Developments in CARS microscopy

The CARS microscopy field

Contrast

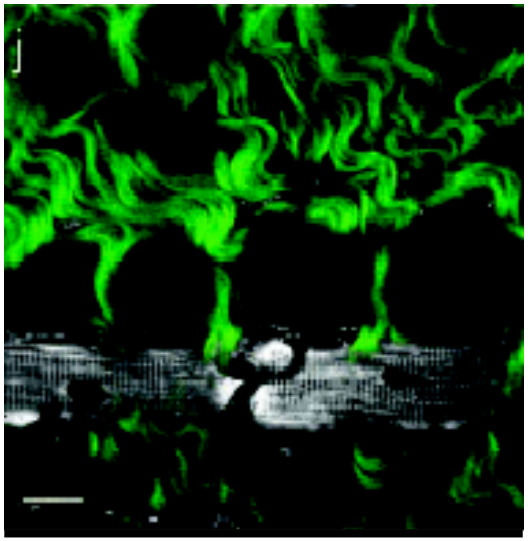
- Transmission microscopy
- Reflection microscopy
- Fluorescence microscopy
- Nonlinear microscopy

Nonlinear Contrast

- Multi-photon fluorescence
- Second harmonic (SHG)
- Third harmonic (THG)
- CARS !

CARS and the rest

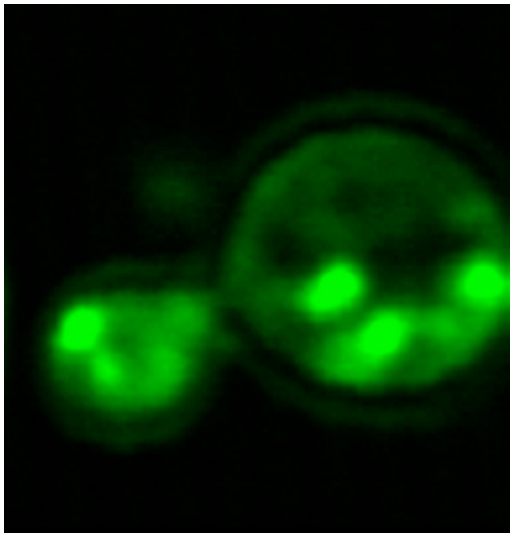
SHG microscopy



- interfaces ($\chi^{(2)}$)
- chiral structures

Zipfel et al., PNAS 100, 7075 (2003)

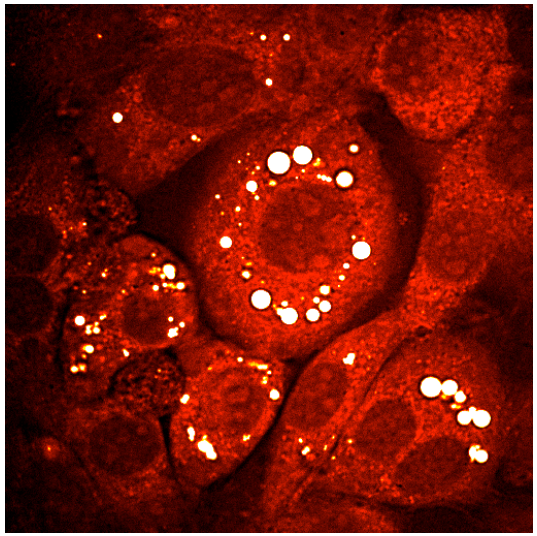
THG microscopy



- spatial $\chi^{(3)}$ distribution
- interfaces & spatial inhomogeneities

Oron et al., J. Struct. Biol. (2003)

CARS Microscopy

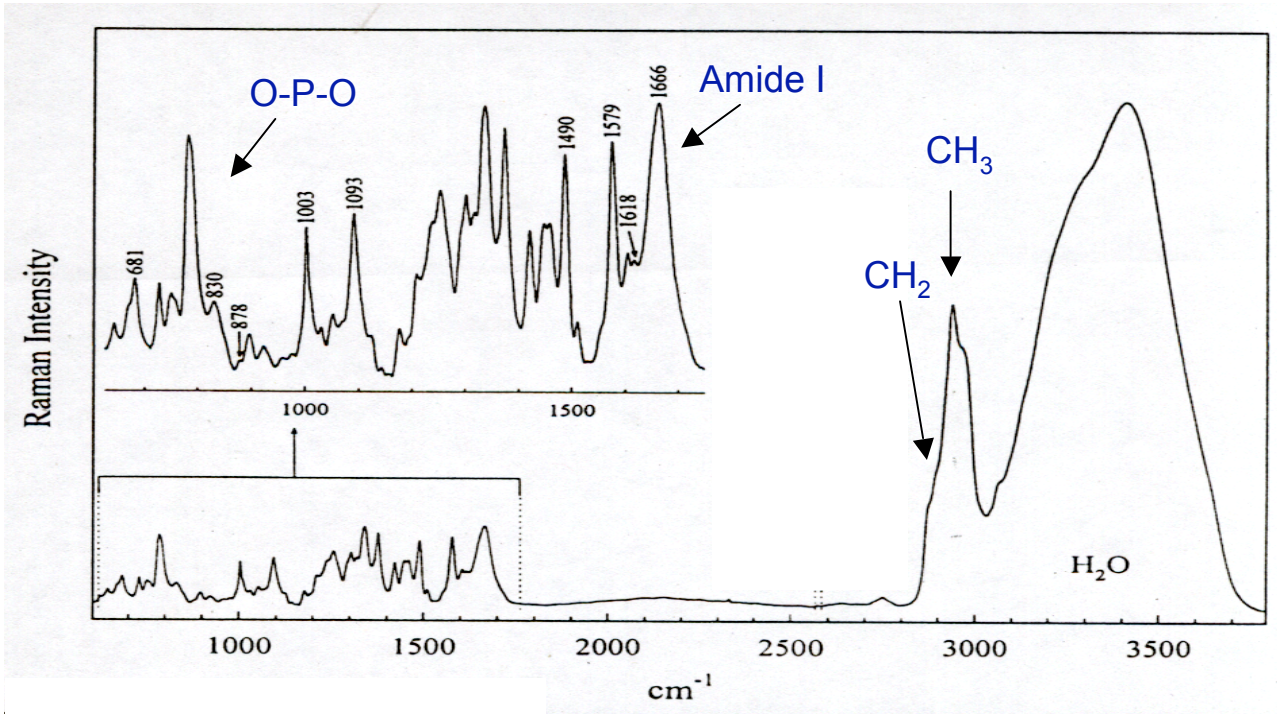


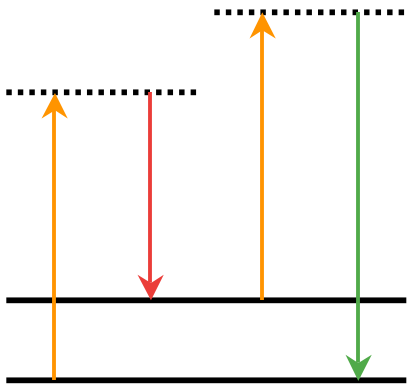
- molecular vibration
- spatial $\chi^{(3)}$ distribution

Nan et al., J. Lipid Res. 44, 2202 (2003)

The ingredients

Raman spectrum Bacteriophage P22





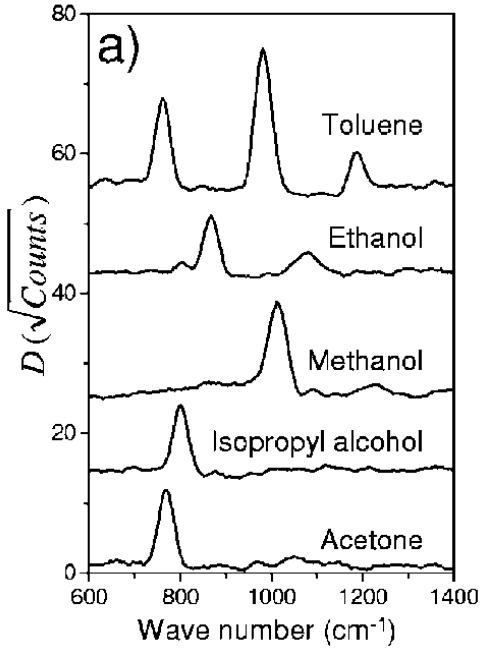
>10^4 times more efficient

Coherent emission

Background problems

Two flavors

CARS microspectroscopy

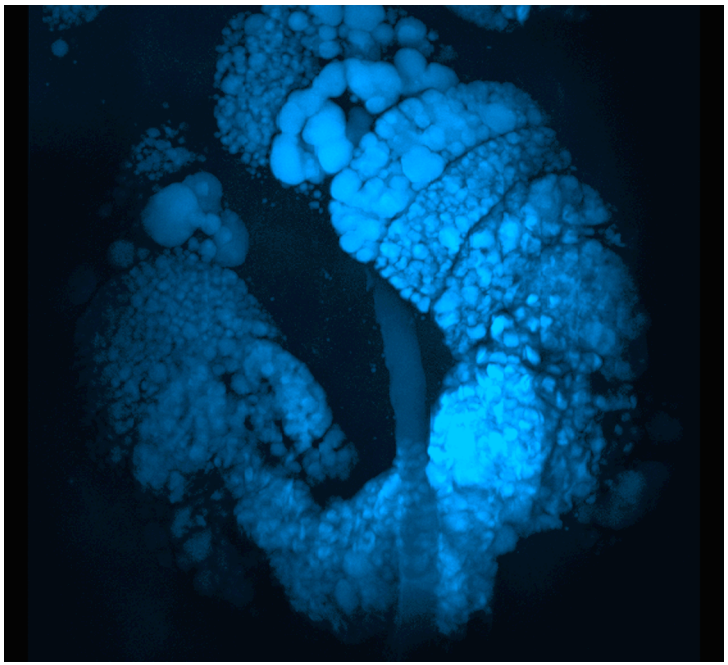


Broad band light source

High nonresonant background

'Slow' acquisition times (10 ms/spectrum)

CARS imaging



Narrow band light source

Lower background

Fast acquisition times (0.1 μs/pixel)

Challenges in CARS

Ultimate light source

Reduce nonresonant background

Increase signal strength of weak modes

CARS interferometry

Broad band

Dudovich et al., *Nature* **418**, 512 (2003)

Marks et al., *Appl. Phys. Lett.* **85**, 5787 (2004)

Evans et al., *Opt. Lett.* **29**, 2923 (2004)

Lim et al., *Phys. Rev. A* **72**, 041803 (2005)

Narrow band

Yacoby and Fitzgibbon., *J. Appl. Phys*. **51**, 3072 (1980)

Potma et al., *Opt. Lett*. **31**, 241 (2006)

Fourier Transform CARS

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Fourier-transform coherent anti-Stokes Raman scattering microscopy

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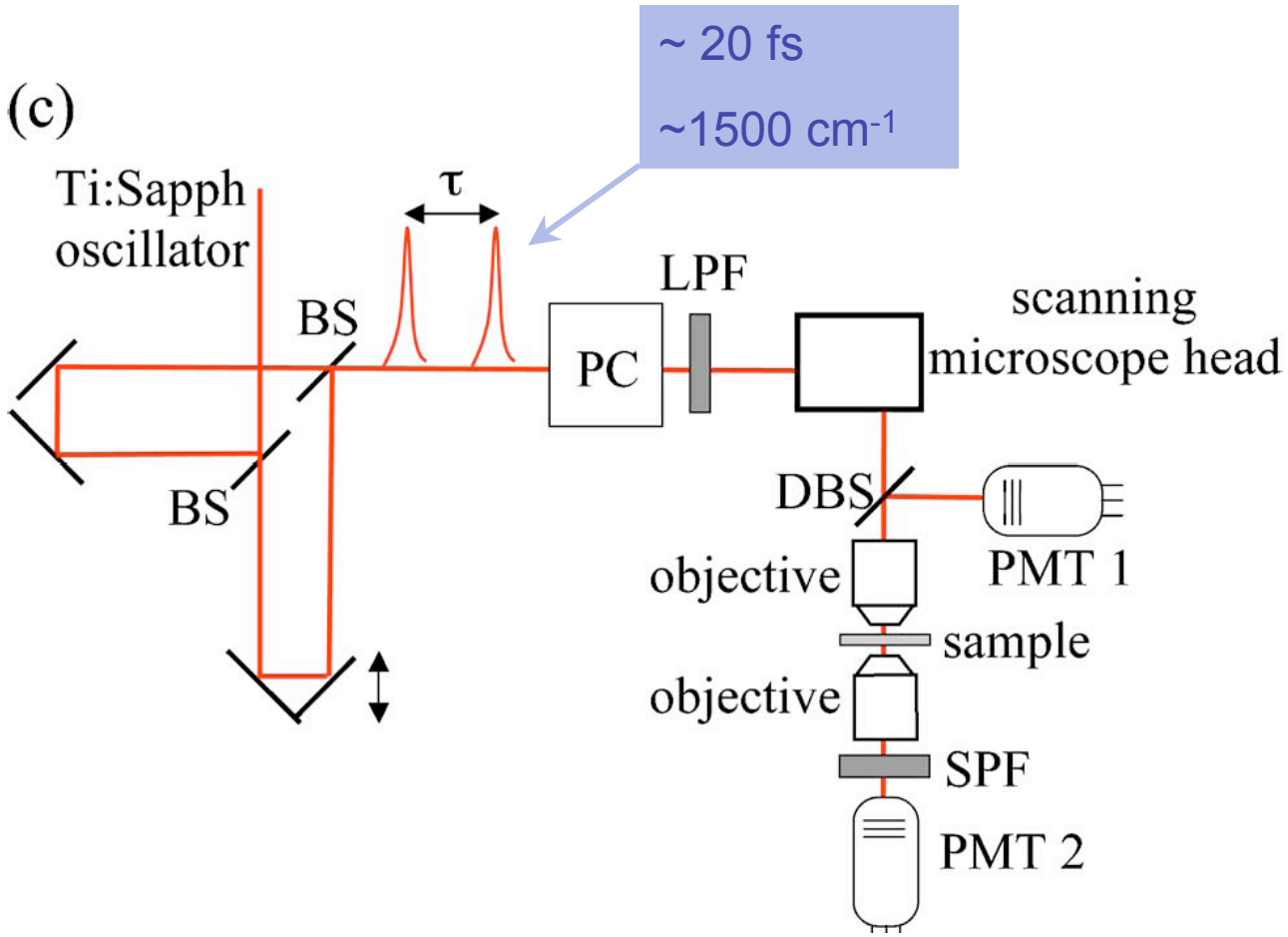
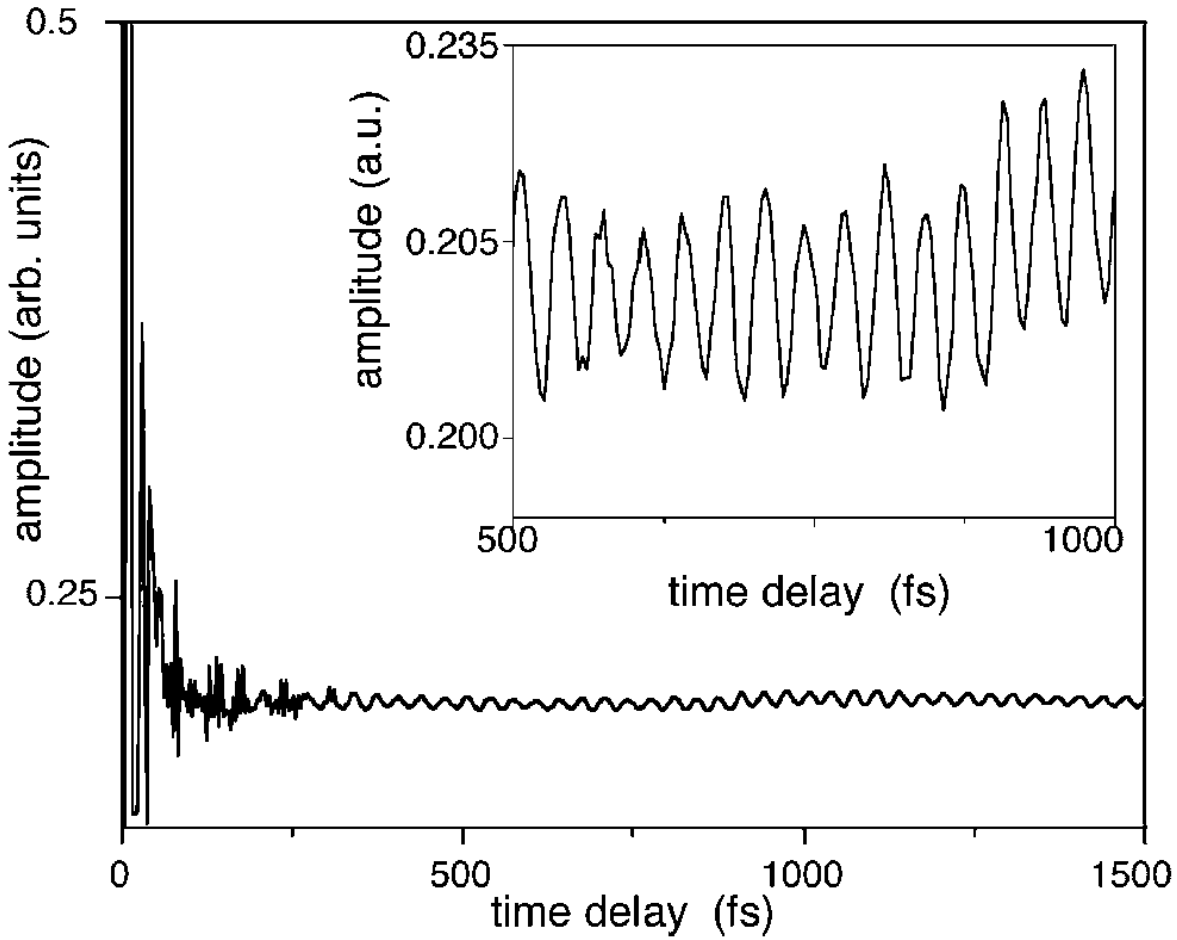
We report a novel Fourier-transform-based implementation of coherent anti-Stokes Raman scattering (CARS) microscopy. The method employs a single femtosecond laser source and a Michelson interferometer to create two pulse replicas that are fed into a scanning multiphoton microscope. By varying the time delay between the pulses, we time-resolve the CARS signal, permitting easy removal of the nonresonant background while providing high resolution, spectrally resolved images of CARS modes over the laser bandwidth ($\sim$1500 cm^{-1}). We demonstrate the method by imaging polystyrene beads in solvent.

OCIS codes: 170.5660, 020.4180, 180.6900, 020.1670, 300.6410, 300.6450.

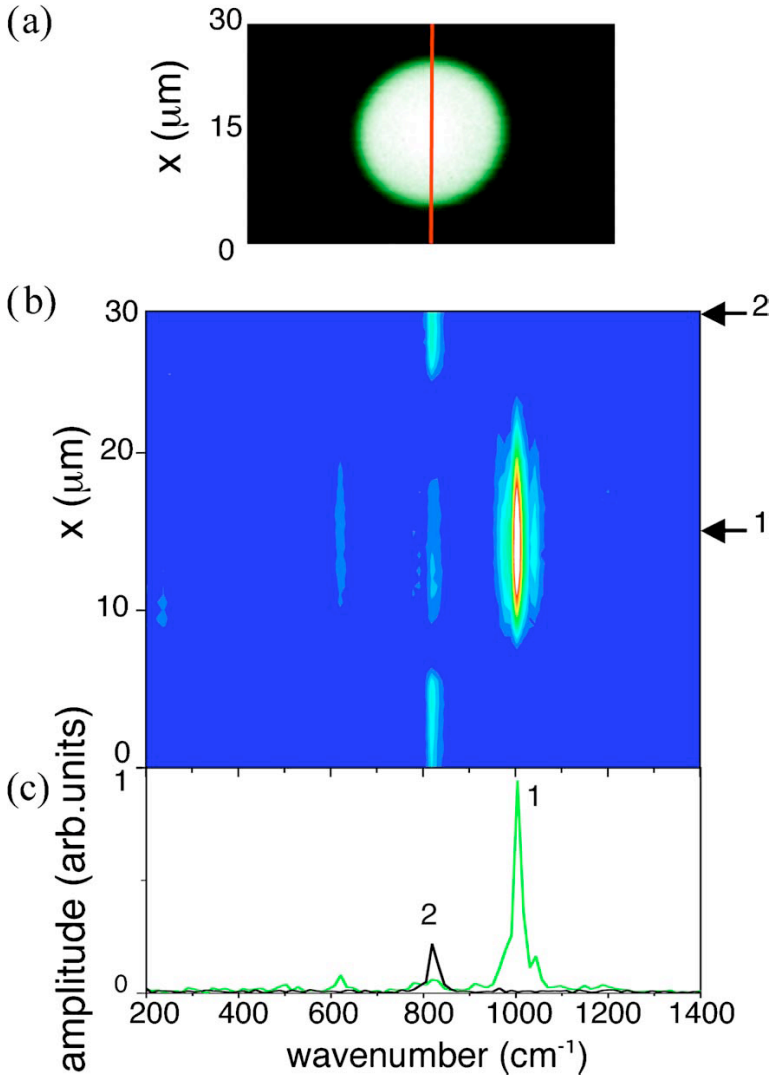
Fourier Transform CARS



Fourier Transform CARS



Fourier Transform CARS



~10 minutes