3-D reconstruction. Ten optical sections (2µm apart), each image is 700x700 points.

FOM map of laser sources



More compact, lower cost lasers for imaging

Large, fully flexible laboratory systems

Available hands-off industrial systems

Evolving to compact, optimized low-cost systems for specific applications

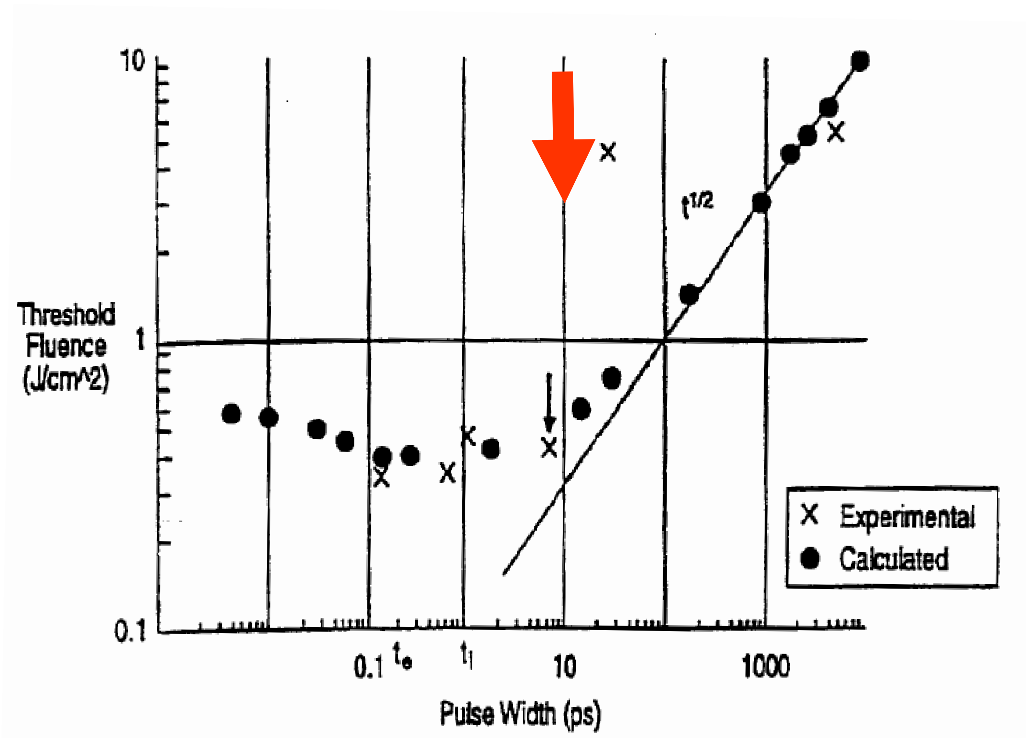
Cutting:

ultrashort pulsewidth with high peak power

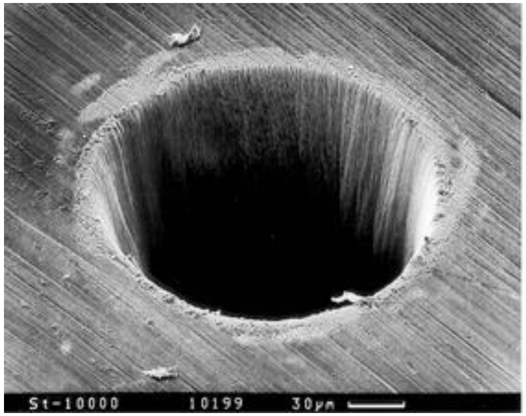
Material processing: "long" versus "short"

Picosecond to femtosecond pulses can cut through "anything" with a very low amount of heating / residual damage

"Cold ablation" starts at around 10 ps pulsewidth

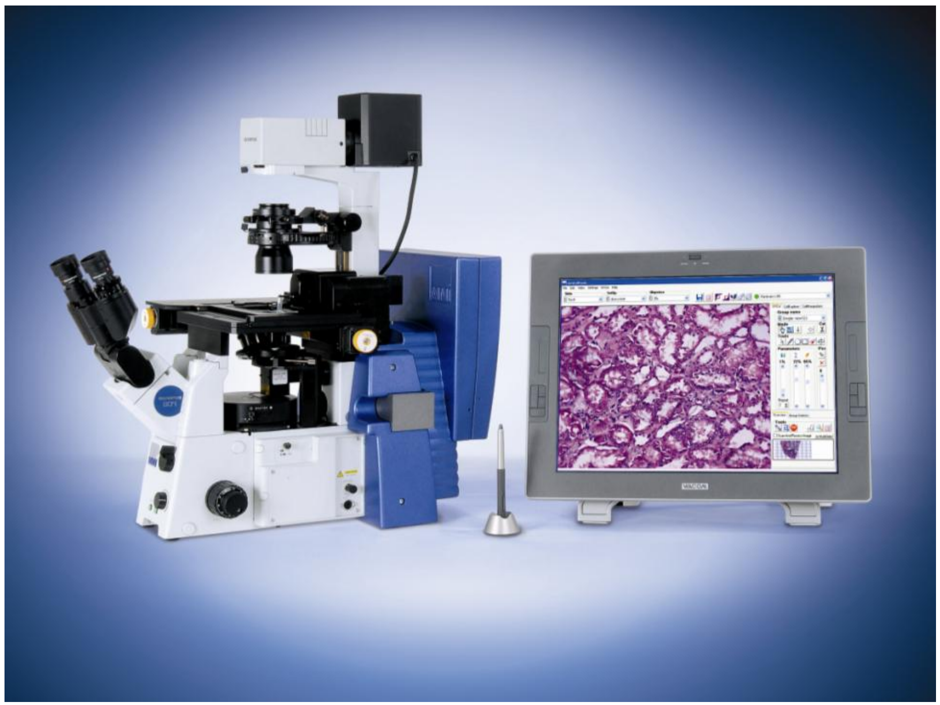


Why? Peak Power required to start ablation is reached at lower pulse energy with shorter pulses

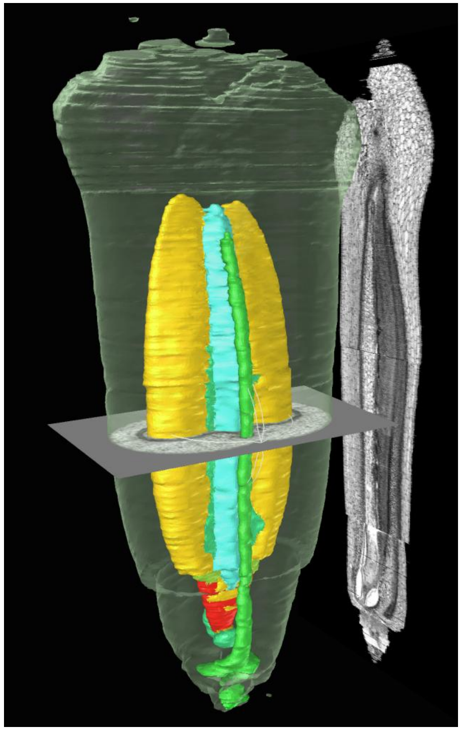


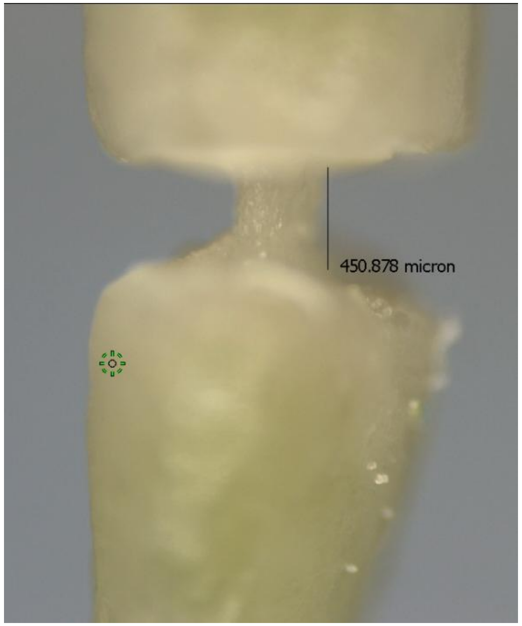
Time-Bandwidth® Products

mmi CellCut Movie



3-D laser cryo-mikrodissection of barley grains

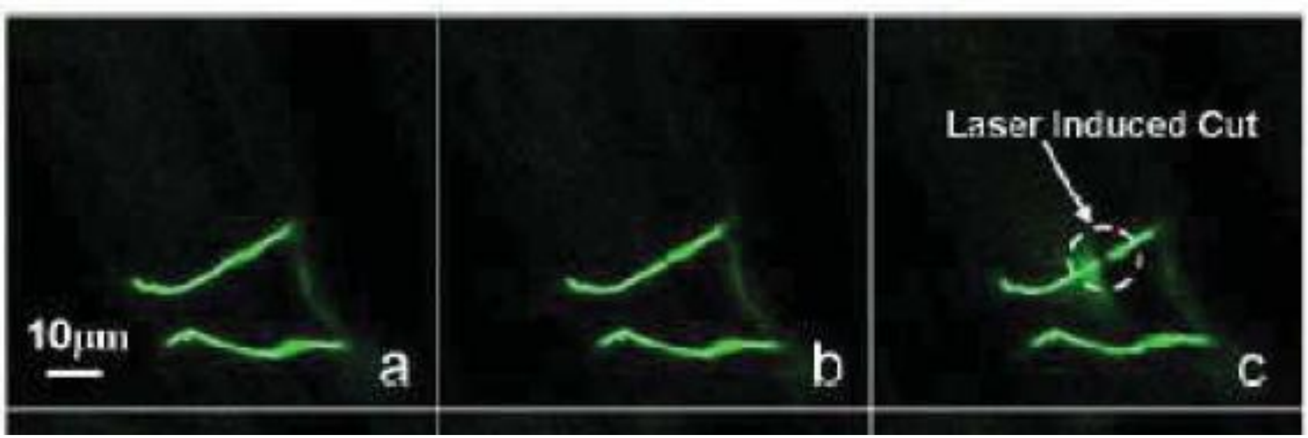




Use 3D models to select volume of interest

Sub-cellular manipulation

- **Targeted transfection (photo-perforation) for optical gene transfer**
- **Intra-cellular chromosome dissection**
- **Separation of single cells from histological sections**
- **Knock-out of cellular components**

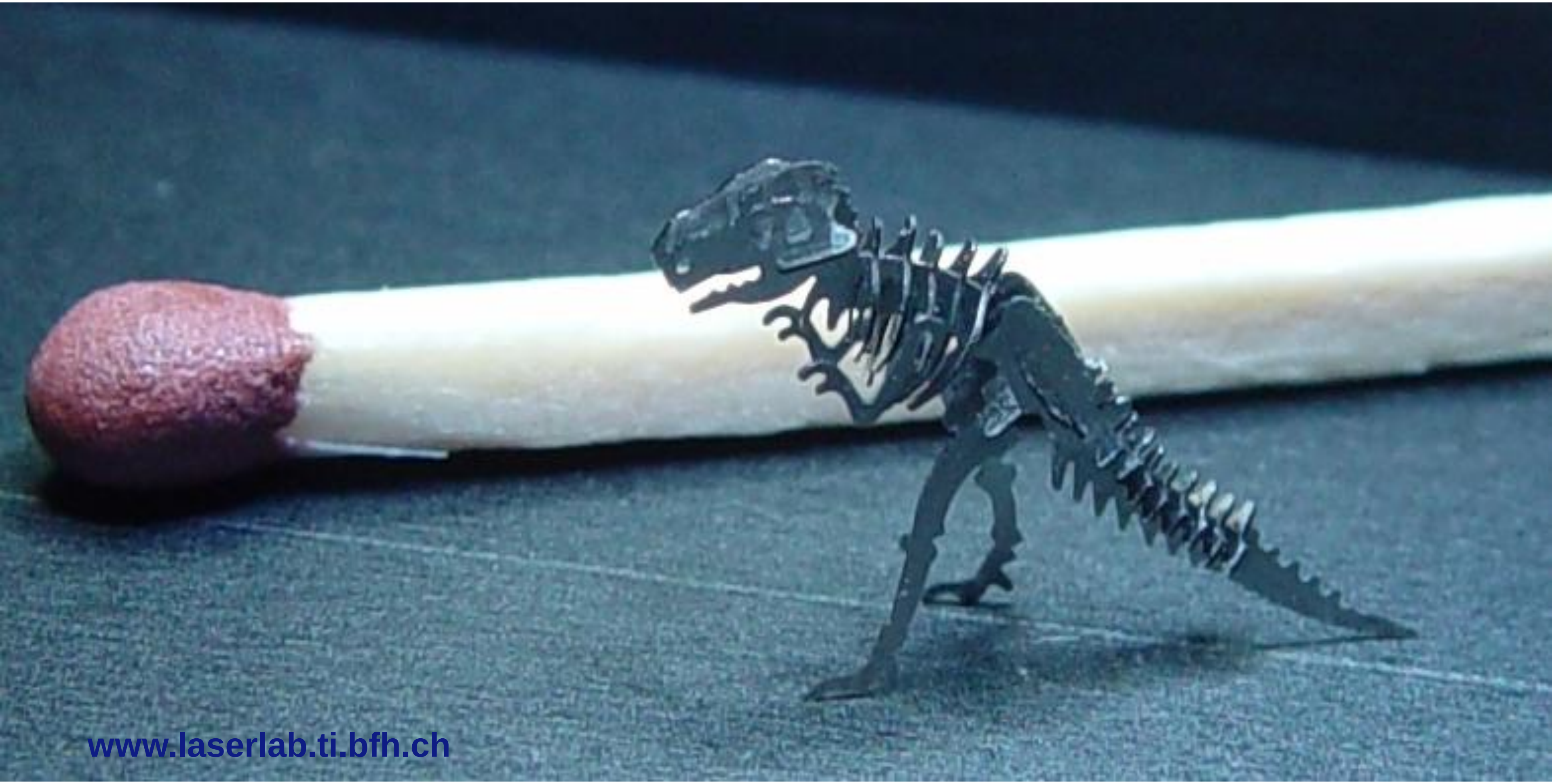


Santos et. al. 4 January 2010 / Vol. 18, No. 1 / OPTICS EXPRESS 364

Summary

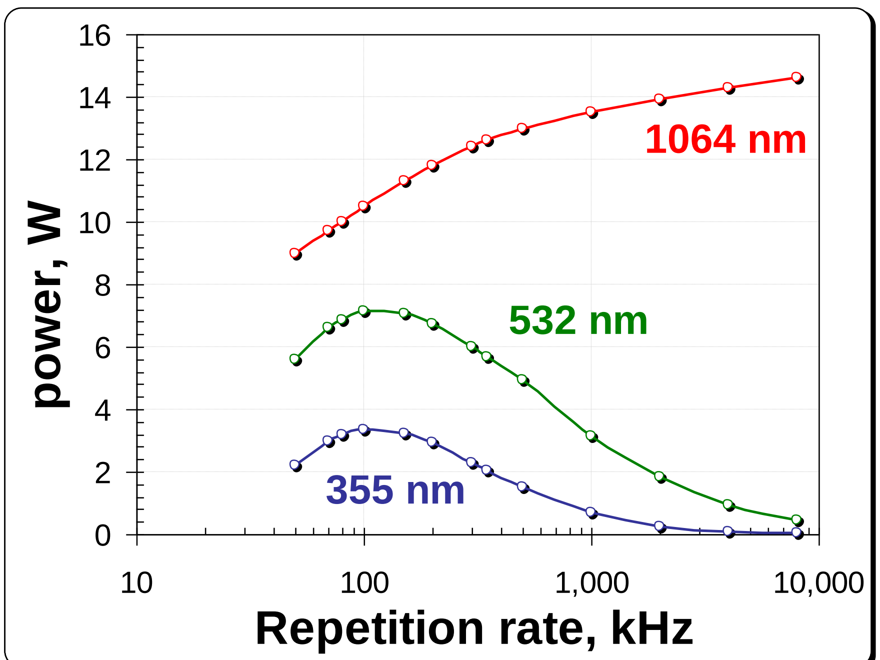
- **There are many commercial and laboratory techniques today to use a laser to**
  1) **move**
  2) **image**
  3) **cut**
- **However, an optimized high-repetition rate ultrafast laser could be used as optical tweezers, as precision sources for nonlinear microscopy, and for cellular nanosurgery, allowing one source to replace all of the above for specialized applications**

Many thanks for your attention!

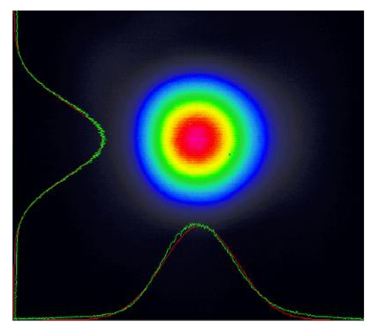


www.laserlab.ti.bfh.ch

DUETTO - key performance parameters



output power	> 10 W
repetition rate	50 kHz – 8 MHz
pulse energy	up to 200 µJ
pulse width	10 ps
peak power	up to 20 MW
wavelength	1064 nm
M^2 (TEM_{00})	< 1.3



Applications

- **Metals**
  - very thin (thin-film)
  - precision holes (sub-100 μm)
  - surface feature structuring / tribology
- **Ceramics**
  - precision cutting / structuring without cracking (resulting in low-yields)
- **Semiconductor / Photovoltaic**
  - hole / via drilling
  - ablative processes / structures
  - singulation
- **Dielectric**
  - structuring
  - selective ablation
  - hard dielectrics like sapphire and diamond
  - glass welding
- **"Mixed" materials**
  - picosecond (IR or UV) can cleanly cut / ablate through combinations of the above materials
  - semiconductor: low-k coated chips
  - solar: thin-film technologies (CIGS, CdTe, etc)
  - medical: coated stents
  - etc, etc.

Other applications

- Analysis
  - Wafer inspection, Multi-photon microscopy, CARS, FLIM
- Medical applications
  - Ophthalmology, Laser dissection
- Metrology
  - Optical clocking, Optical sampling, Laser ranging
- Optical communication
  - Special high-performance data transmission
- Wavelength conversion
  - Visible / UV wavelengths, optical parametric oscillators, THz generation
- High-Energy Physics
  - Photocathode illumination, EUV & X-ray generation

Using 3D models to select the volume of interest