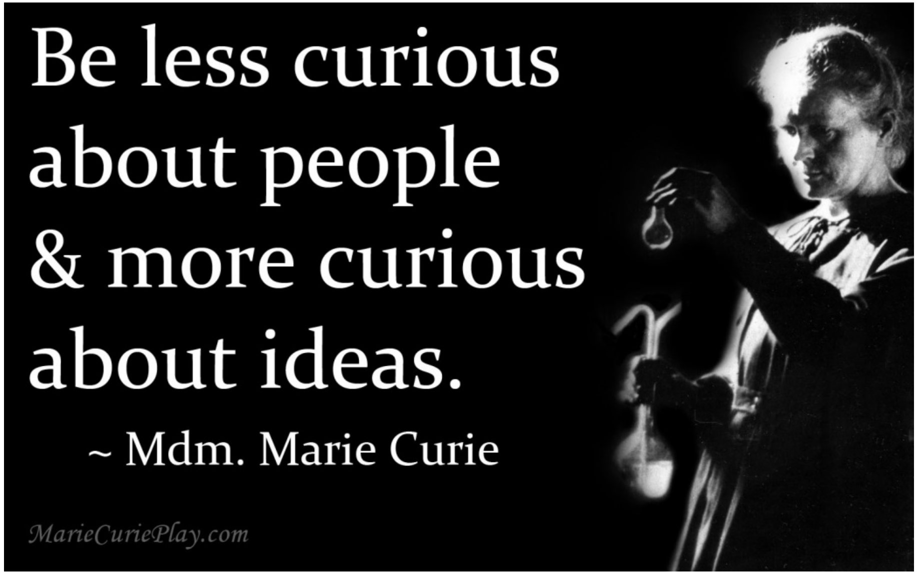
Femtosecond laser: From frequency combs to Deep Brain Imaging

An alternative career path in Photonics

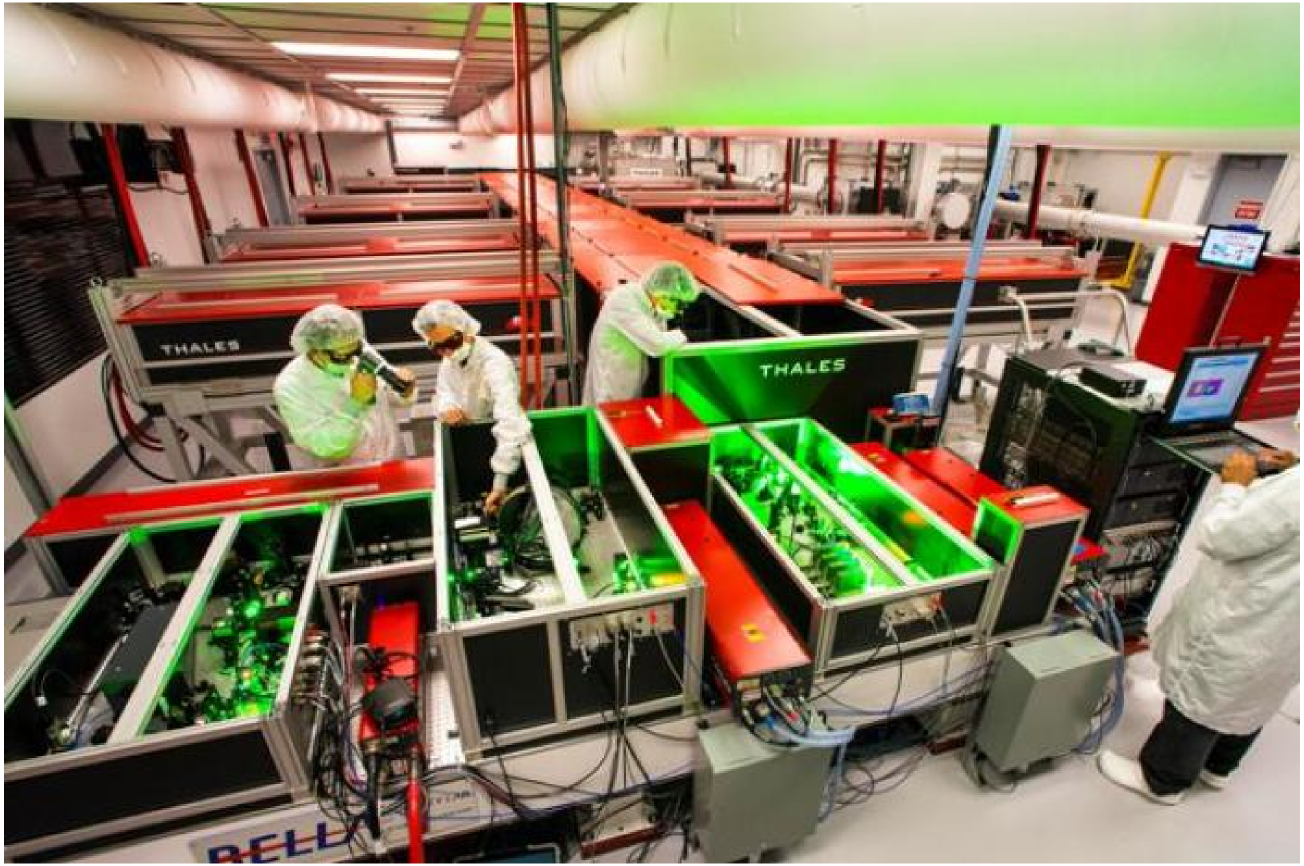
Peter Fendel

What is he going to talk about??

- Brief history of Ti:Sa
- Precision Spectroscopy
- Exo-planet search
- Two Photon Imaging



Ti:Sa lasers – A remarkable success story in just 25 years



Bella Peta Watt Laser System @ LBL: >40 J, < 30 fs

History of Ti:Sa-Laser:

Peter F. Moulton Lincoln Labs MIT: Spectroscopic and Laser Characteristics of Ti-Al2O3, JOSA B 1986

Wilson Sibbet St Andrews: Sub-100fs Pulse Generation from A Self-Modelcoked Ti:Sa Laser, CLEO 1990

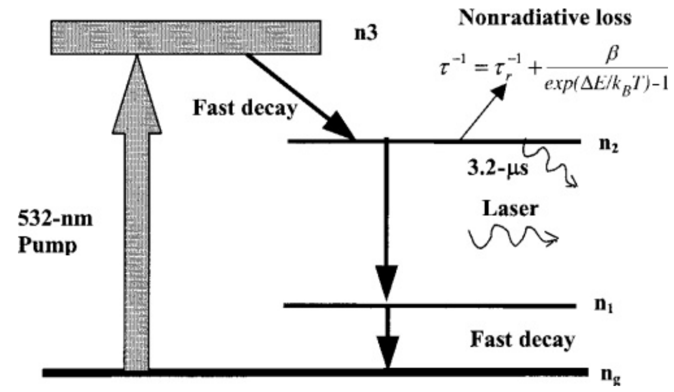
Ti:Sa – The 'god given' laser material

Sapphire (Al_2O_3) is an important substrate in the LED and consumer electronic industry and can be grown by three techniques:

- Czochralski growth
- Heat exchanger method (HEM)
- Kyropoulos technique

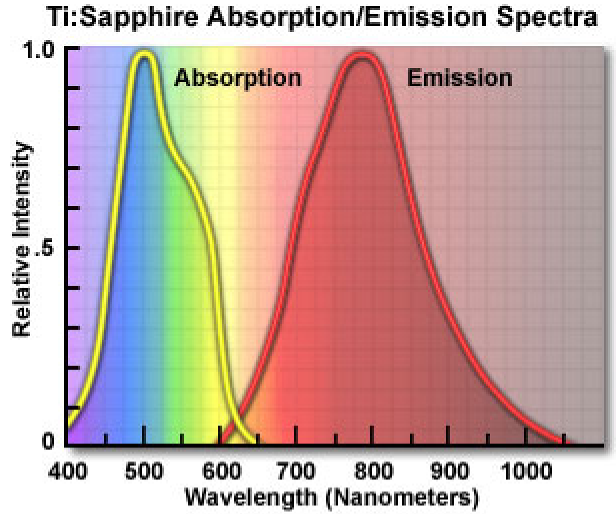
Apple consumes 1/4 of the world's supply of sapphire to cover the iPhone's camera lens and fingerprint reader

Ti:Sa – The 'god given' laser material



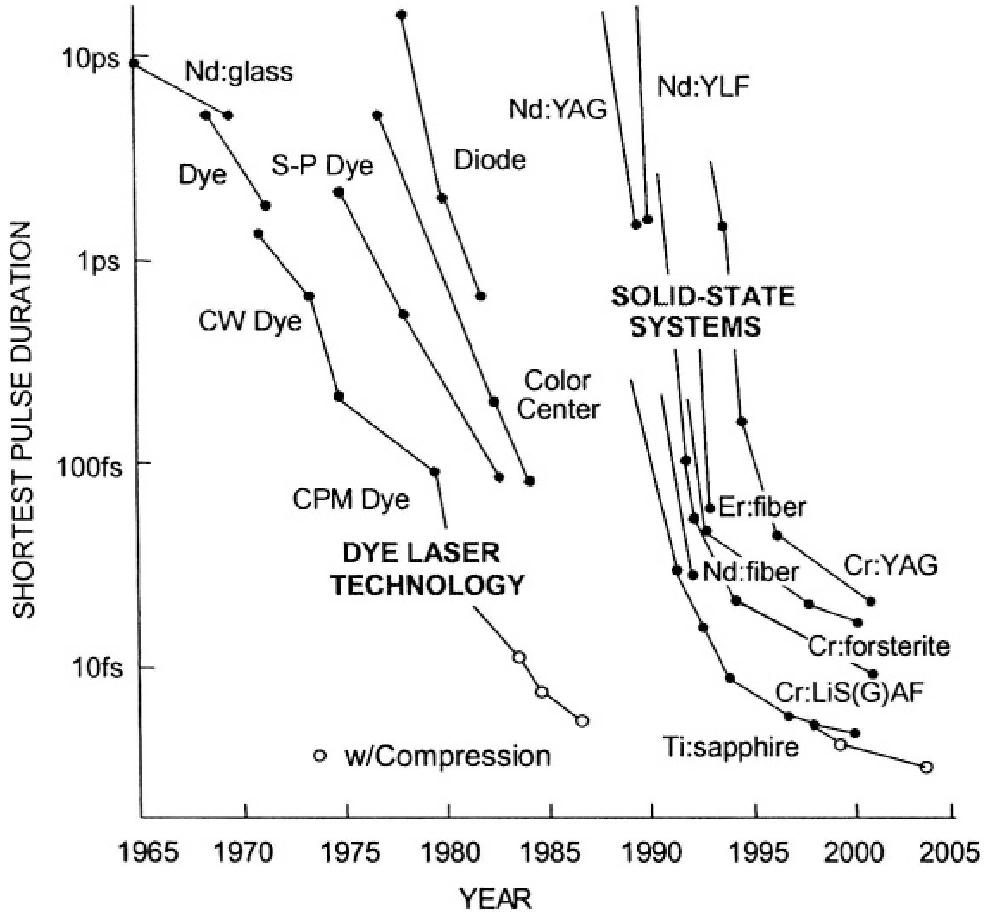
Important properties as a laser material:

- Mohs hardness: 9
- Thermal Conductivity: 33 W /(m K)
- Upper State lifetime 3.2 us
- >400 nm of Gain Bandwidth
- Non-linear refractive index: 3 x 10^16 cm2 /W



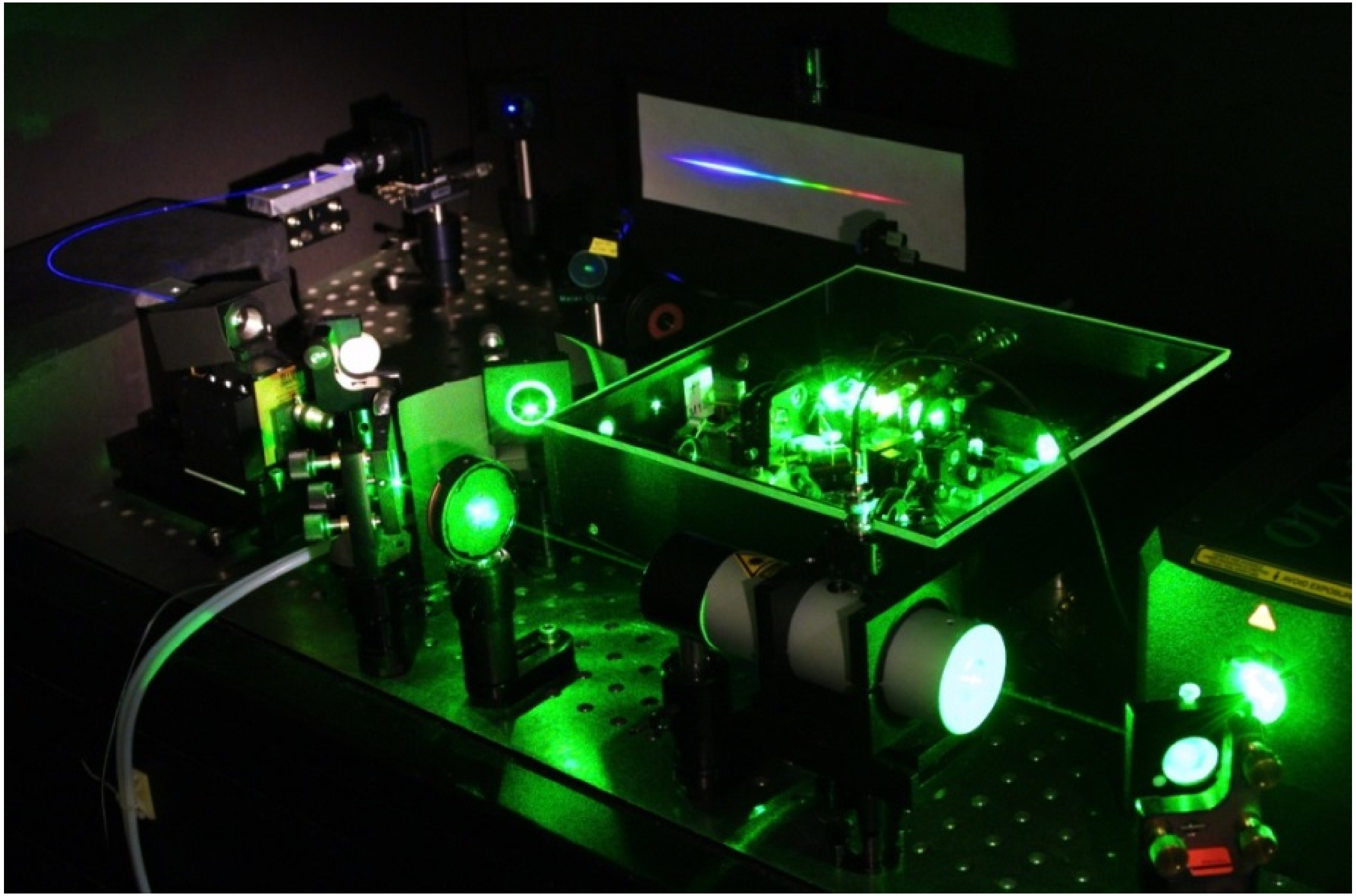
6 fs Ti:Sa Output spectrum

Ti:Sa – History of Short Pulse lasers



Courtesy of F. Kärtner

Frequency Combs and Precision Spectroscopy



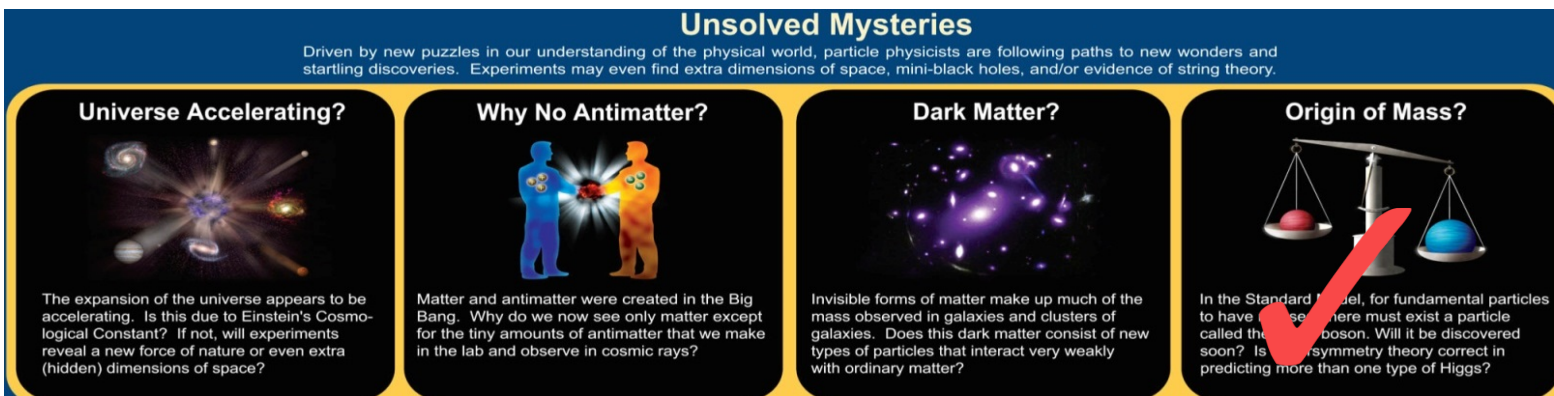
Why precision spectroscopy?

Our understanding of physics is based on the Standard Model. Extremely successful since the late 1960-ties

Properties of the Interactions

The strengths of the interactions (forces) are shown relative to the strength of the electromagnetic force for two u quarks separated by the specified distances.

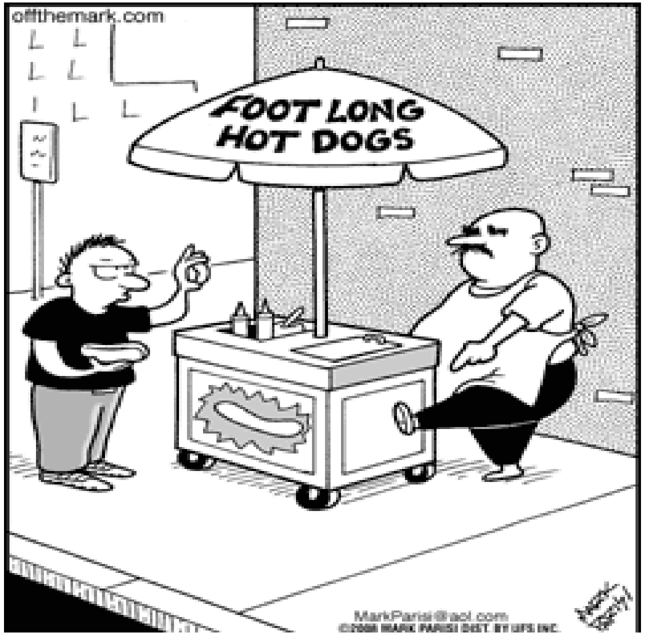
Property	Gravitational Interaction	Weak Interaction (Electroweak)	Electromagnetic Interaction (Electroweak)	Strong Interaction
Acts on:	Mass – Energy	Flavor	Electric Charge	Color Charge
Particles experiencing:	All	Quarks, Leptons	Electrically Charged	Quarks, Gluons
Particles mediating:	Graviton (not yet observed)	W^+ W^- Z^0	γ	Gluons
Strength at 10^{-18} m	10^{-41}	0.8	1	25
Strength at 3×10^{-17} m	10^{-41}	10^{-4}	1	60



Why precision spectroscopy?

In fundamental science researchers test our understanding of nature by comparing predictions from current theories with measured data.

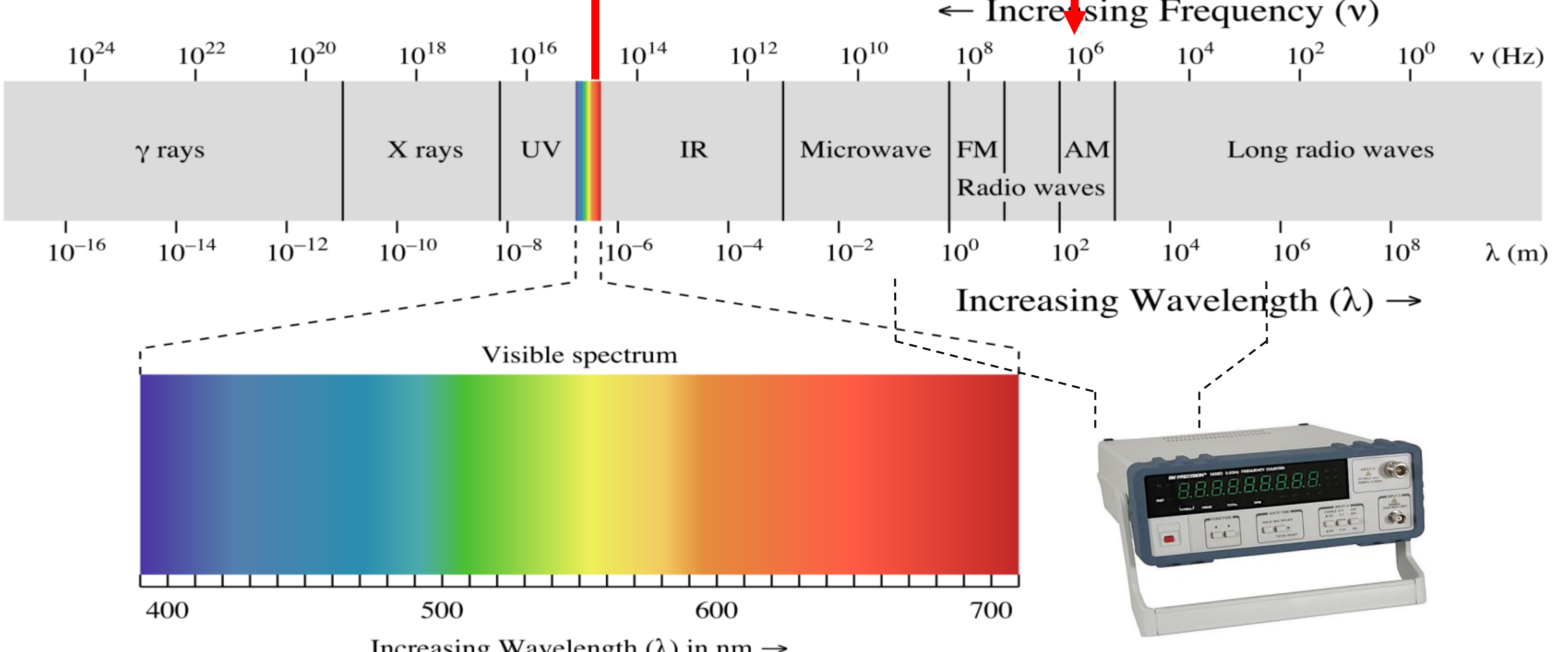
Wiki: ***Measurement*** *is the process or the result of determining the ratio of a physical quantity, such as a length, time, temperature etc., to a unit of measurement, such as the meter, second or degree Celsius. The science of measurement is called metrology.*



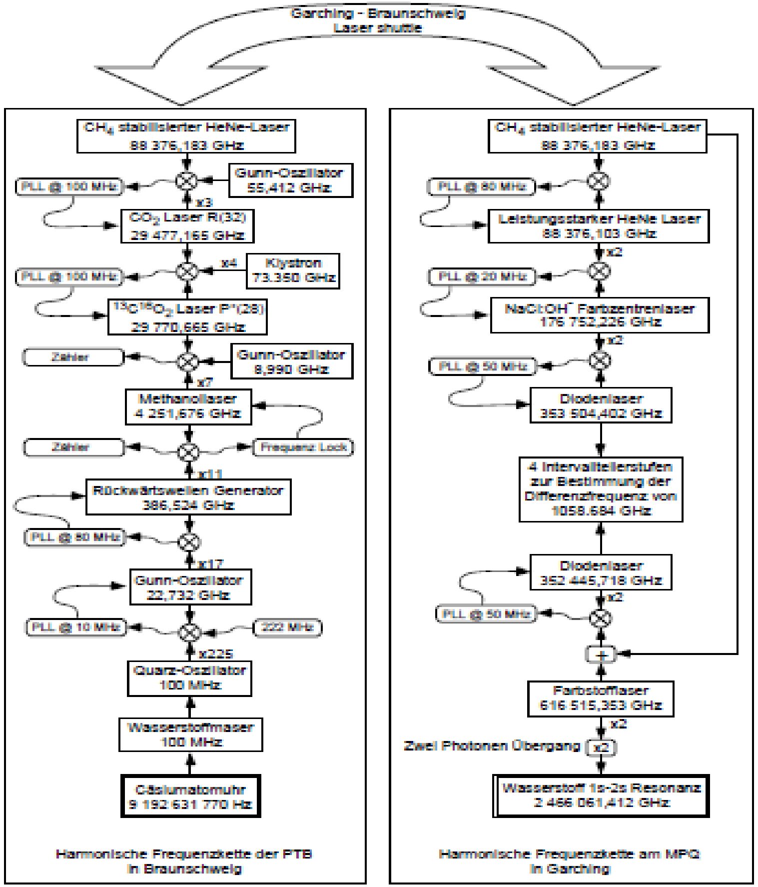
Time intervals and therefore frequencies are measurable with the highest possible accuracy and therefore a great candidate to test fundamental theories.

How are optical frequencies measured?

Optical Clockwork needs to bridge
6 orders of magnitude

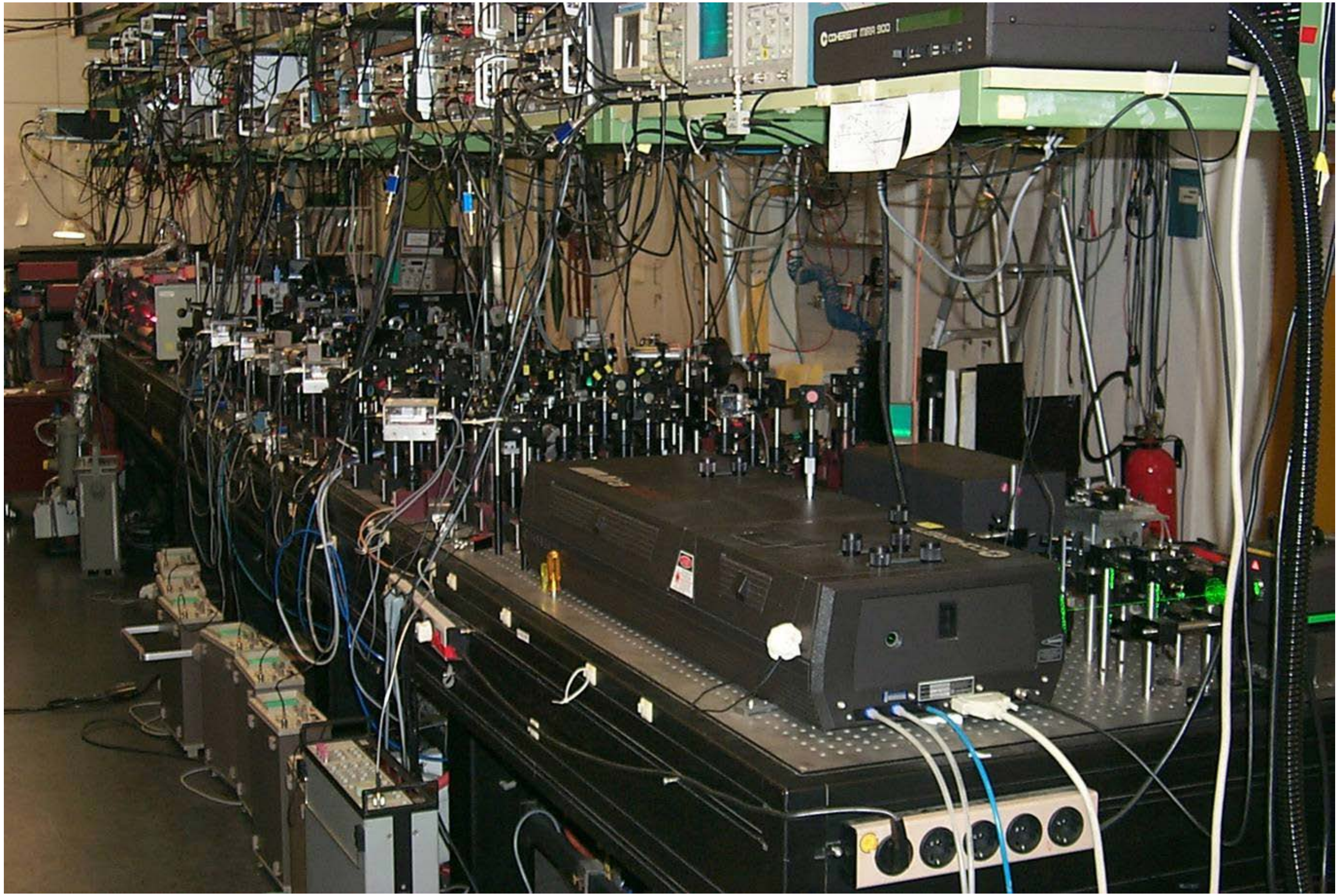


Optical Clockwork prior to Frequency combs

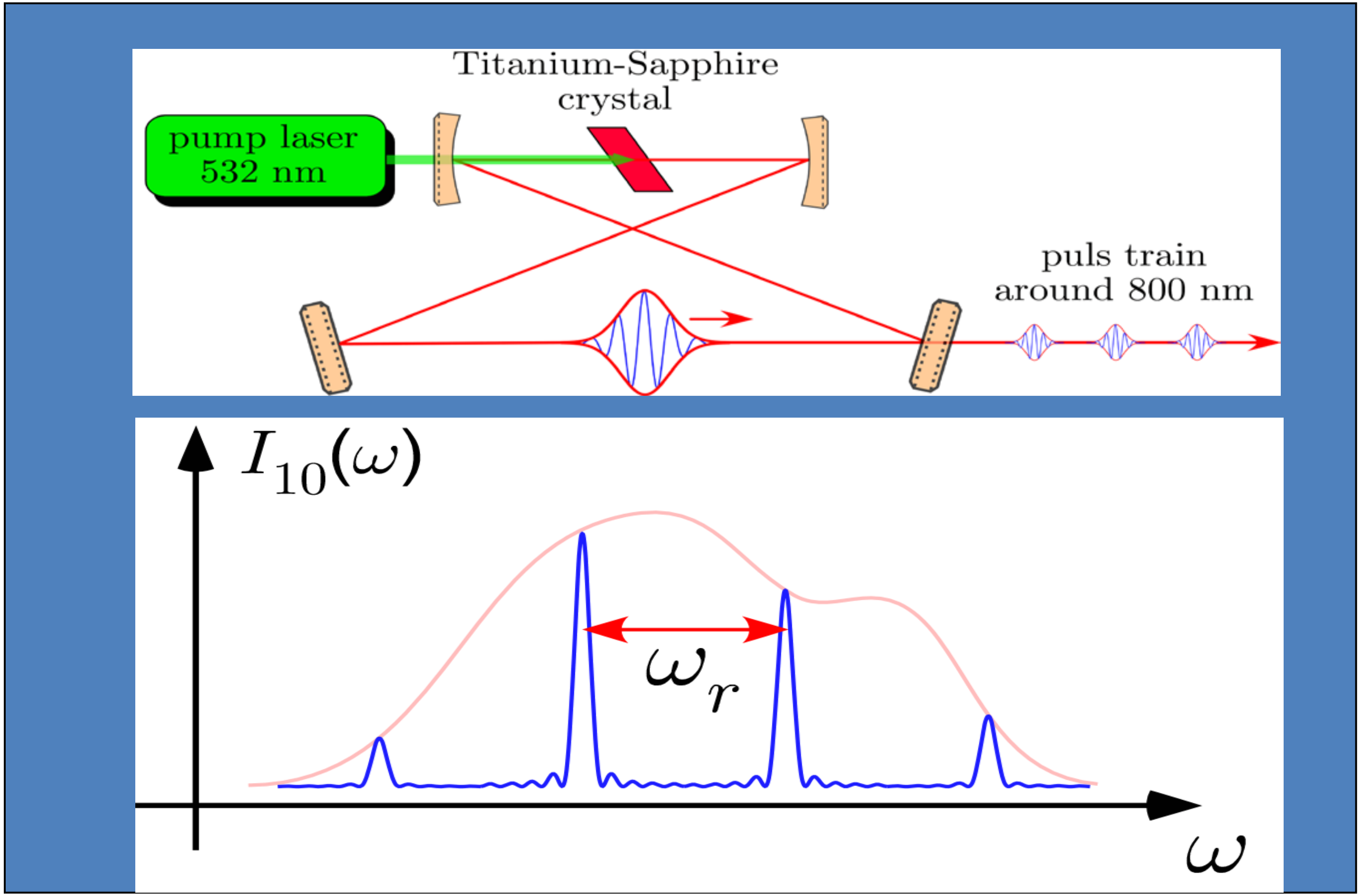


- 9 phase lock loops
- 1 frequency lock
- 14 local oscillators
- 4 optical frequency interval divider setups

Frequency Chain at MPQ in Garching

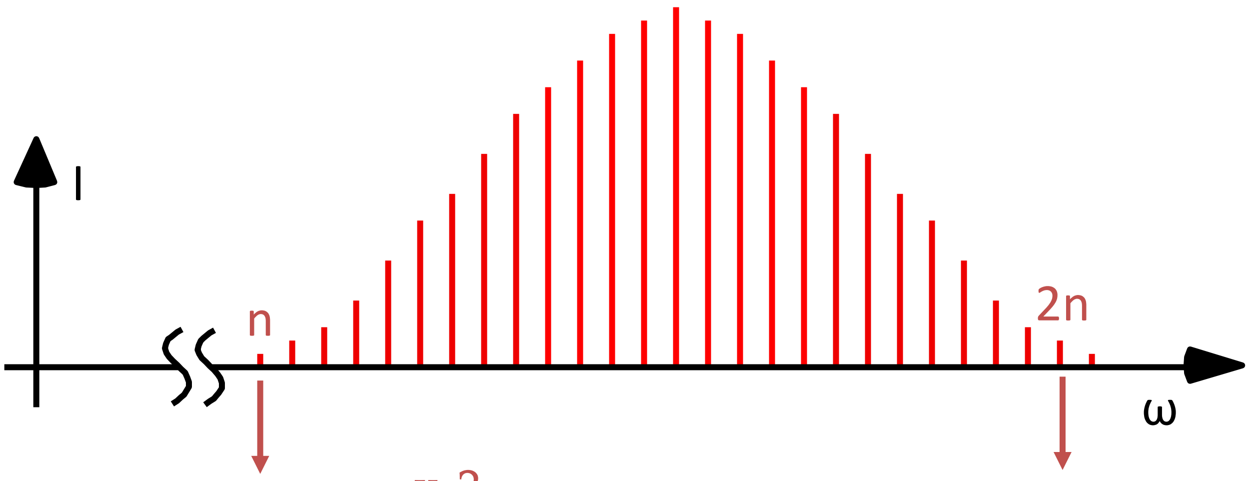


The frequency comb



The frequency comb

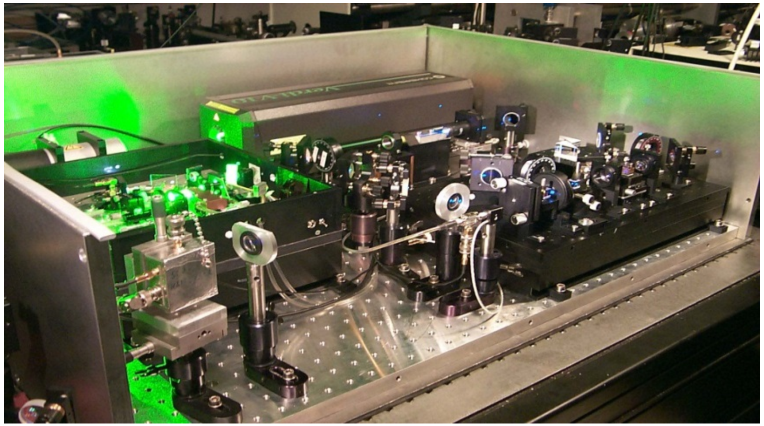
It is simple to detect ω_{CE} of an octave wide frequency comb:



$\omega_{rep} + \omega_{CE}$ —x 2→ $2(\omega_{rep} + \omega_{CE})$ − $2n\omega_{rep} + \omega_{CE}$

$$\omega_{CE} = 2(\omega_{rep} + \omega_{CE}) - (2n\,\omega_{rep} + \omega_{CE})$$

Implementations of frequency combs



Original 800 MHz Ti:sapphire ring laser based frequency comb

Commercial Er-doped fiber laser based frequency comb 2016

Take away messages:

- Replaces large and complex laser harmonic frequency chains.
- One system to measure virtually any optical frequency.

Hydrogen Spectroscpoy

"To understand Hydrogen is to understand all of Physics"

Viktor Weiskopf

Fraunhofer, Balmer, Bohr, Schrödinger, Dirac, Lamb, Feynman,…

were inspired by the hydrogen spectrum to develop "new physics"

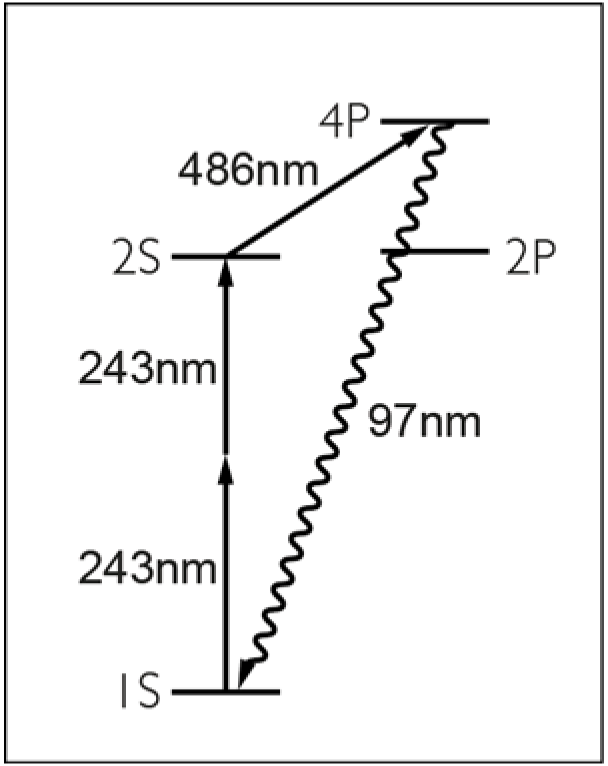
The Energy levels are given by:

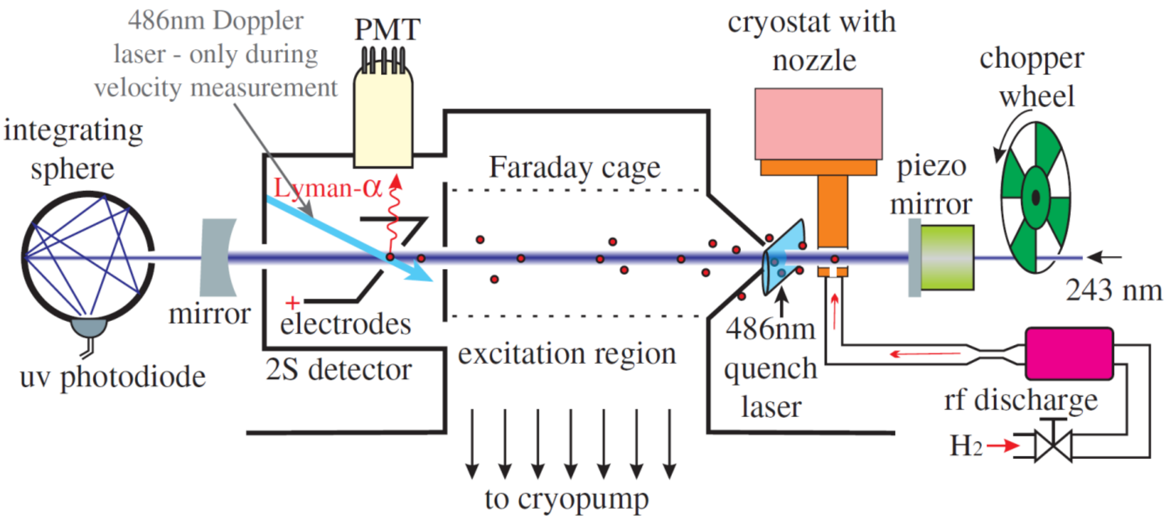
$$\begin{aligned} E = {} & R_\infty E_{\mathrm{DR}}(n,j) \\ & + E_{\mathrm{HFS}}(n,j,l,F) \\ & + L(n,j,l) \end{aligned}$$

We can learn something about:

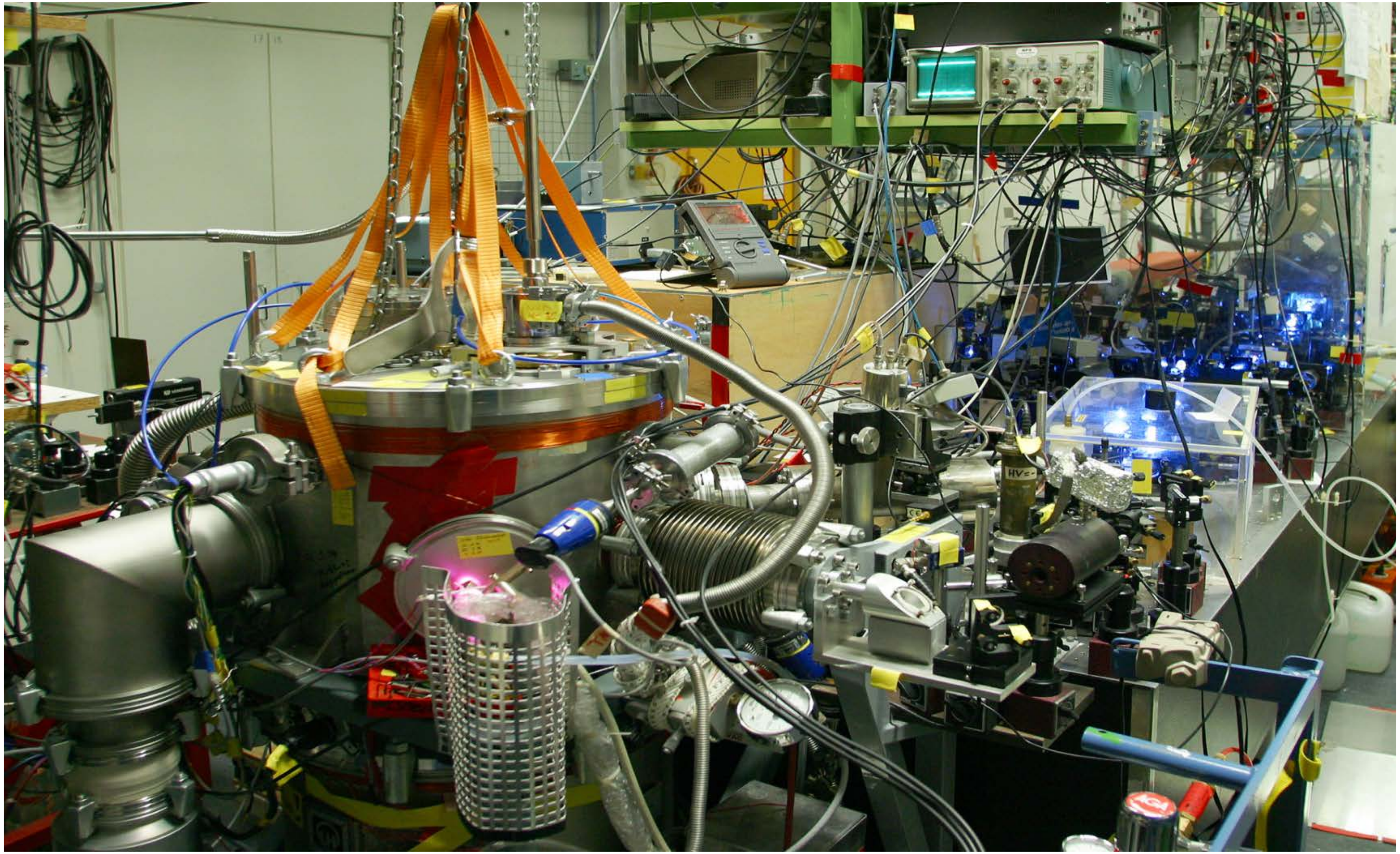
- QED
- QCD

Hydrogen Spectroscopy setup

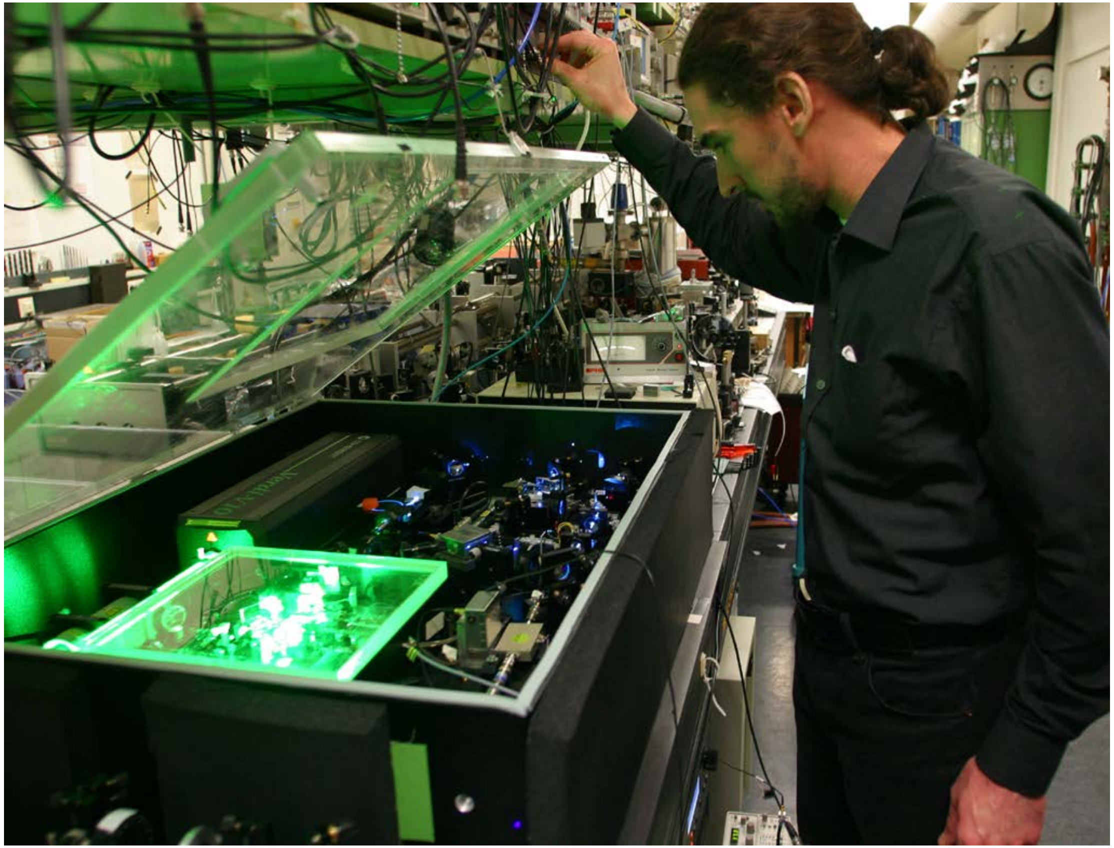




Hydrogen spectroscopy setup



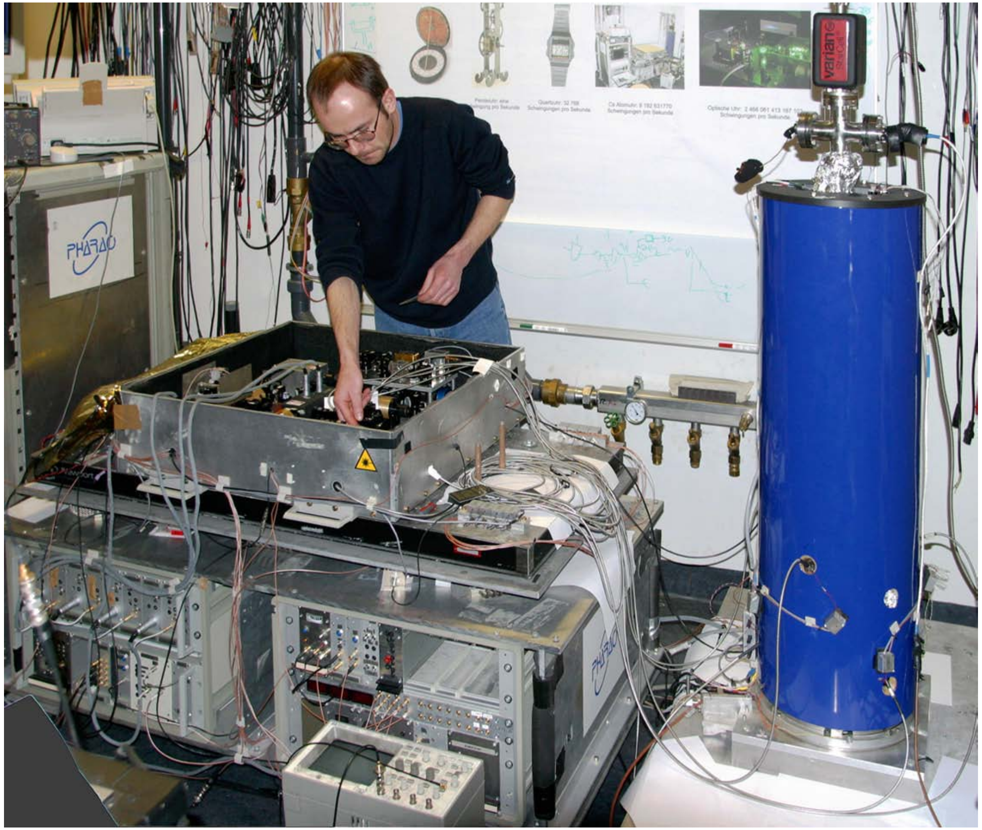
Optical Clockwork: Frequency comb



Marcus Zimmermann

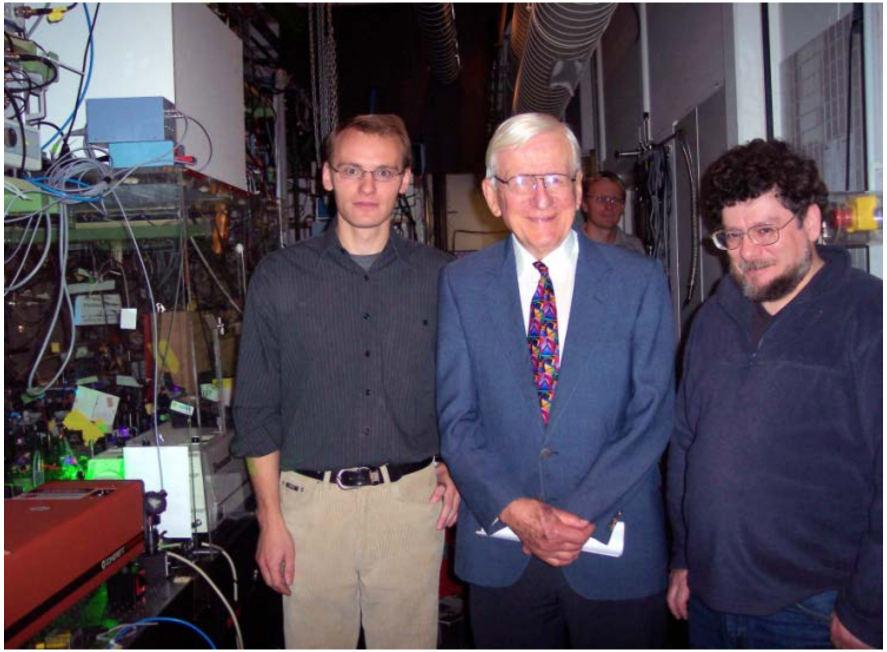
Cs-Frequency Standard:

PHARAO cesium fountain clock from. Collaboration with Christoph Salomon from ENS, Paris

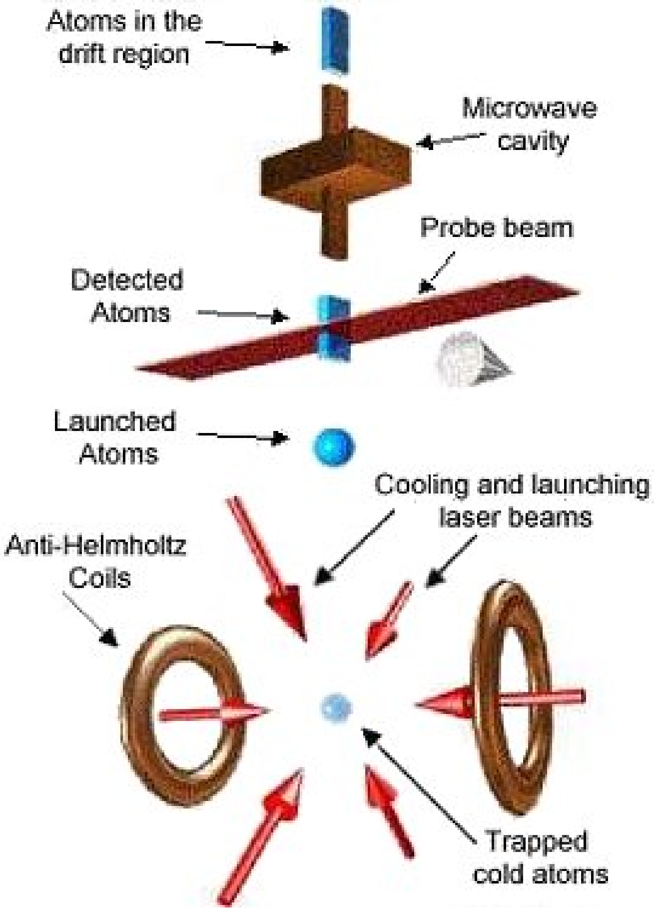


Micheal Abgrall

The Cs-fountain clock: Today's frequency standard



Norman Ramsey and Savely Karchenboim

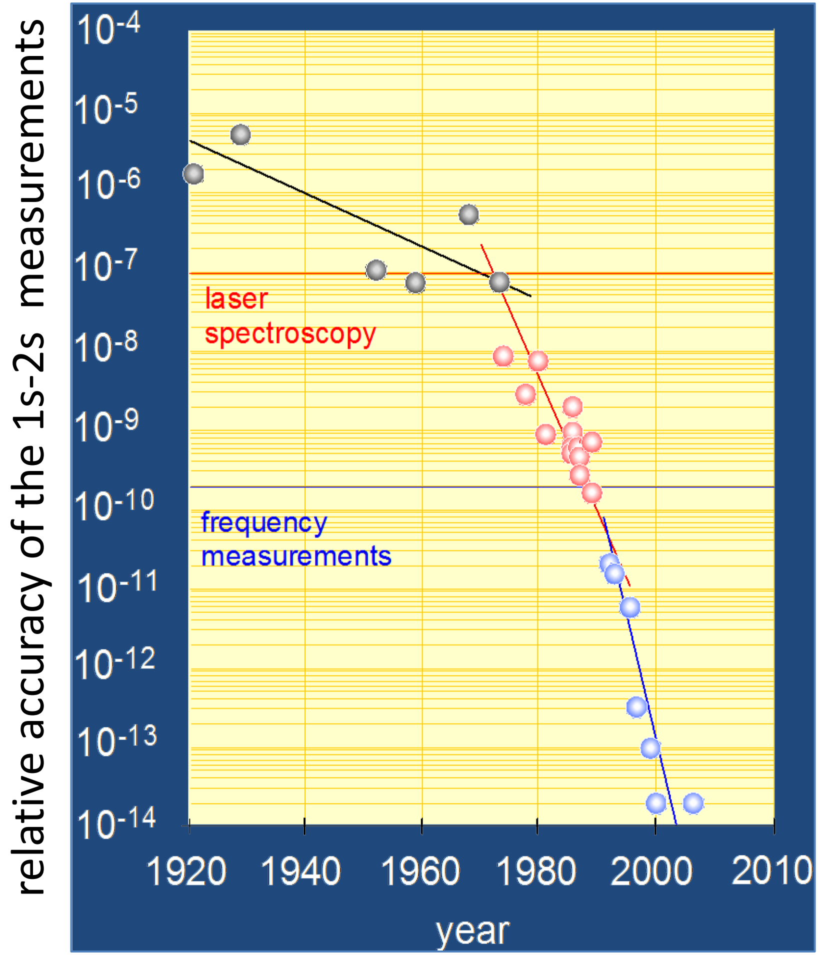


Hydrogen spectroscopy

- 1s – 2s: 4.2 x 10^{-15}
- (2s – 4s) - (1s – 2s) : 2 x 10^{-11}
- 2s-HFS: 4 x 10^{-8}

What did we learn?

- Rydberg Constant
- Lamb Shift
- Isotopic Shift
- Drift of fundamental constants
- CPT reversal theorem when compared to antihydrogen

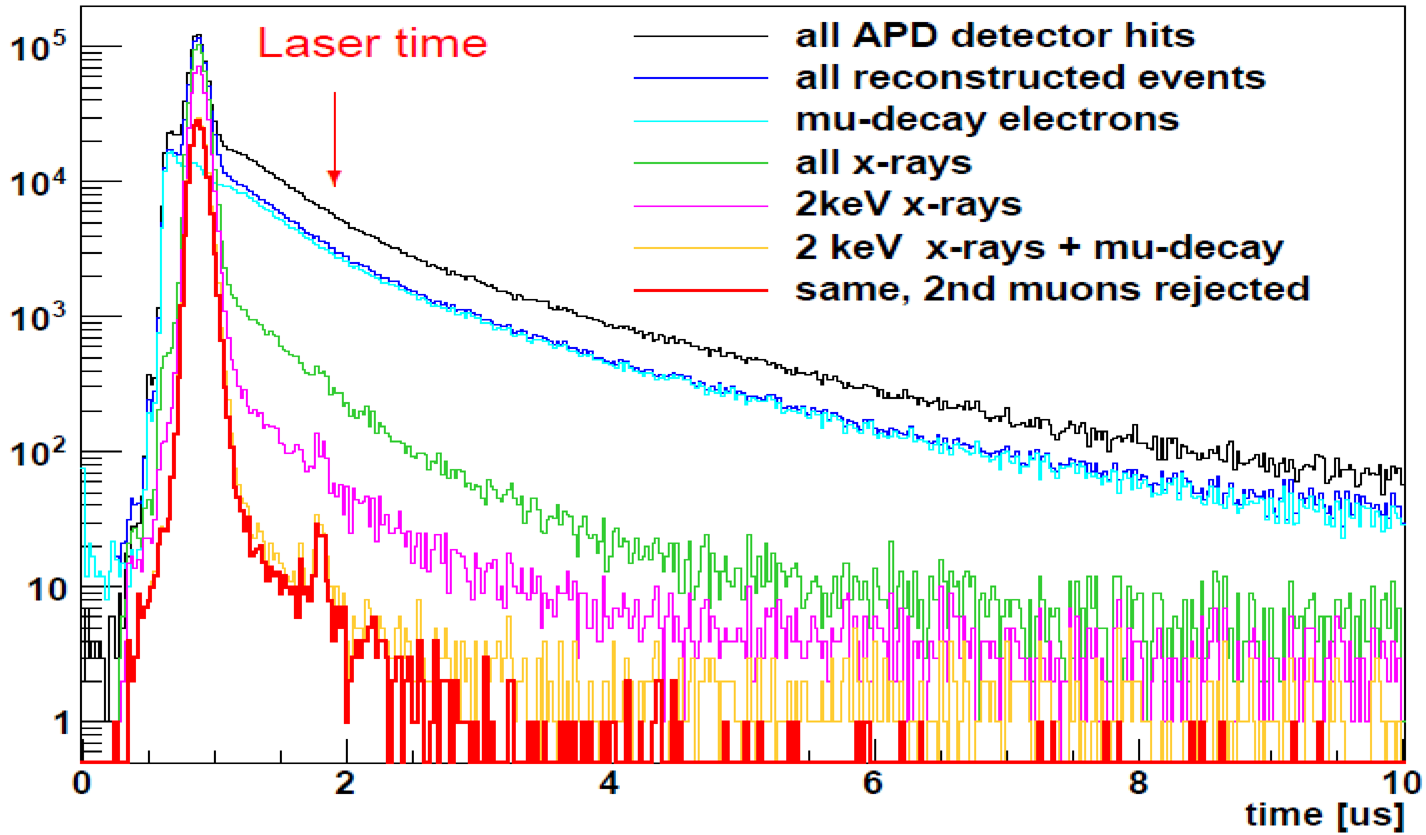


Proton Charge Radius limits currently QED-Tests: -> PSI - Experiment

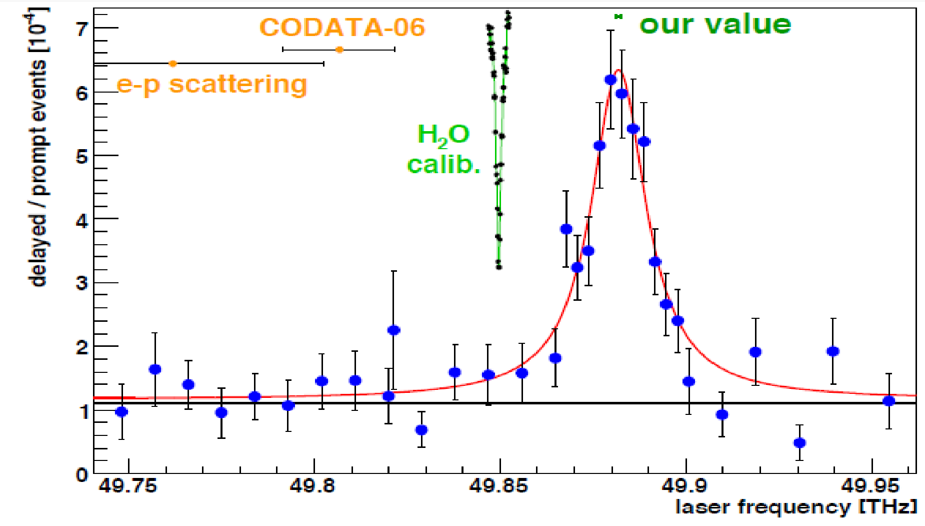
The proton charge radius

Randolf Pohl

Understanding your Experiment:
860 000 laser shots
1.56 Million detector clicks – 20 real events



The munoic hydrogen $2s_{1/2}$-$2p_{3/2}$ resonance:



Discrepancy:

$$5.0\,\sigma \;\leftrightarrow\; \sim 75\text{ GHz} \;\leftrightarrow\; \delta\nu/\nu = 1.5\times 10^{-3}$$

6 events per hour on resonance

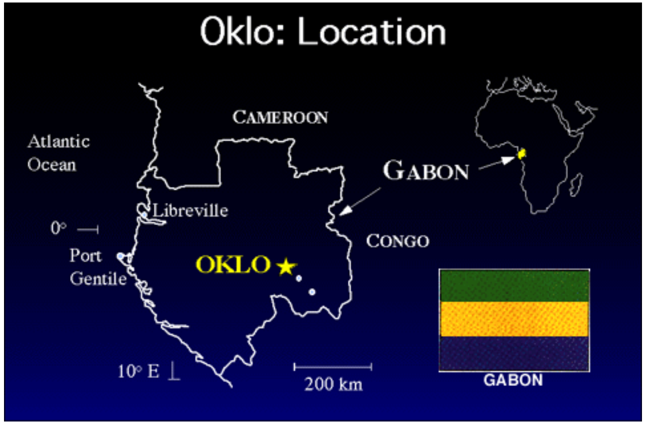
010).

Drift of fundamental constants

Natural fission $^{235}U/^{238}U$ reactor
$2{\cdot}10^9$ years ago

$$n + {}^{149}_{62}\mathrm{Sm} \rightarrow {}^{150}_{62}\mathrm{Sm} + \gamma$$

A.I. Shlyakhter, *Nature* (London), **264**, 340 (1976)



Abundance ratio:

$${}^{149}_{62}\mathrm{Sm}/{}^{147}_{62}\mathrm{Sm}$$

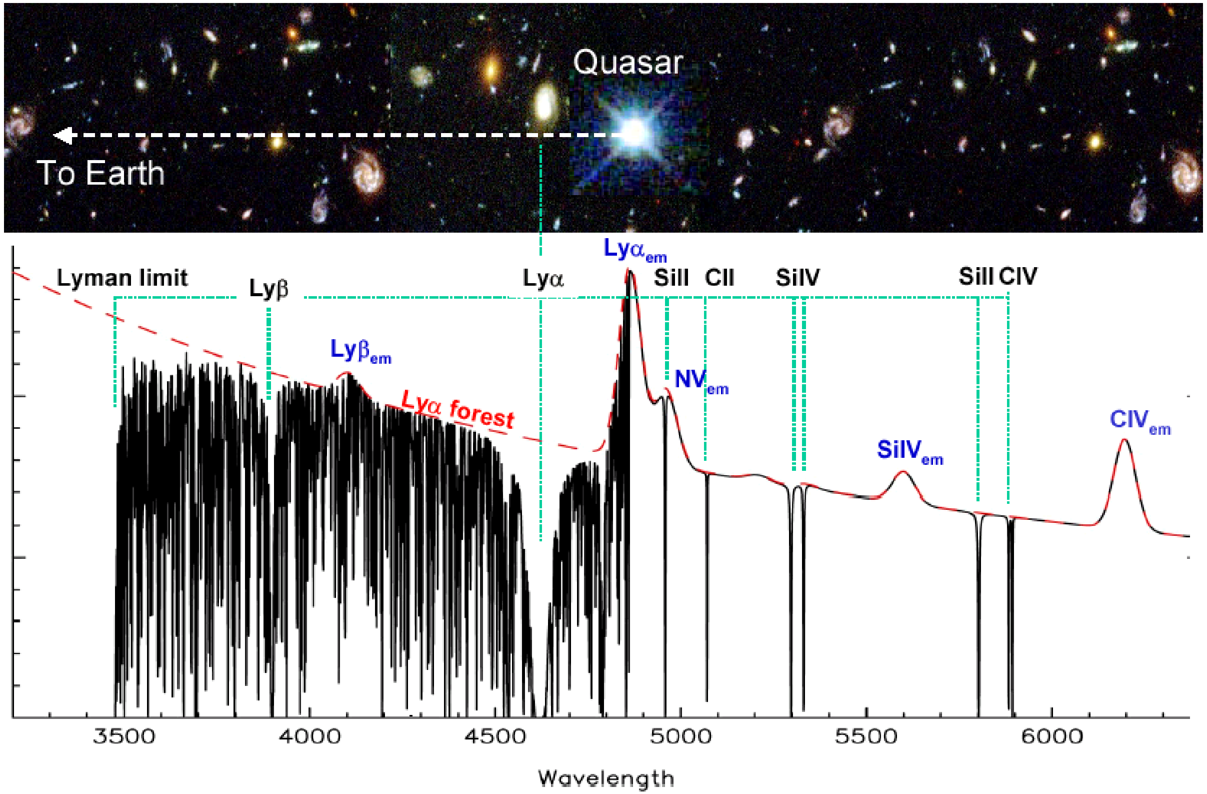
0.02 (Oklo)

0.9 (typical)

$\Delta\alpha/\alpha=(-0.36 \pm 1.44) \times 10^{-8}$

Y.Fujii *et al.*, *Nucl. Phys*. B, **573, 377 (2000)**

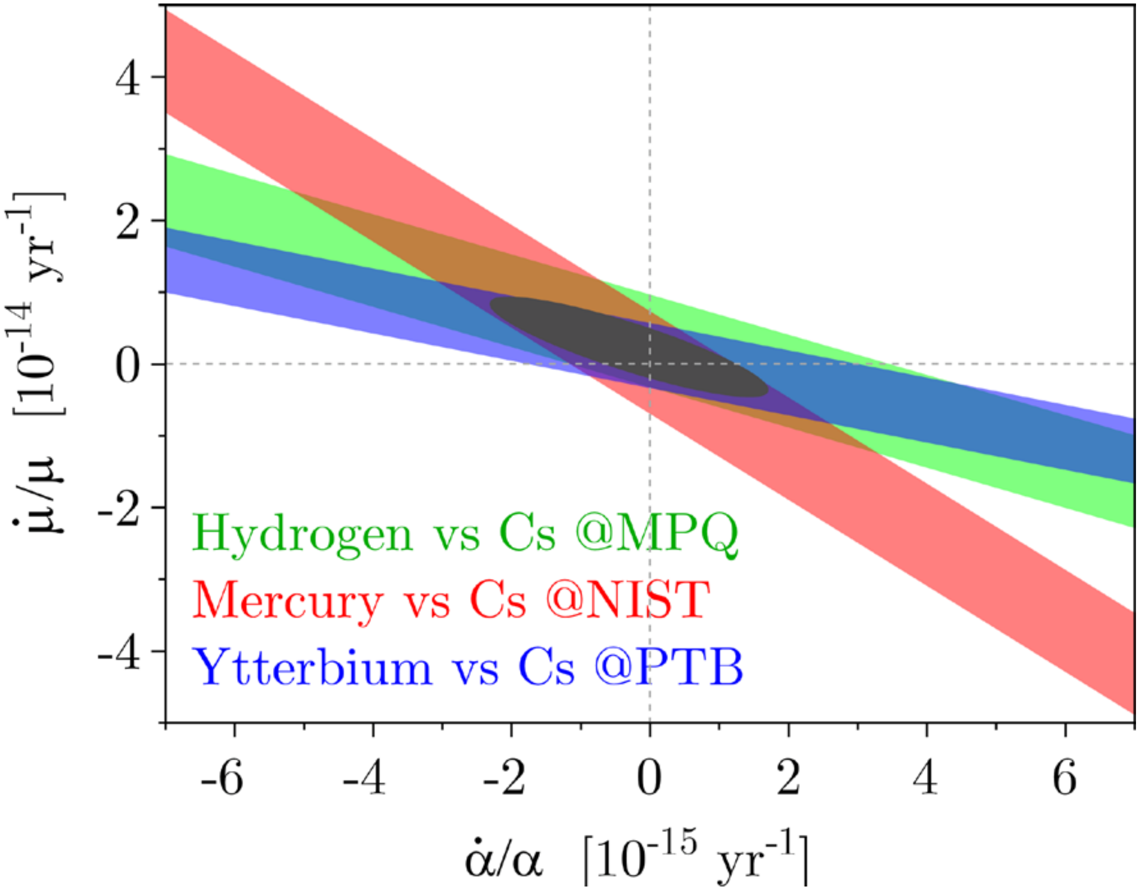
Drift of fundamental constants



J.K. Webb *et al.*, *Phys. Rev. Lett.* **87**, 091301 (2001)

$\Delta\alpha/\alpha = (-0.72 \pm 0.18) \times 10^{-5}$

Drift of fundamental constants



Fischer et al. Phys. Rev. Lett. **92**, 230802

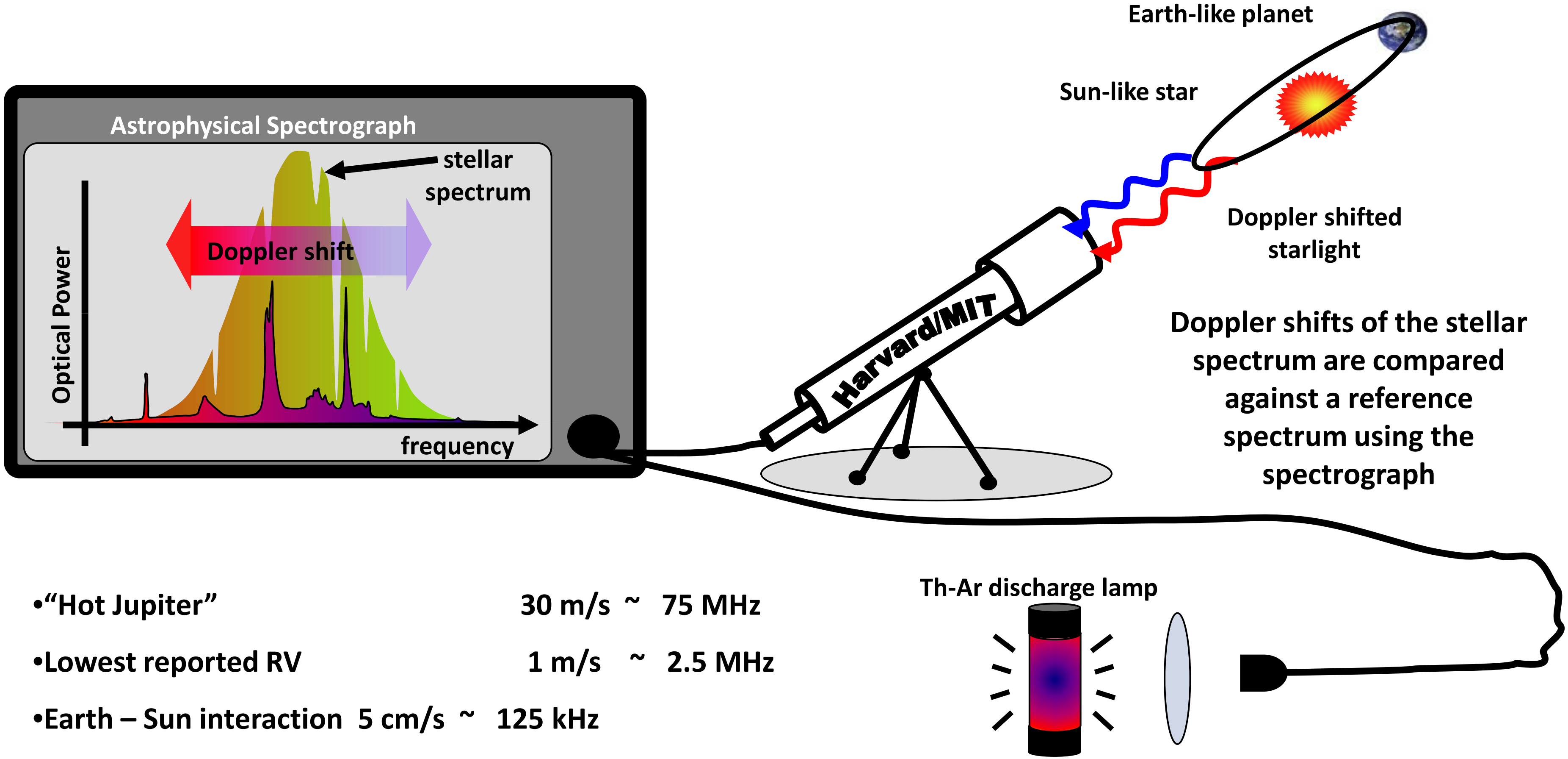
Astro-combs: Search for Exo-planets

Harvard – Smithsonian
Center for Astrophysics
60 Garden Street, Cambridge, MA 02138

MIT

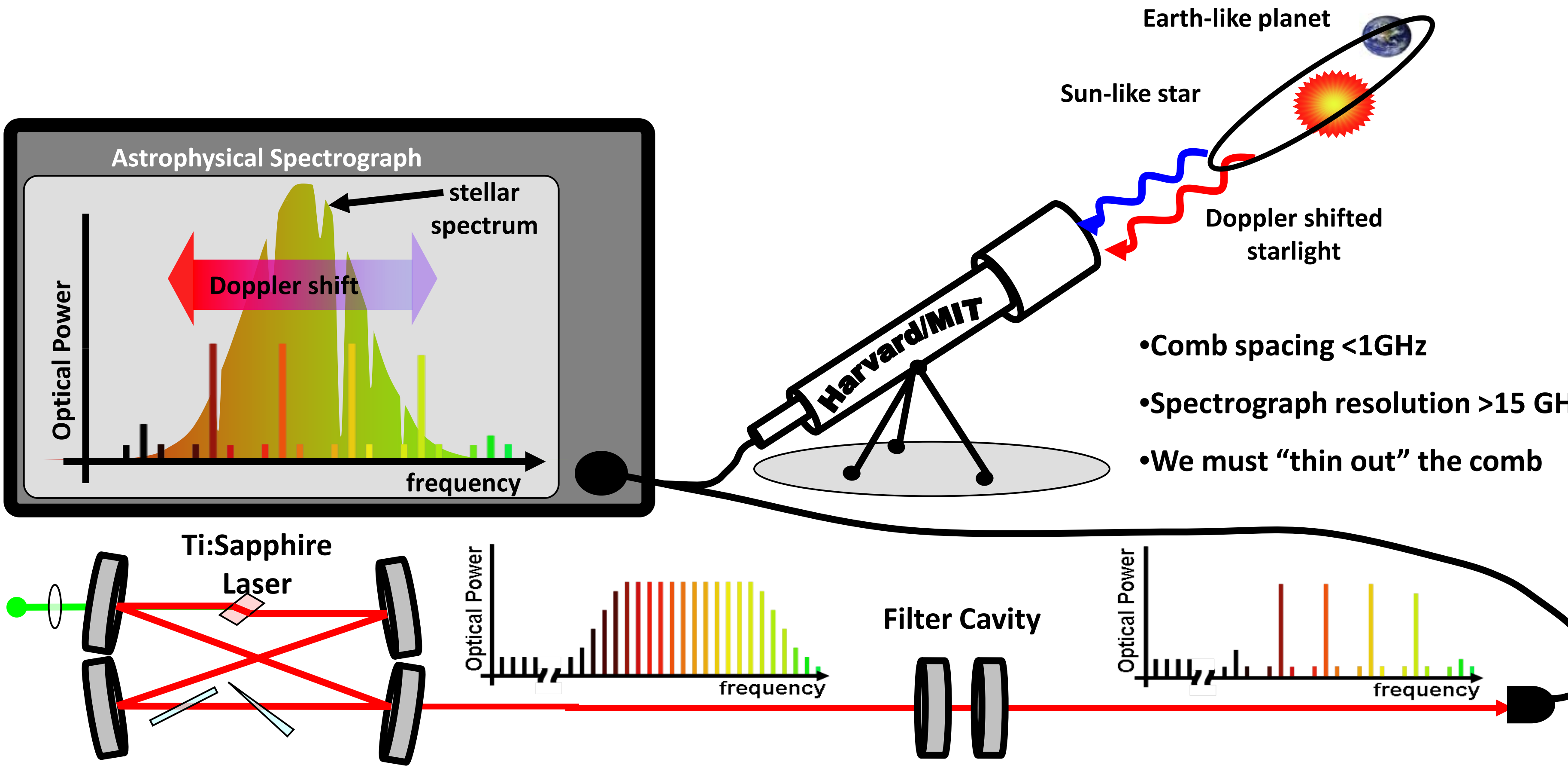
idestaQE
quantum electronics

Astro-combs: Search for Exo-planets



- "Hot Jupiter" 30 m/s ~ 75 MHz
- Lowest reported RV 1 m/s ~ 2.5 MHz
- Earth – Sun interaction 5 cm/s ~ 125 kHz
- Th-Ar discharge stability minimum 1 m/s ~ 2.5 MHz

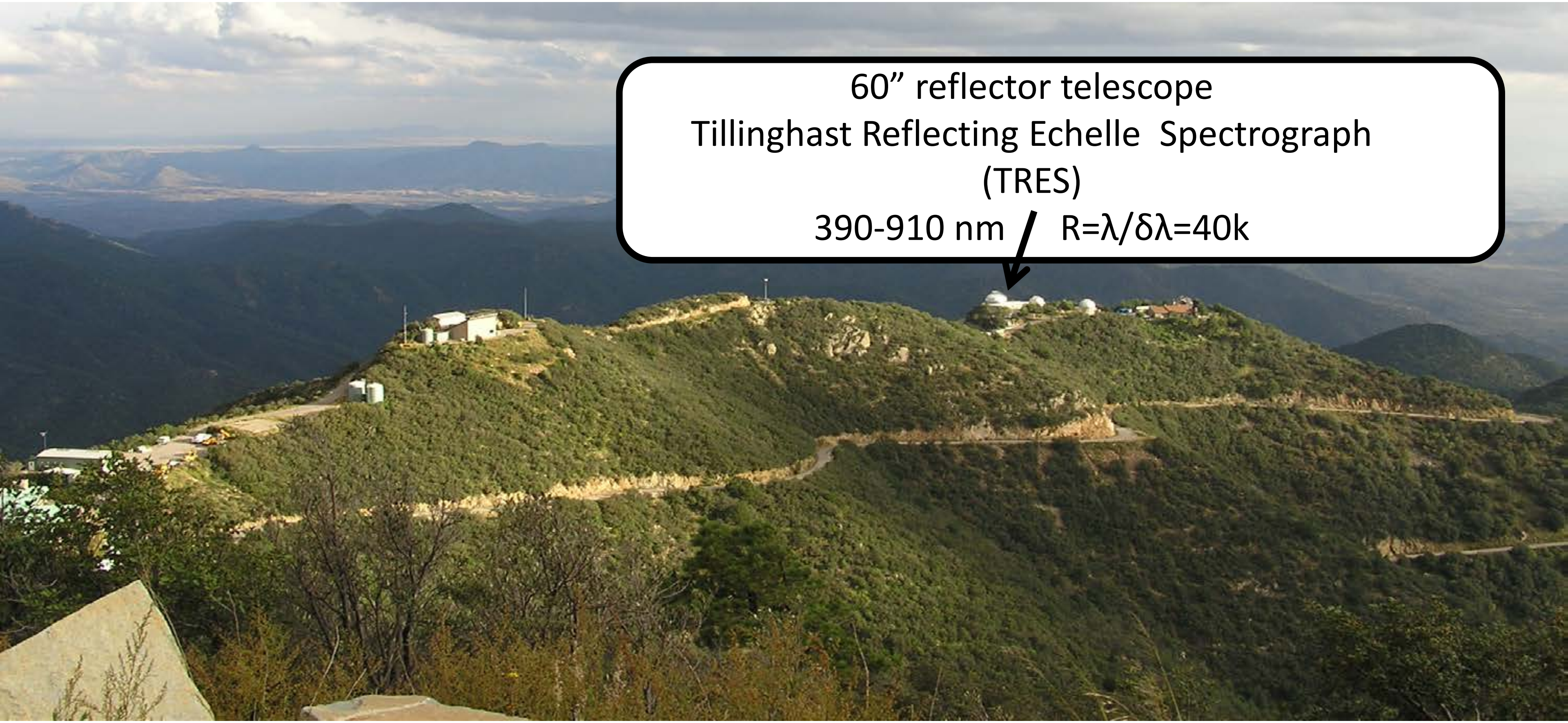
Astro-combs: Search for Exo-planets



- Comb spacing <1GHz
- Spectrograph resolution >15 GHz
- We must "thin out" the comb

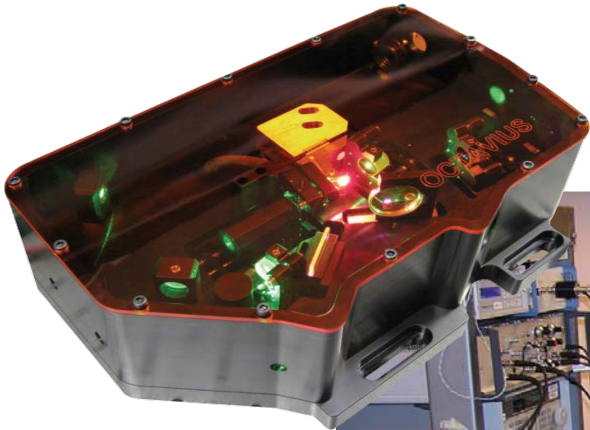
Courtesy A. Benedick

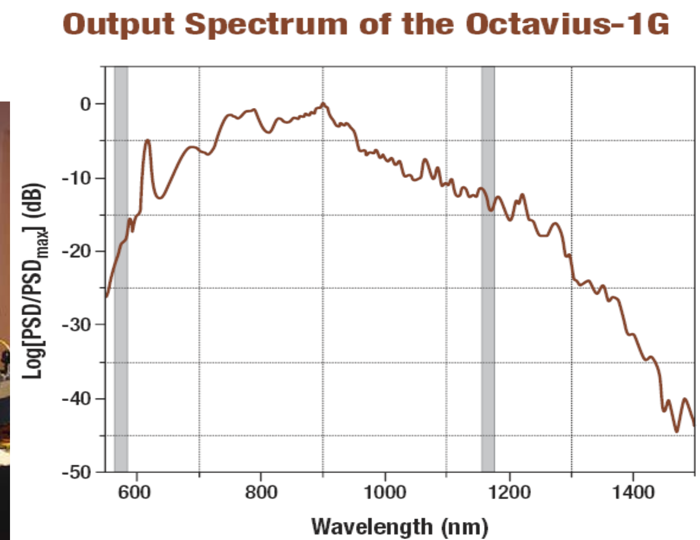
Fred Lawrence Whipple observatory



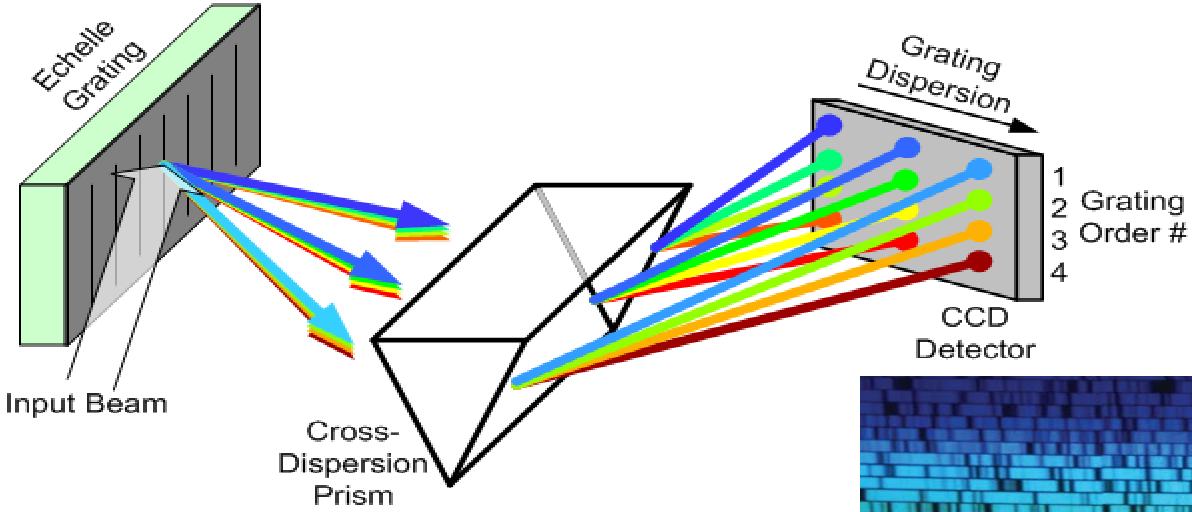
Andrew Benedick & Chi-Hao Li

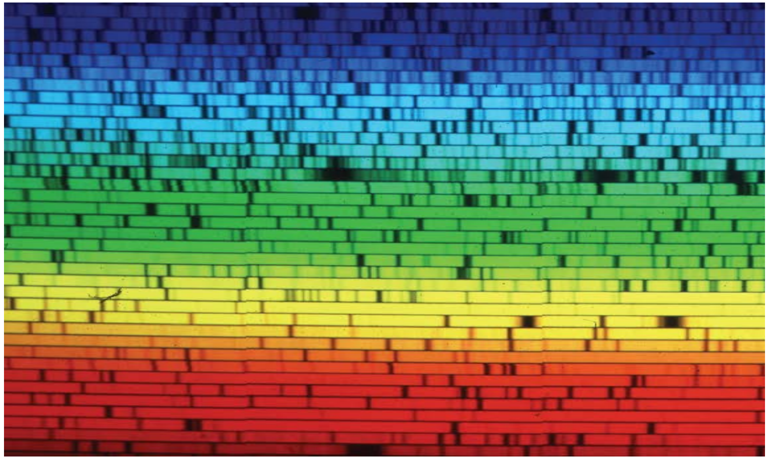
Astro Comb Experimental setup:





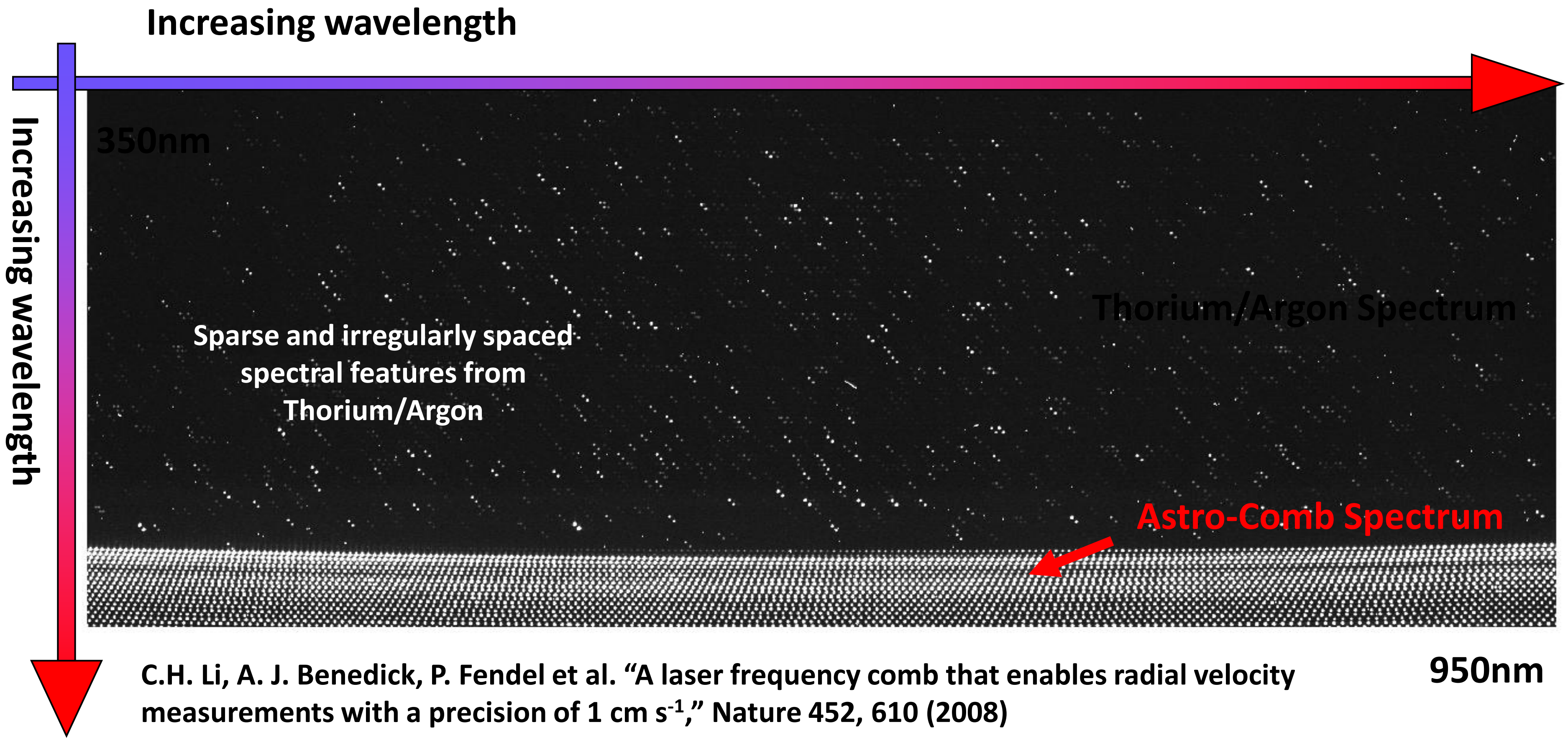
Basic principle of Echelle Spectrographs:





Typical Feature	~50 GHz
Resolution	~15 GHz
Pixel width	~1 GHz
Earth-Sun Interaction	~125 kHz

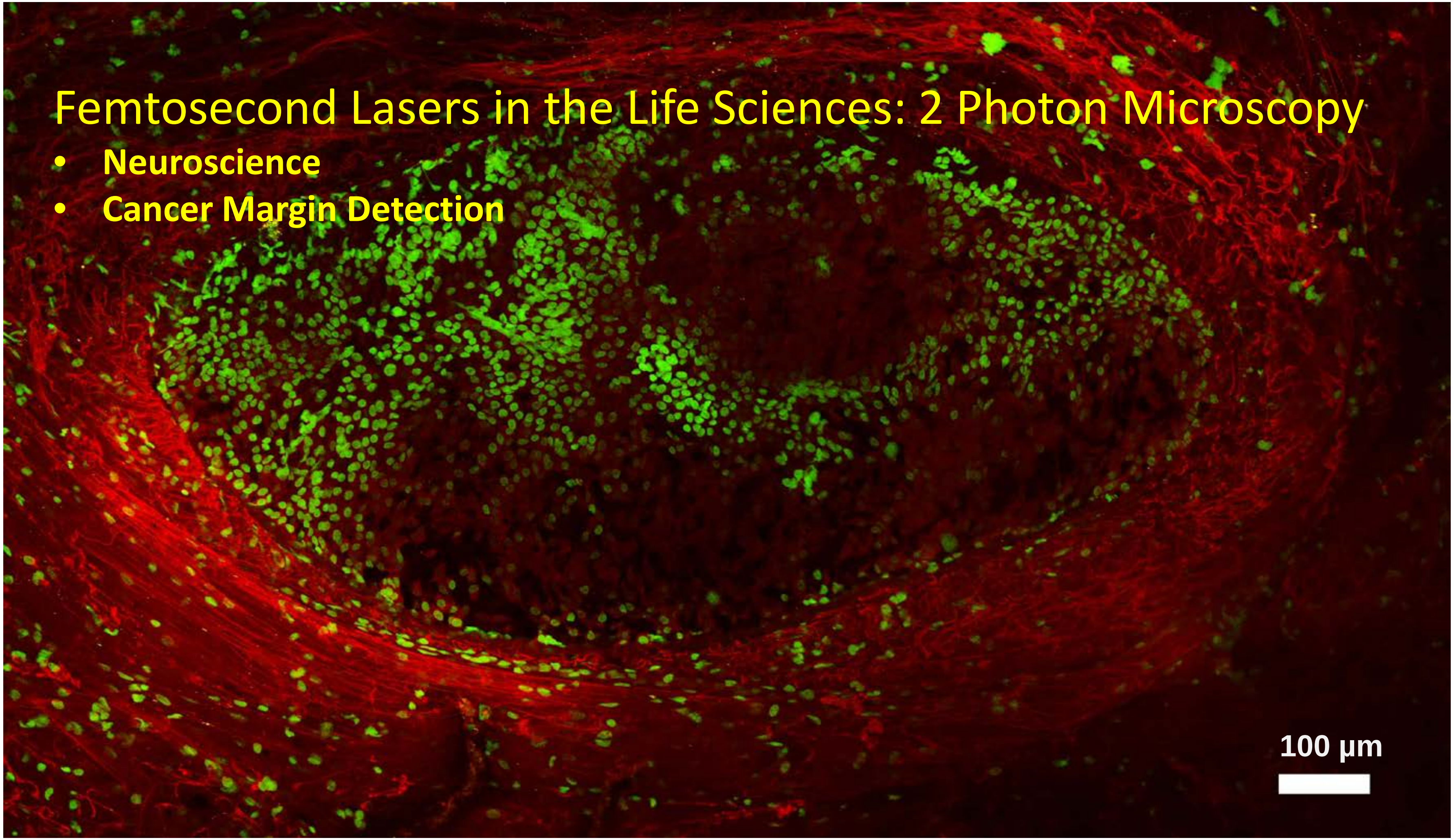
CCD image from the TRES



C.H. Li, A. J. Benedick, P. Fendel et al. "A laser frequency comb that enables radial velocity measurements with a precision of 1 cm s^{-1}," Nature 452, 610 (2008)

Femtosecond Lasers in the Life Sciences: 2 Photon Microscopy

- **Neuroscience**
- **Cancer Margin Detection**

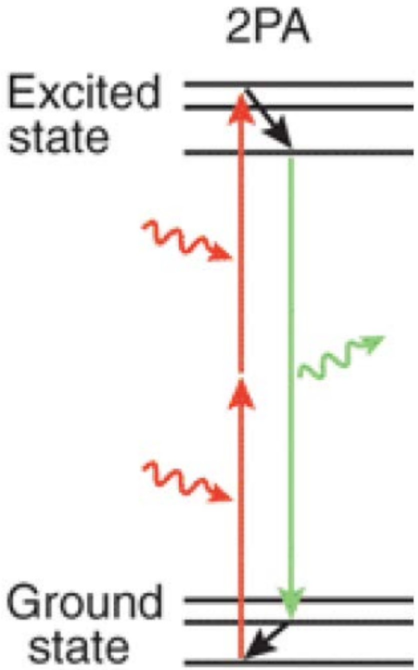


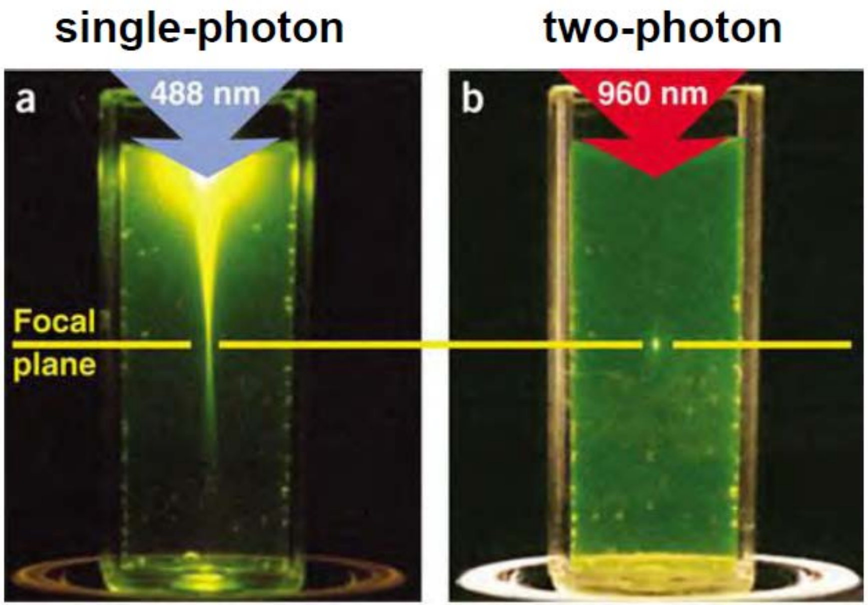
Carcinoma In Situ

Why 2p microscopy?

2p microscopy is based on a non linear absorption process first described in 1931:

Maria Göppert-Mayer

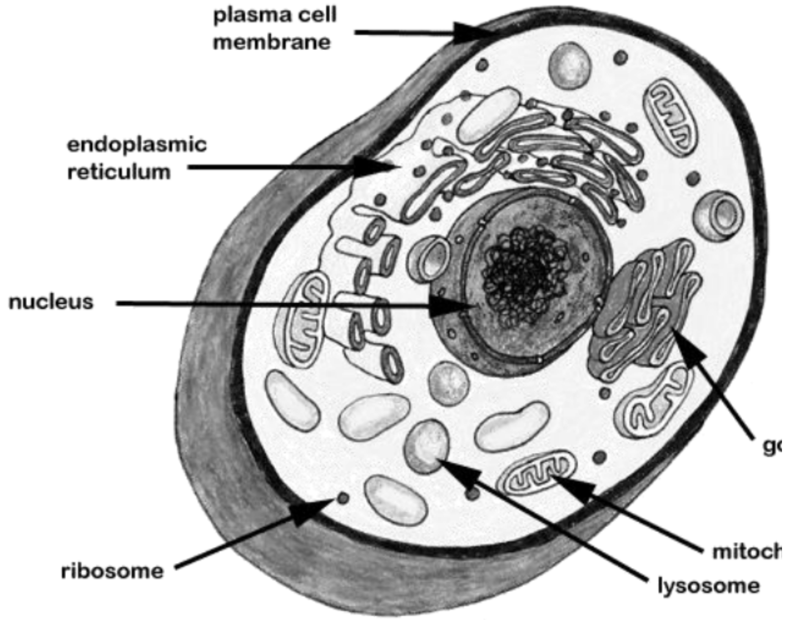


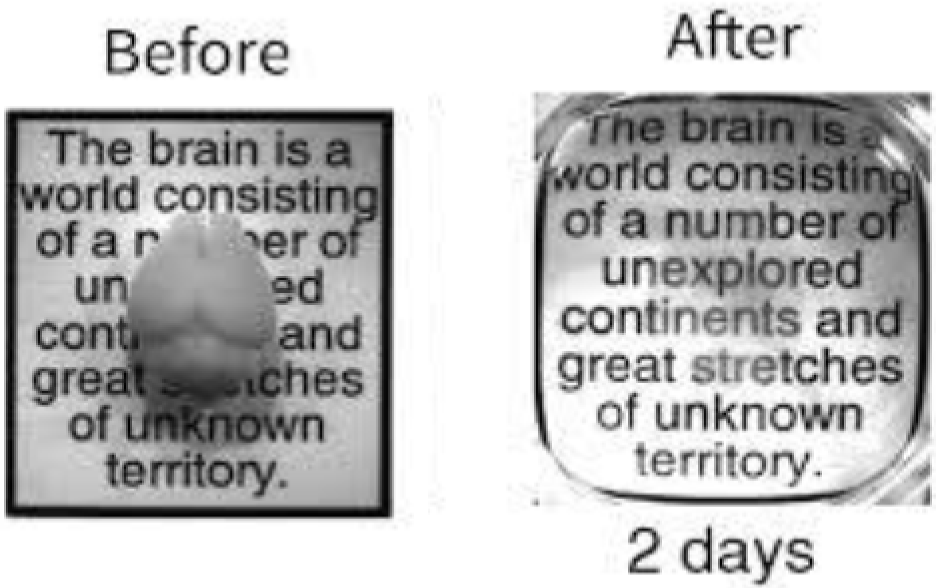


Zipfel et al. 2003

Intrinsic optical sectioning (3D resolution)

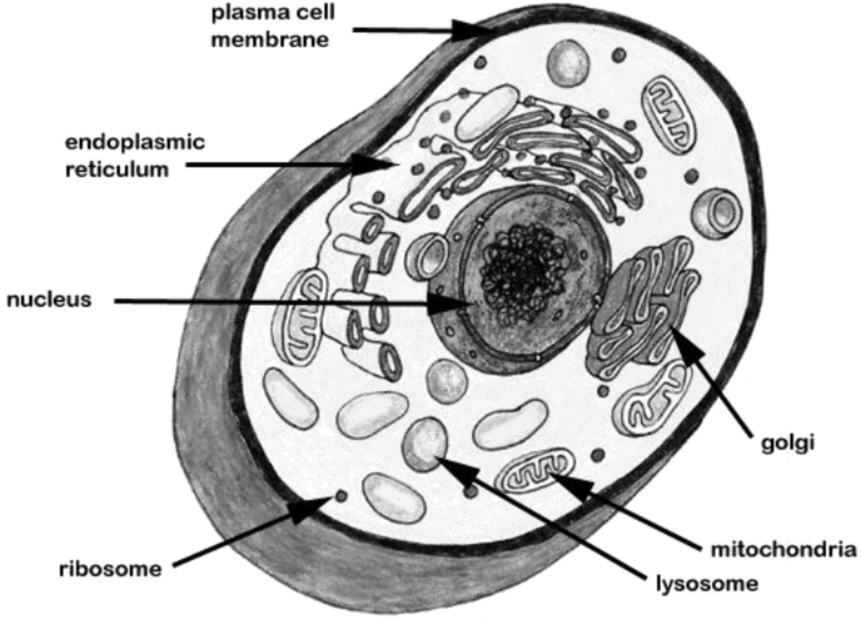
Imaging through highly scattering media:

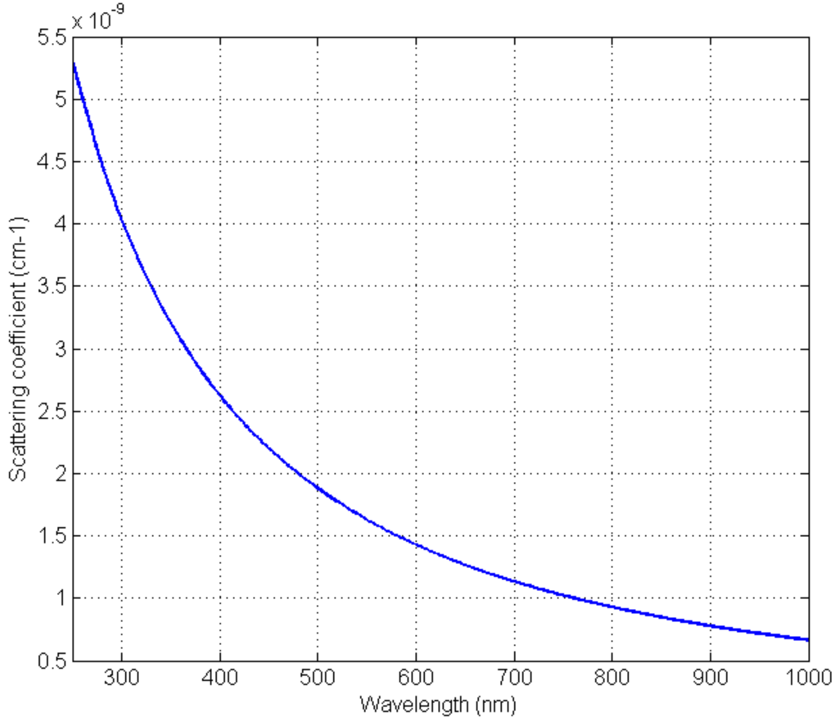




Clearing the Brain of Scattering Tissue: Clarity (Nature 2013)

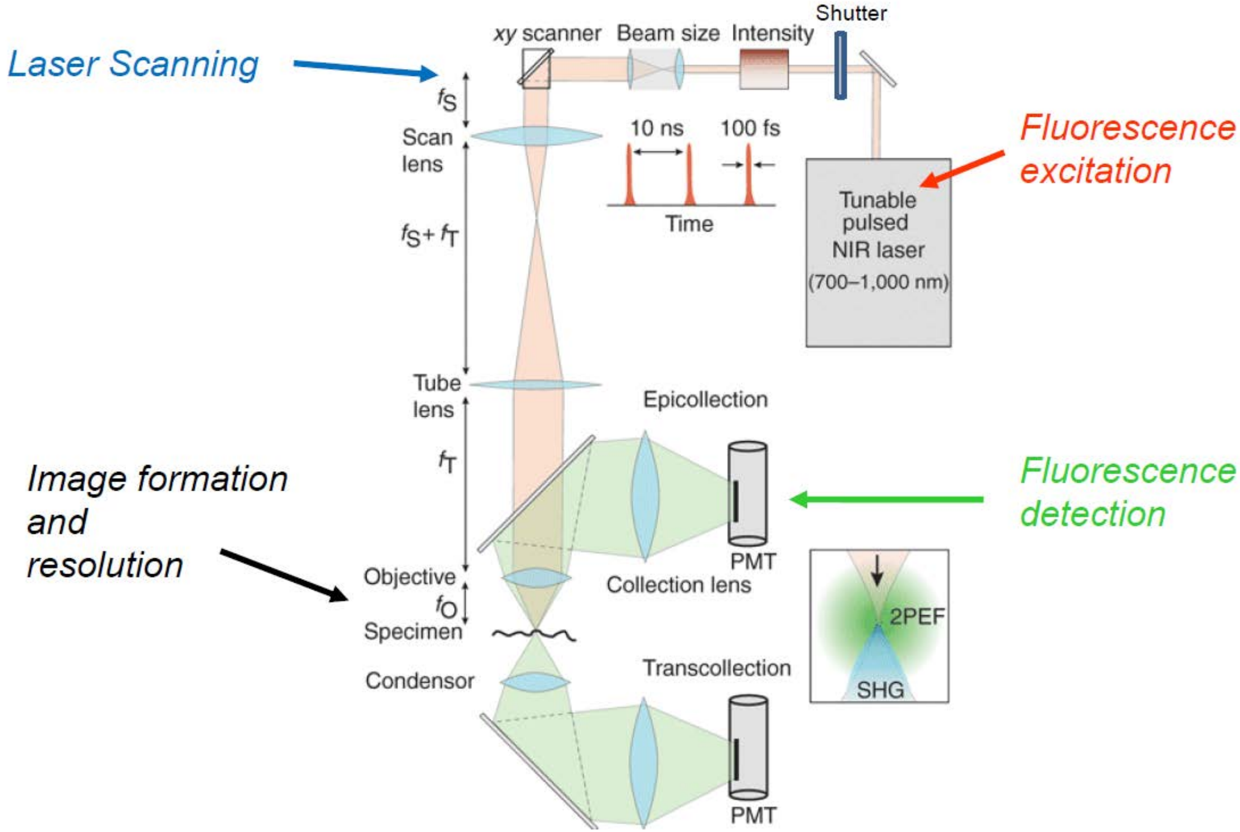
Mie Scattering on Organelles





The scattering coefficient spectrum of biological tissue

Generic Two Photon Microscope:

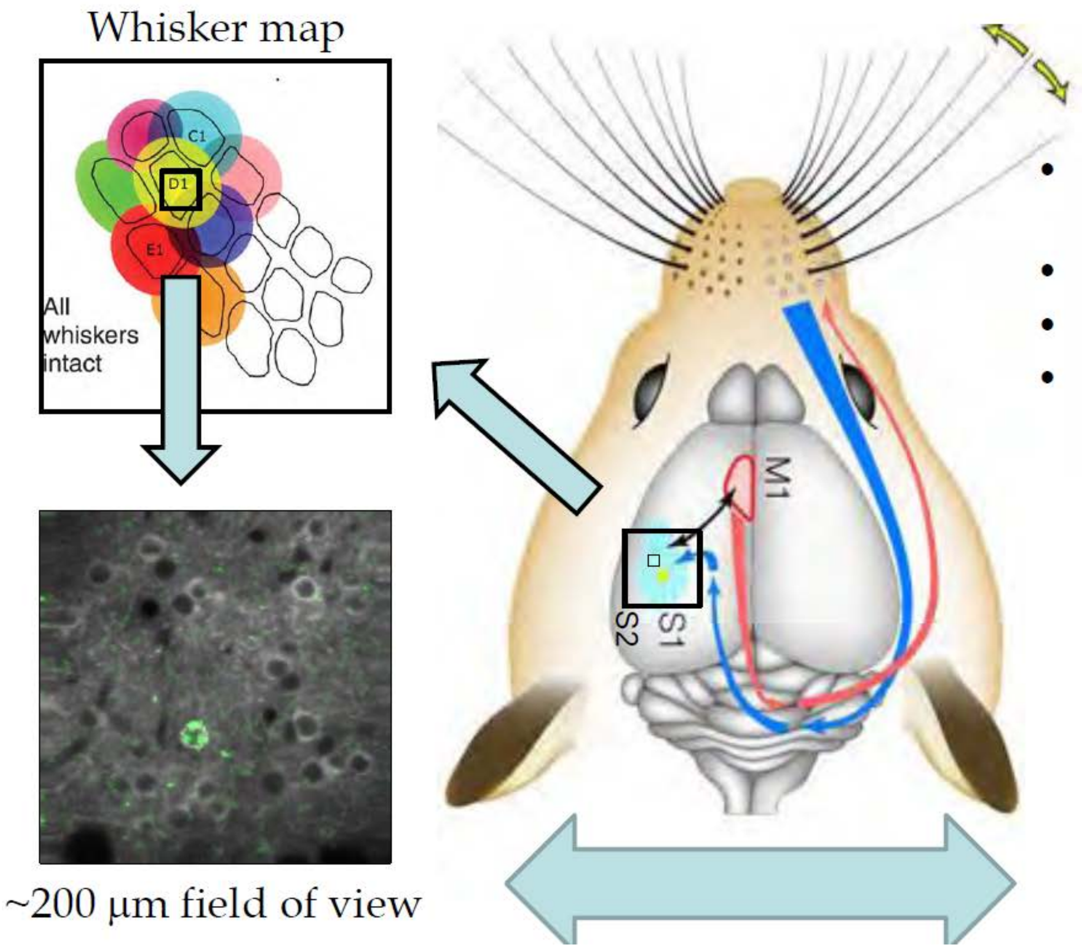


Early Papers:

Denk, Strickler and Webb, Science 1990 (Colliding pulse dye laser)

Yuste R, Denk W. Dendritic spines as basic functional units of neuronal integration. Nature 1995

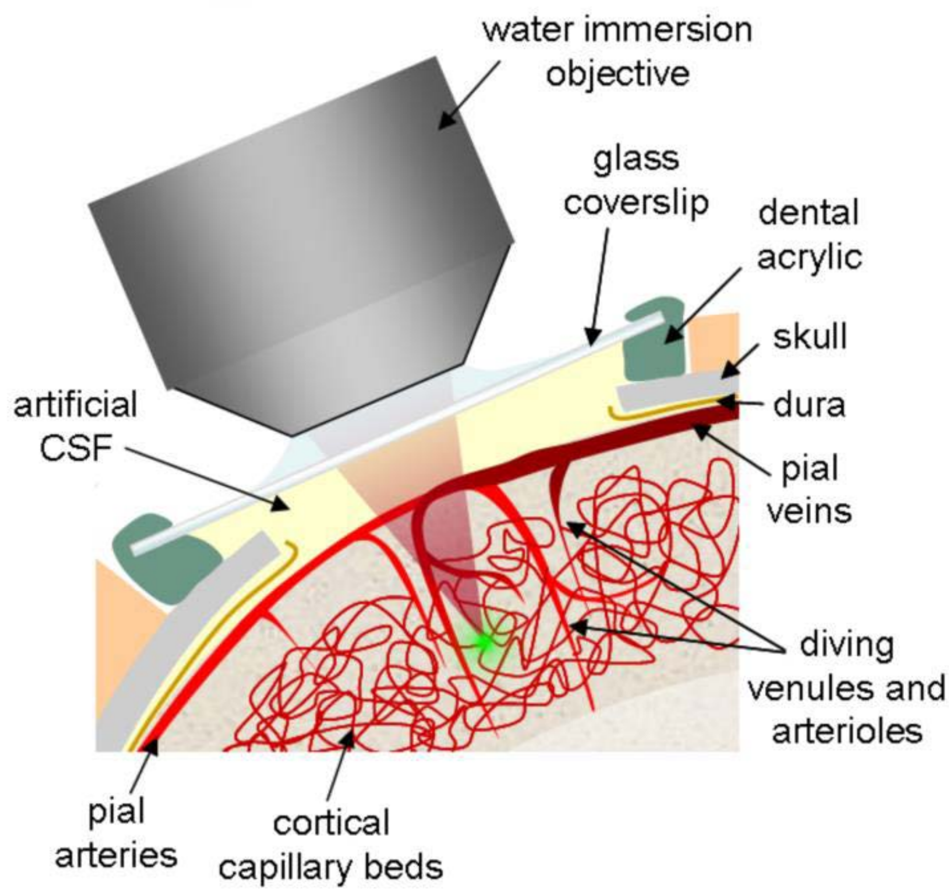
Two-Photon Microscopy: THE tool for understanding the Brain



- Model system sensorimotor integration
- Clear topography
- Easy whisker trimming
- Active whisking behavior

Courtesy F. Helmchen

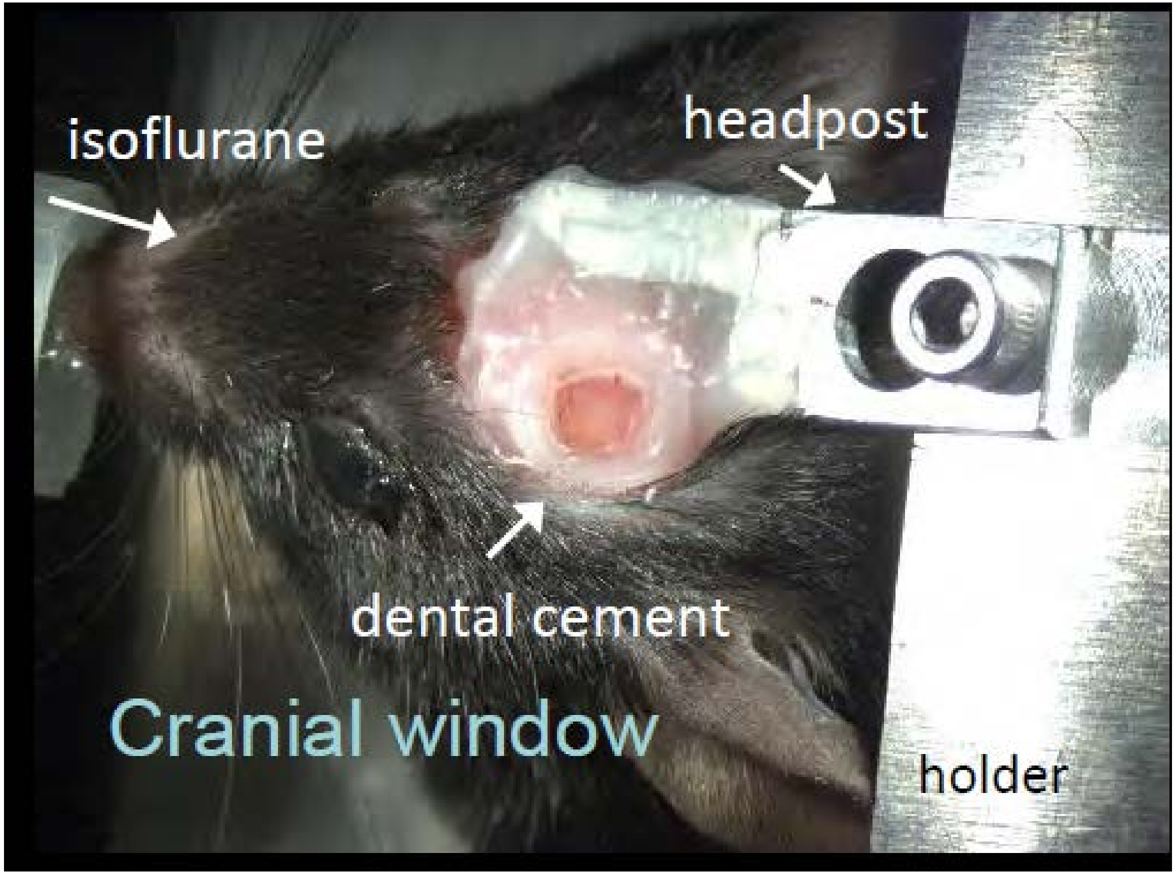
Typical Experimental Setup



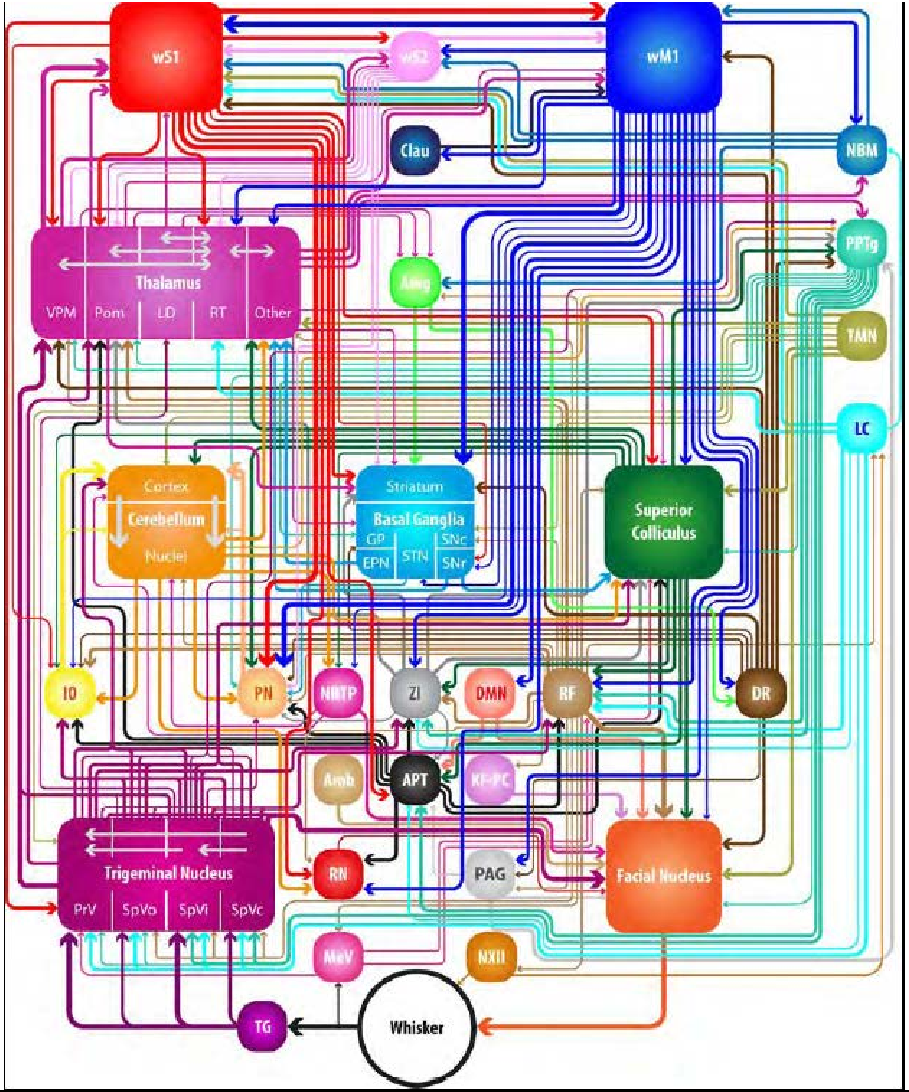
Cranial Window

Courtesy E. Hillman

Typical Experimental Setup

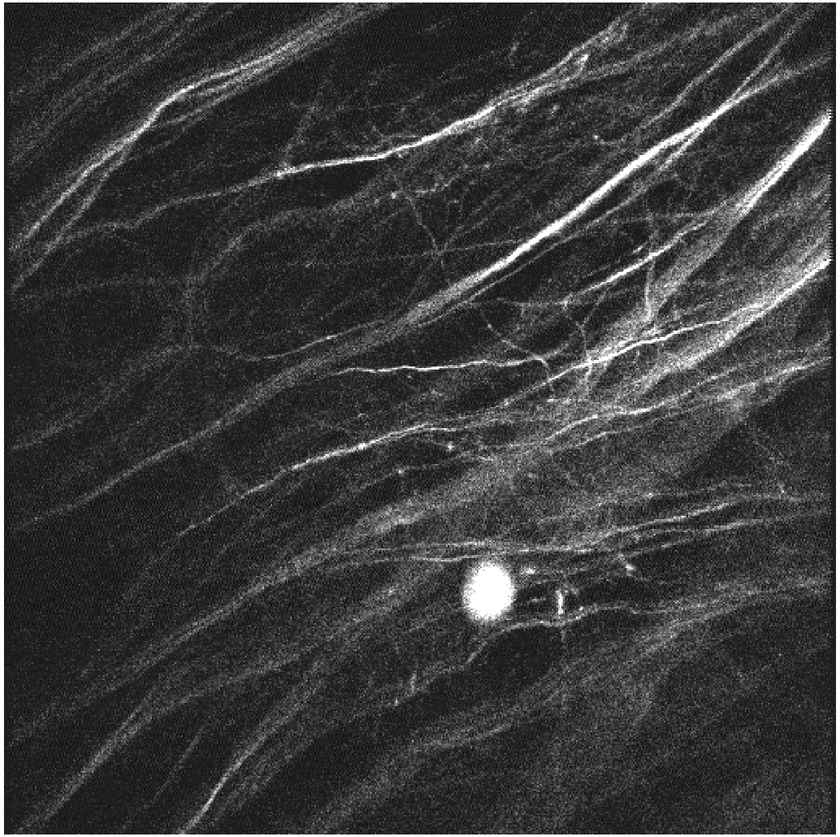


Brain-wide network for processing whisker information:



Bosman et al, 2011

Deep Brain Imaging

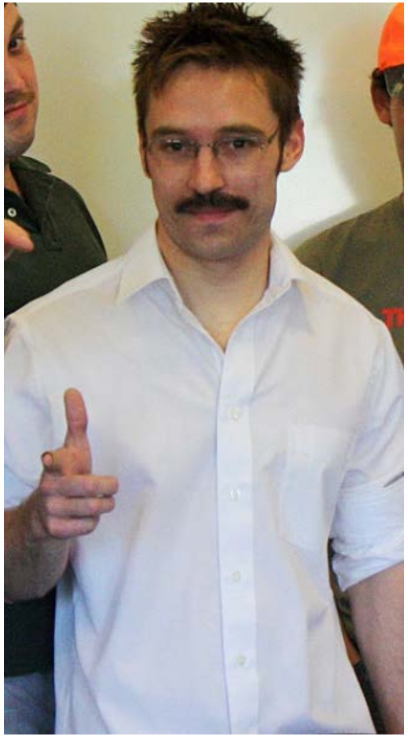


Imaging CA1 of the hippocampus

Neurons labeled with thy1-YFP, 510um stack

Courtesy of the Neurobiology Course at the Max Planck Institute for Neurobiology, Jupiter FL

Cancer Boundary Detection: Breast Cancer



Mike Giacomelli

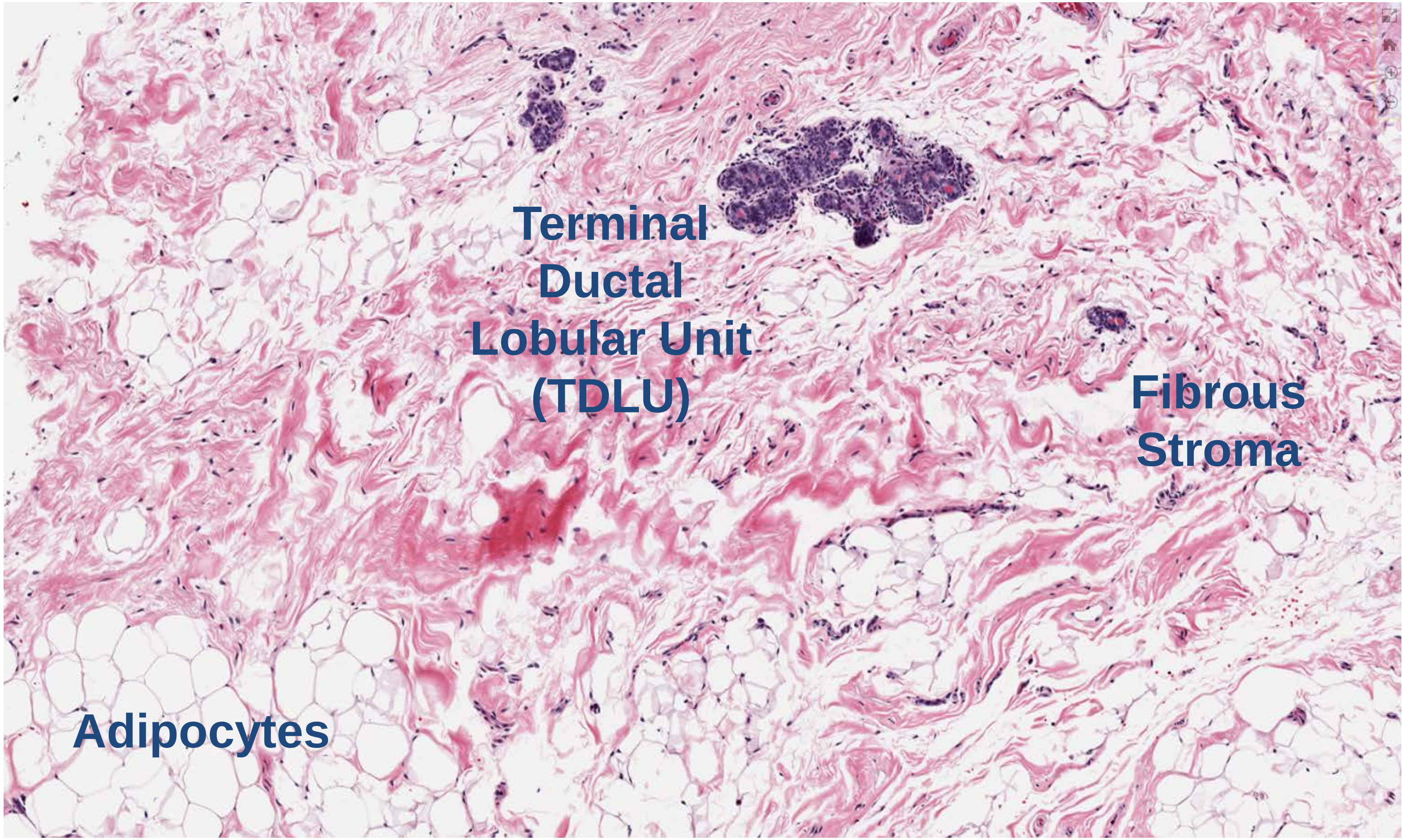
- High failure rate (1 in 3 patients) for early stage breast cancer surgery (lumpectomy)
- Intraoperative imaging is not widely used
- Traditional histopathology:
  Gold standard for cancer diagnoses and tumor boundary evaluation uses hematoxylin (to stain nuclei) and eosin (to stain stroma) takes ~ 1 day for fixation, embedding and sectioning into ~5µm thick slices

Two Photon Imaging:

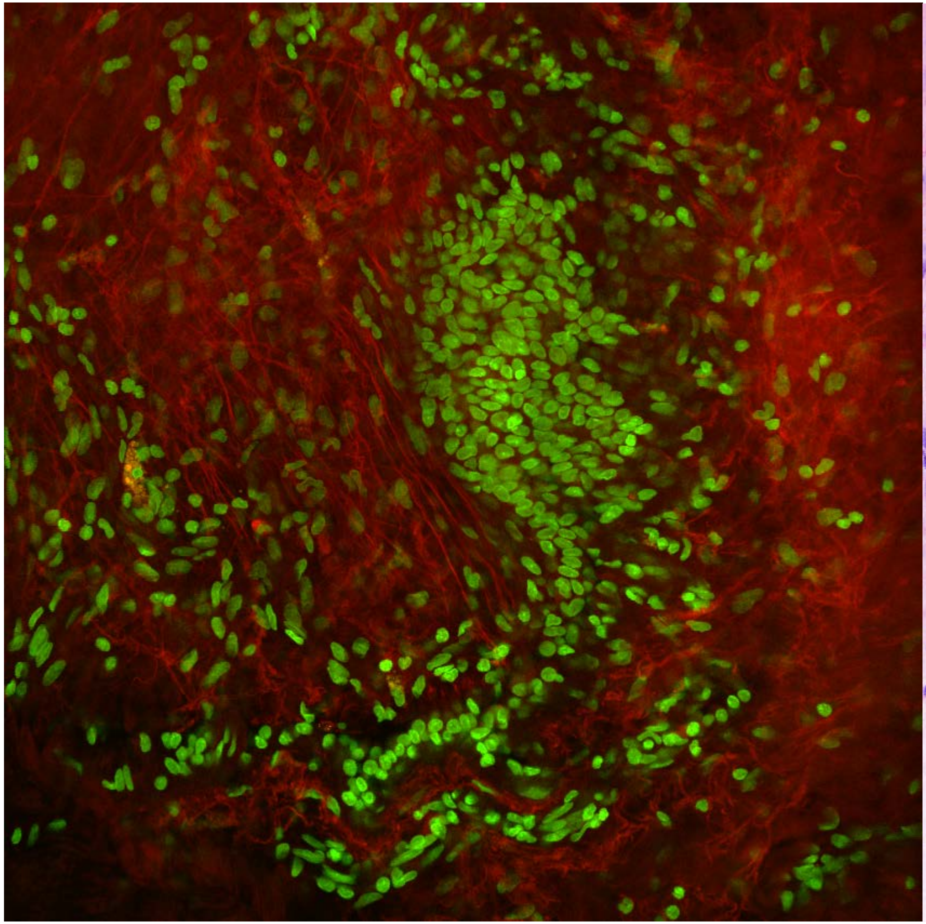
- Provides histology-like axial sectioning
- Good penetration into thick tissue
- Large number of possible fluorescent agents to provide nuclear and stromal contrast like traditional histology

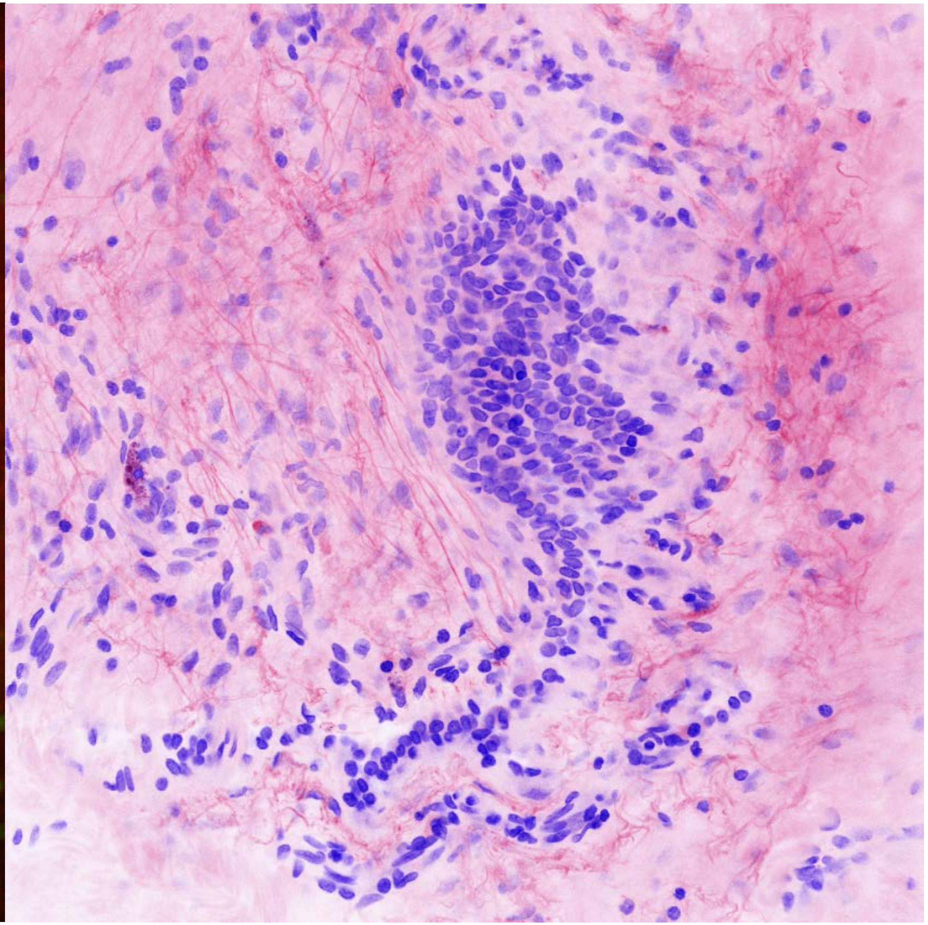
rle AT MIT RESEARCH LABORATORY OF ELECTRONICS AT MIT

Traditional Breast Histology



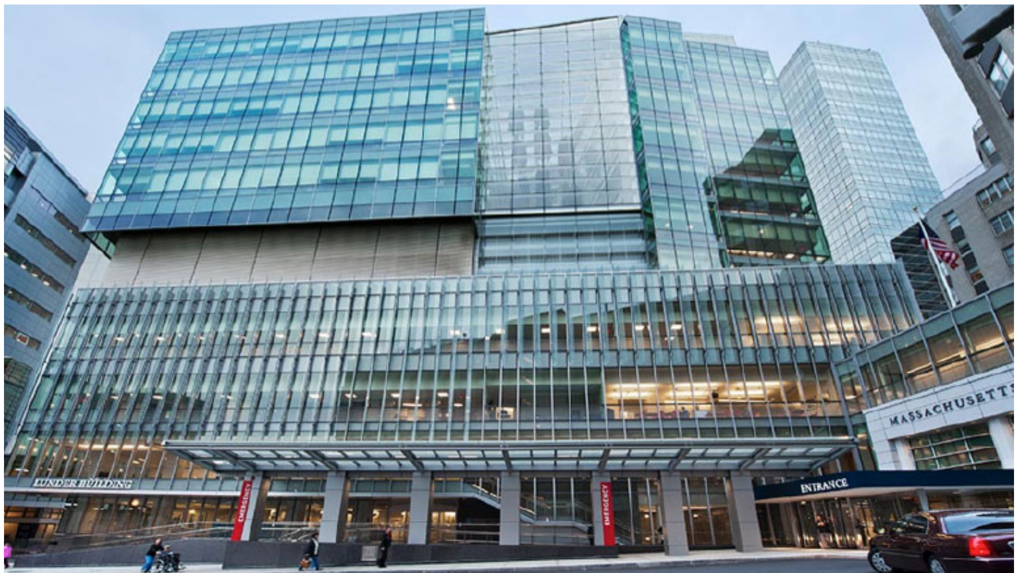
Virtual Transillumination Microscopy





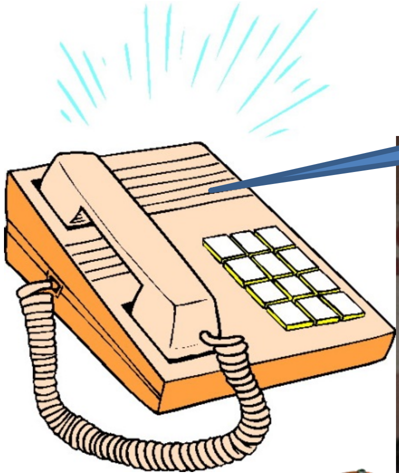
Moving to the Clinic:

MGH 1811 MASSACHUSETTS GENERAL HOSPITAL

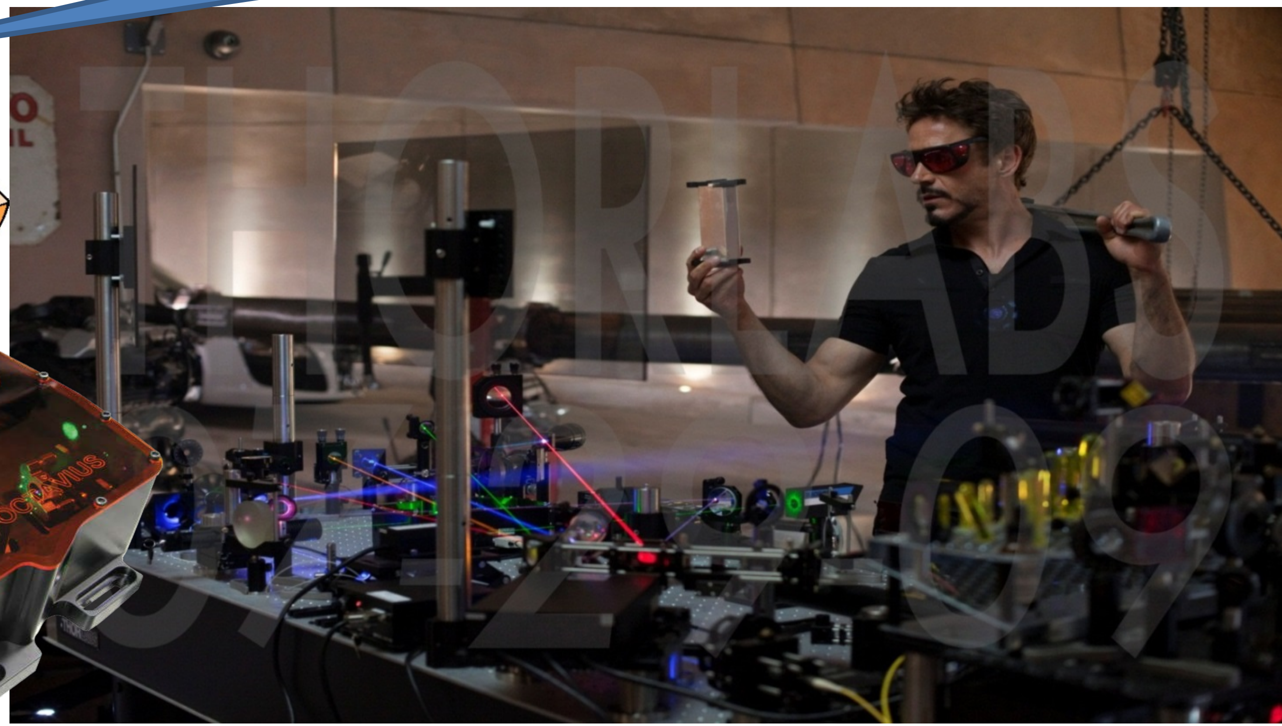


Patient Study is ongoing at MGH

20 years of fun in Photonics

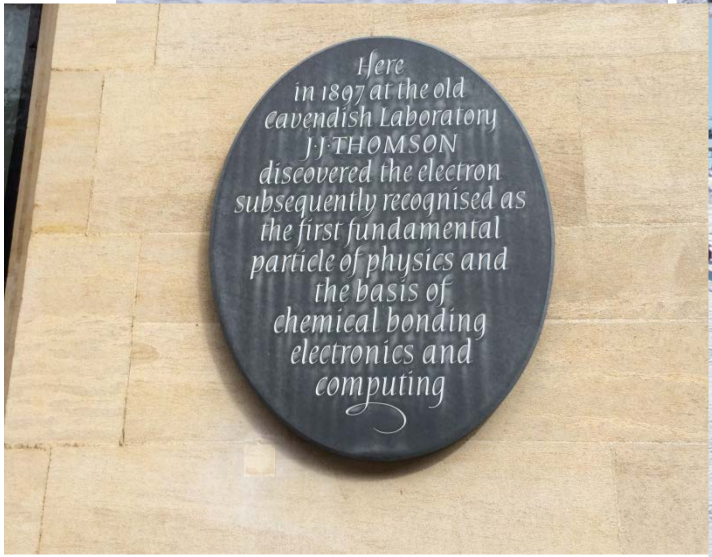


'This is Julie from Marvel Studios…'



From Iron Man II

20 years of fun in Photonics



20 years in Photonics

Stockholm, December 2005

Thank you

Hänsch Group – Kärtner Group – Walsworth Group – Fujimoto Group – Richardson Group – LCLS Laser Group

THORLABS SITES WORLDWIDE

- Corporate Headquarters
- Thorlabs Locations
- Warehousing and shipping centers