Phase-controlled dual-comb coherent anti-Stokes Raman spectroscopic imaging

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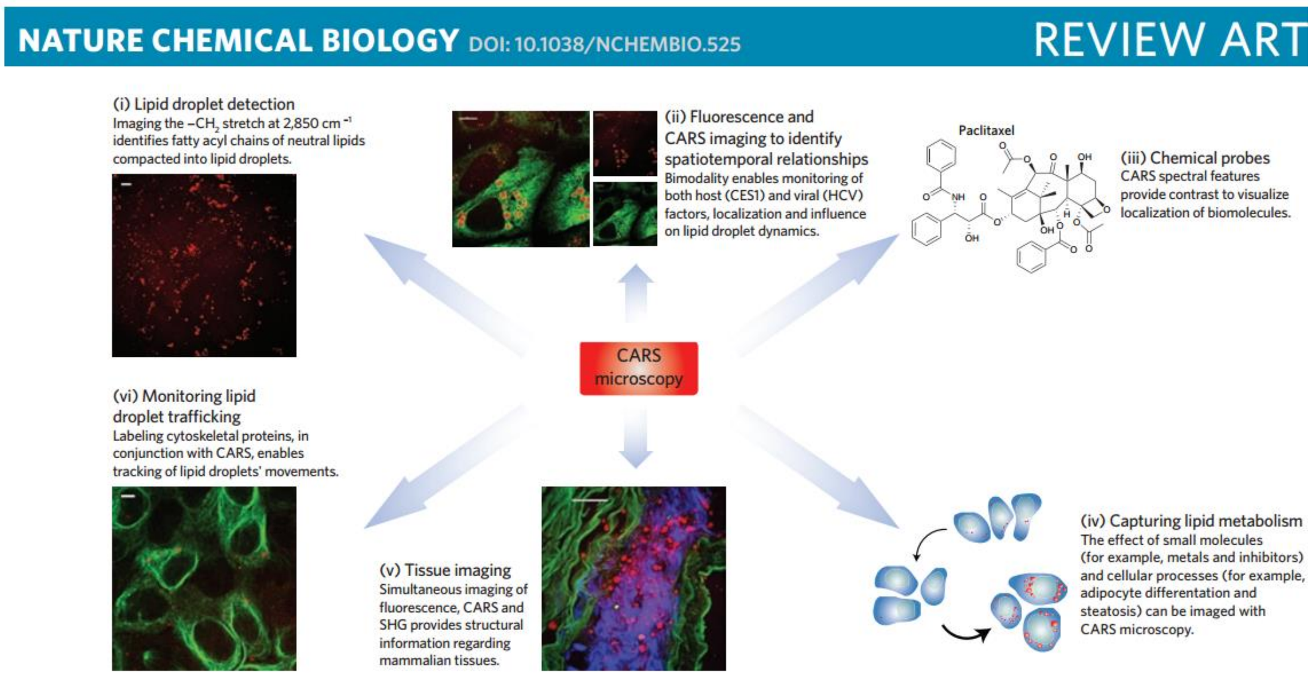
TSINGHUA UNIVERSITY

Advantage of CARS imaging

- Intrinsic vibrational contrast, label-free imaging.
- Coherent signal accumulation, high-speed imaging.
- 3D sectioning capability.
- Near-infrared excitation, allowing deep penetration.



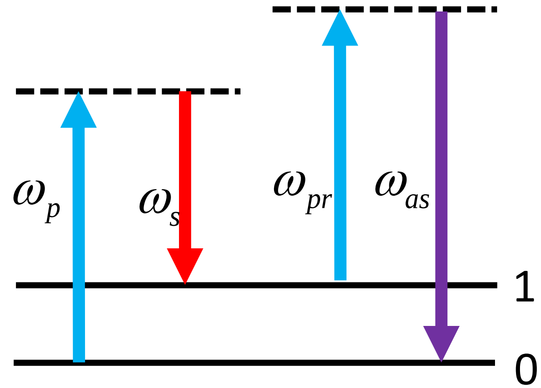
CARS tissue imaging of fresh mouse skin

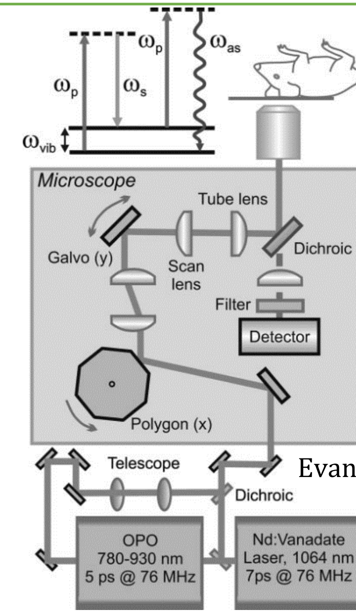
https://bernstein.harvard.edu/research/cars-why.htm

C L. Evans, et al. Annu. Rev. Anal. Chem. 2008
J. Pezacki, et al. Nat. Chem. Bio. 2011
C H Camp Jr, et al. Nat. Photonics. 2014

Multiplex/Broadband vs Narrowband CARS

- Narrowband CARS
  - ☺ High speed~6.4 μs
  - ☹ Narrowband

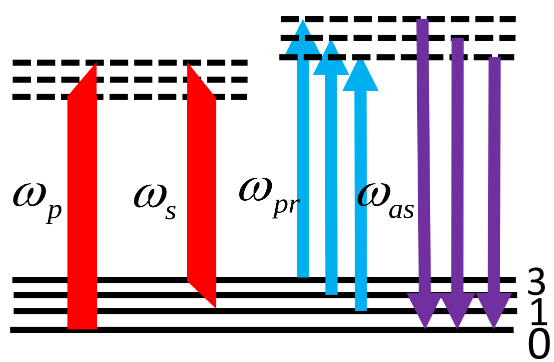


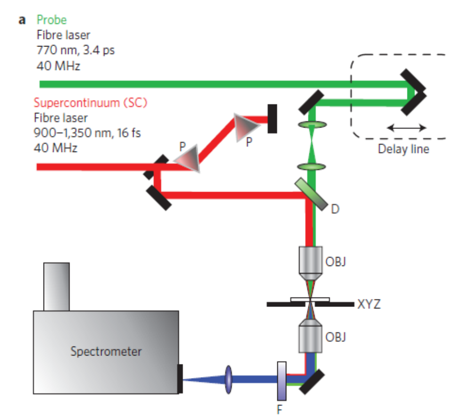


Evans C L, et al. PNAS, 2005

How to achieve broadband and high-speed CARS microscopy simultaneously?

- Broadband CARS
  - ☺ Broadband range
  - ☹ Low speed~3.5 ms





Jr C. H. et al. Nature Photonics, 2014

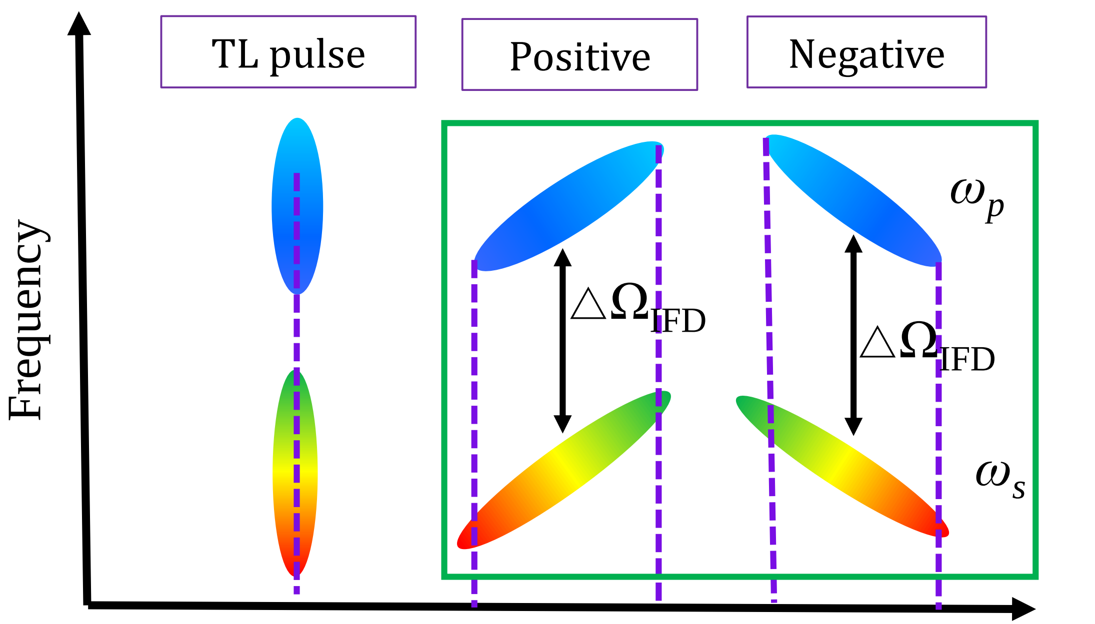
Phase-controlled pulse for CARS excitation

Femtosecond pulse — Picosecond pulse

$E_{p_0}(t)e^{-i\omega_{p0}t}$

$\alpha = \frac{8(\ln 2)^2\Phi_2}{\pi(\tau_0^4 + 16(\ln 2\Phi_2)^2)}$

$E_{p_0}(t)e^{-i\omega_{p0}t - i\frac{\alpha}{2}t^2}$



$\Omega_{IFD} = \omega_{p0} - \omega_{s0} + \alpha\tau$

- Chirp by glass rod

Sellmeier dispersion formula

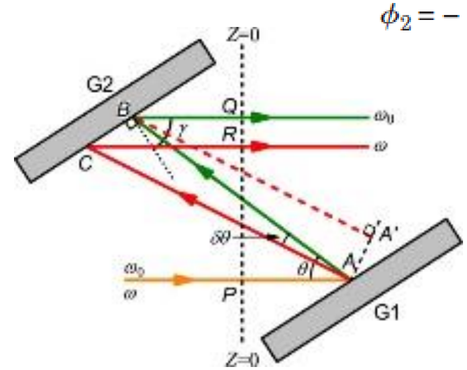
$$n^2(\lambda) - 1 = \frac{B_1\lambda^2}{\lambda^2 - C_1} + \frac{B_2\lambda^2}{\lambda^2 - C_2} + \frac{B_3\lambda^2}{\lambda^2 - C_3}$$

B_1	1.81651371
B_2	0.428893641
B_3	1.07186278
C_1	0.0143704198
C_2	0.0592801172
C_3	121.419942

$$\phi_2 = \frac{\lambda^3}{2\pi c^2}\frac{d^2 n}{d\lambda^2}L$$

- Chirp by grating pairs

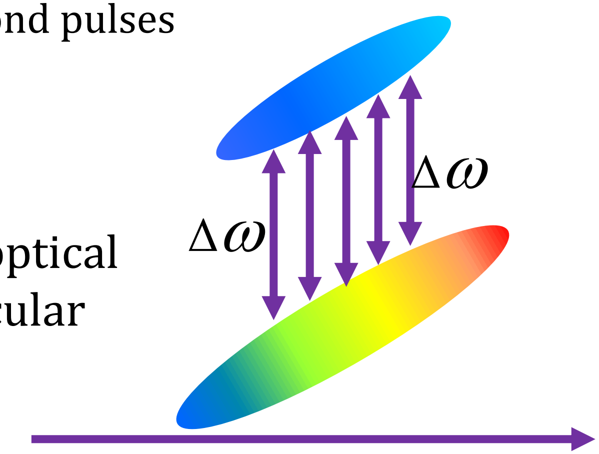
$$\phi_2 = -\frac{\lambda^3 Z}{\pi c^2 d^2}\left[1 - \left(\frac{\lambda}{d} - \sin\theta\right)^2\right]^{-3/2},$$

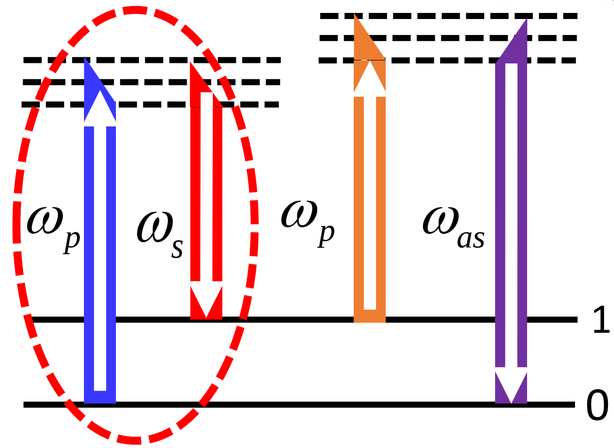


*Concentrate optical power into a single Raman vibrational mode-> **Spectral Focusing***

Spectral focusing CARS

- Two broadband femtosecond pulses
- Same chirp

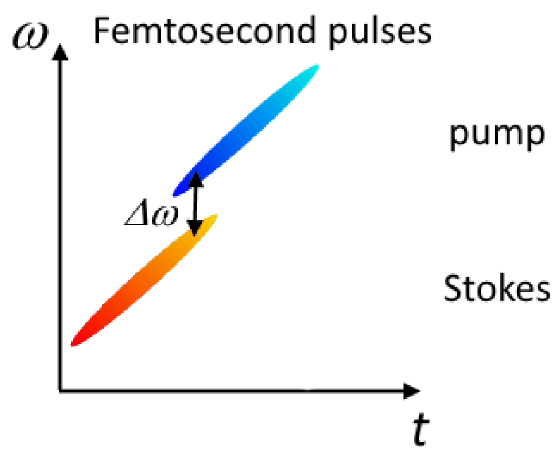


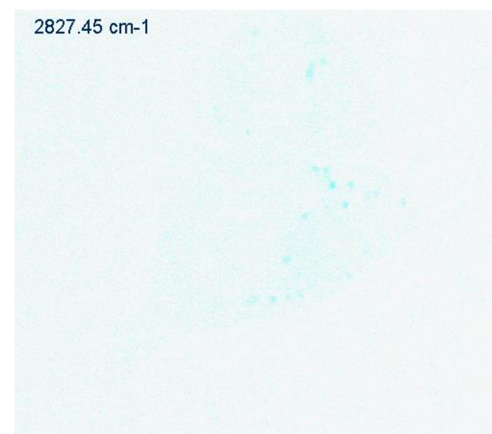


D. Fu, *et al*. J. Phy. Chem. B. 2013

☺ High sensitivity:
Concentrate most of the optical power into a single molecular vibration

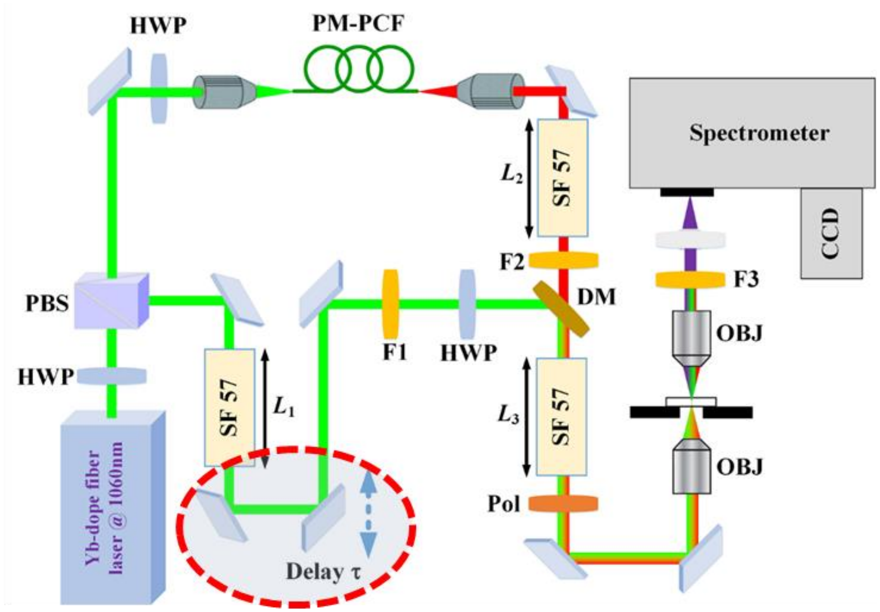
☺ Broadband detection:
Scanning delay-time can excite different molecular vibrations





☺ High resolution:
Flexible and precise control of Linear mapping between delay time and IFD

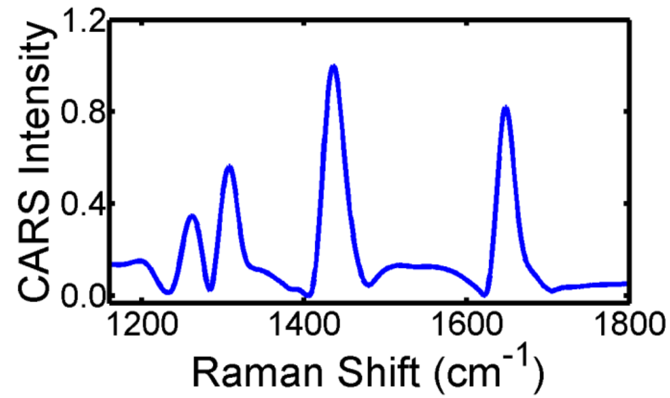
Spectral focusing CARS



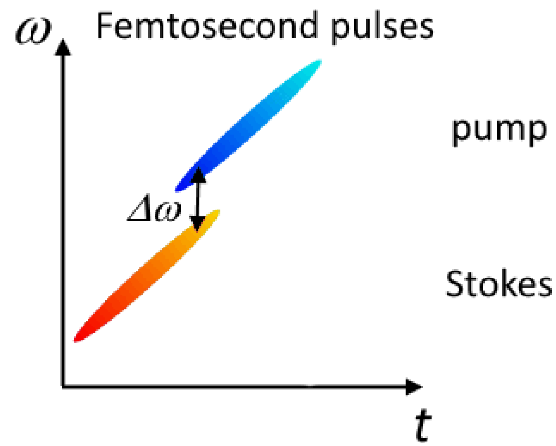
Mechanical motion

UTS Motorized Linear Stages, Newport

Broadband CARS spectra of olive oil



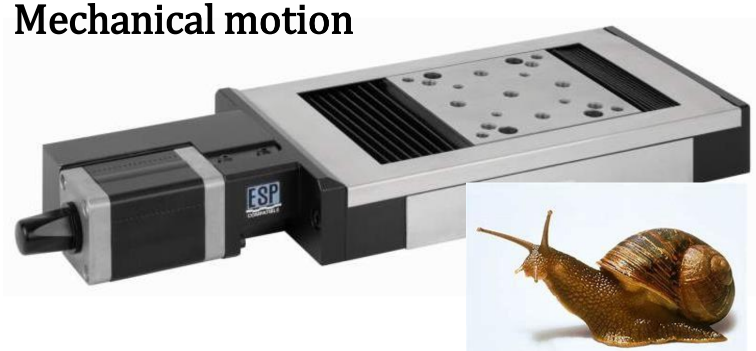
- Travel Range 2 mm
- Maximum Speed 20 mm/s
- Measurement time >100 ms/pixel



K. Chen, T. Wu, HY. WEI, and Y LI, Opt. Lett. 2016

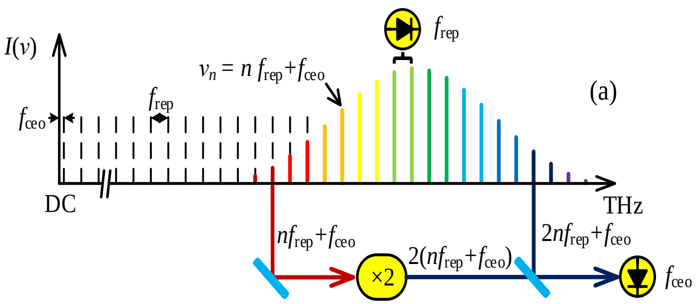
From mechanical scanning to optical scanning

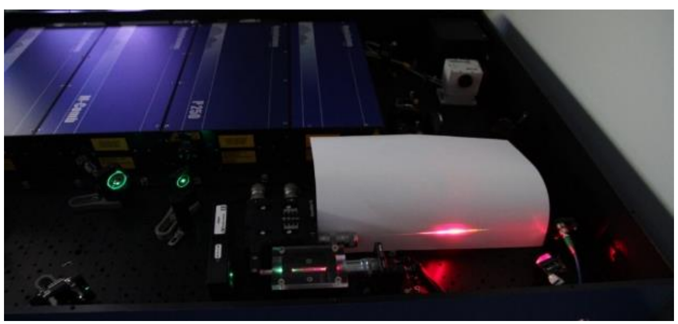
- **Mechanical motion**



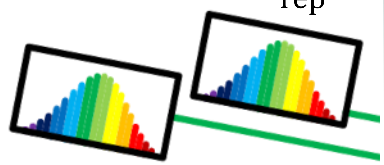
	Mechanical	Optical
Scanning speed	slow	fast
Scanning stability	low	high
Enable dynamics analysis	limited	yes

- **Dual-comb optical scanning**

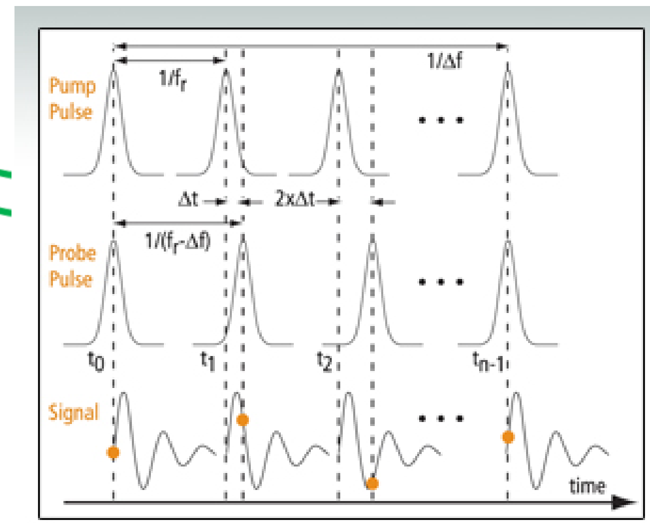




Comb1 f_{rep}



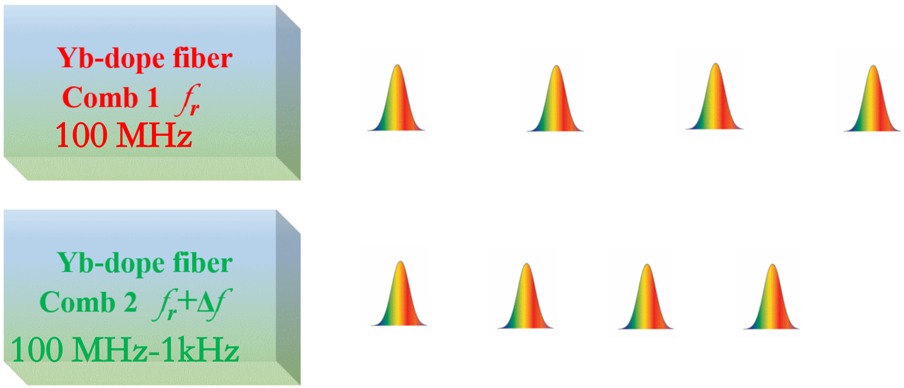
Comb2 $f_{rep}+\delta f_{rep}$



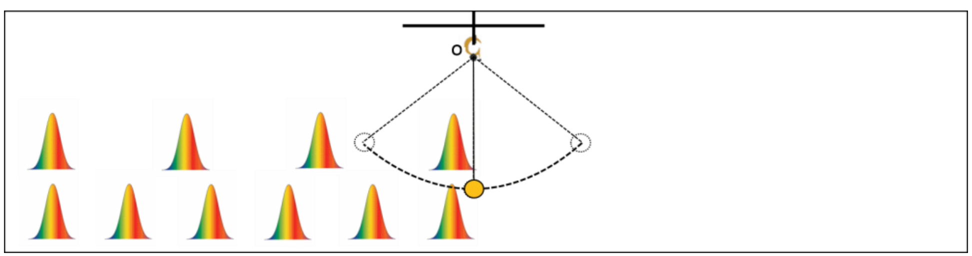
Dual-comb asynchronous optical sampling

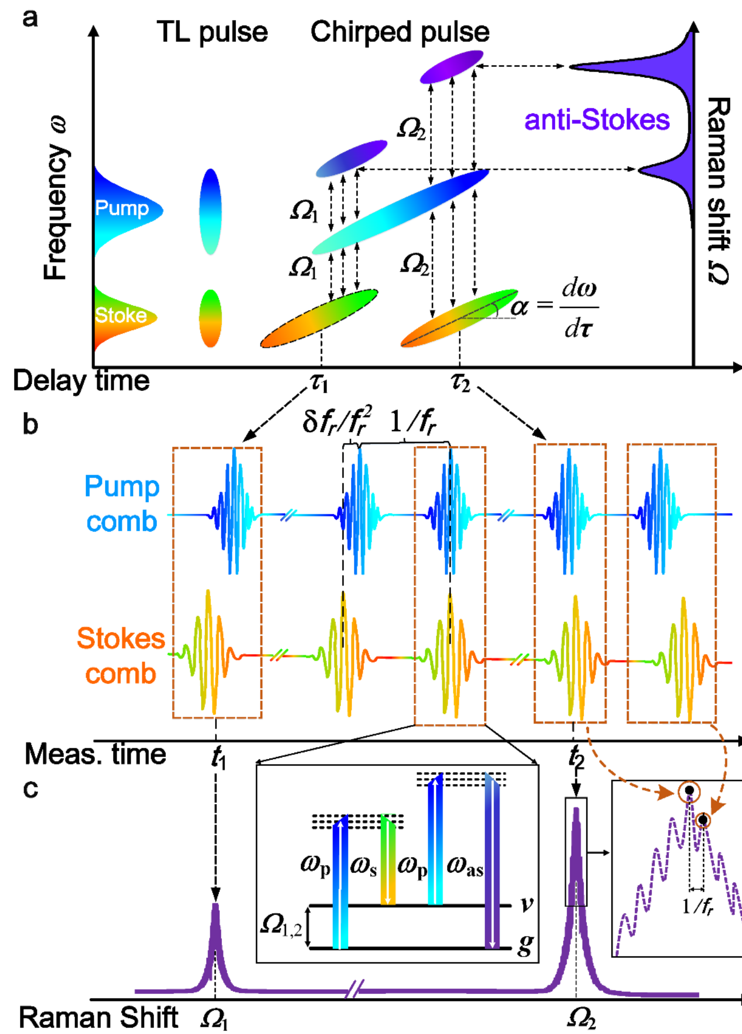
Principle of phase-controlled dual-comb CARS

- Dual-comb asynchronous optical sampling
  ->motionless configuration
  ->High speed scanning



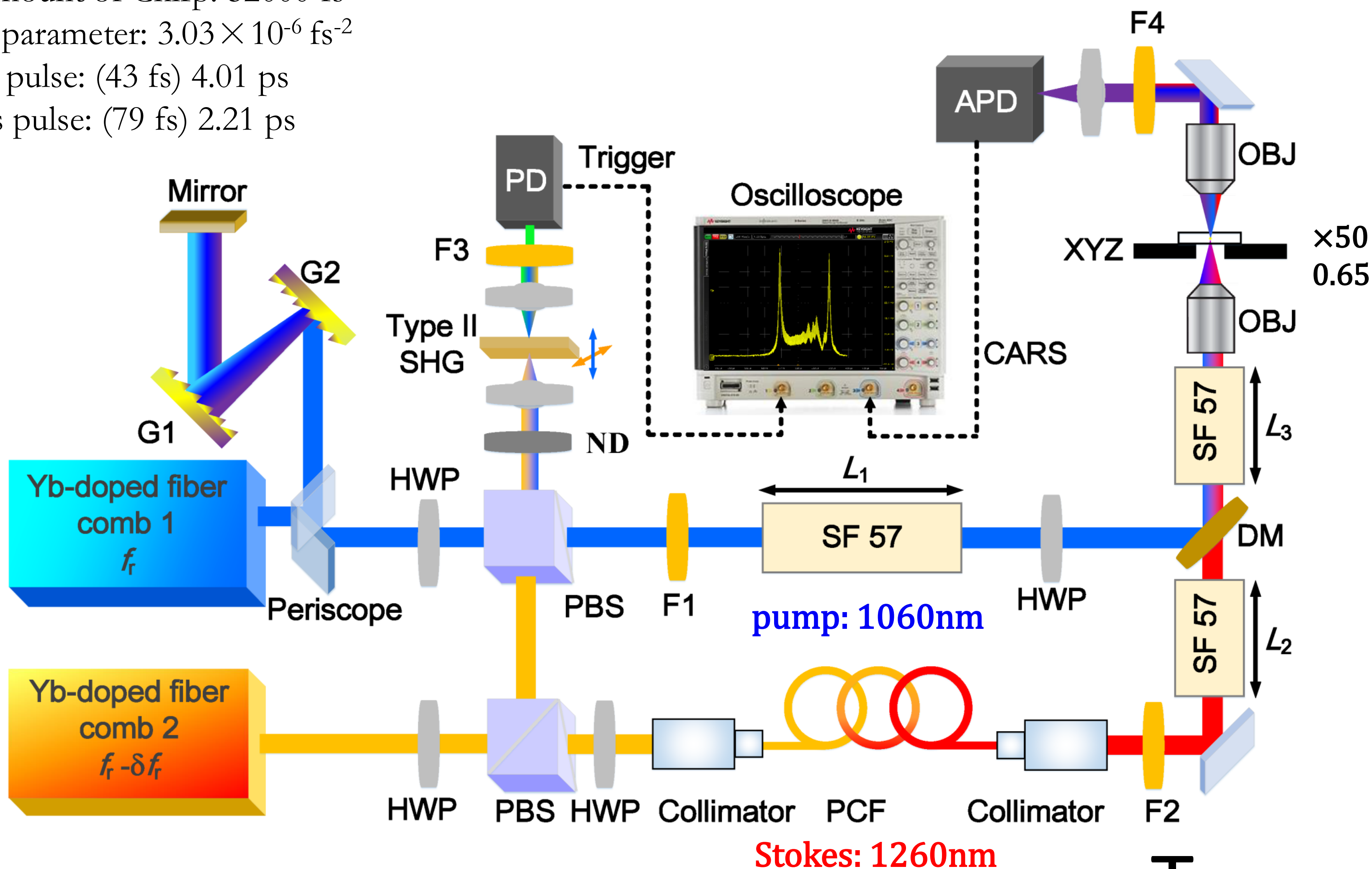
- Phase-controlled dual-comb
  ->Same chirp
  -> Spectral focusing CARS excitation





Dual-comb CARS experimental system

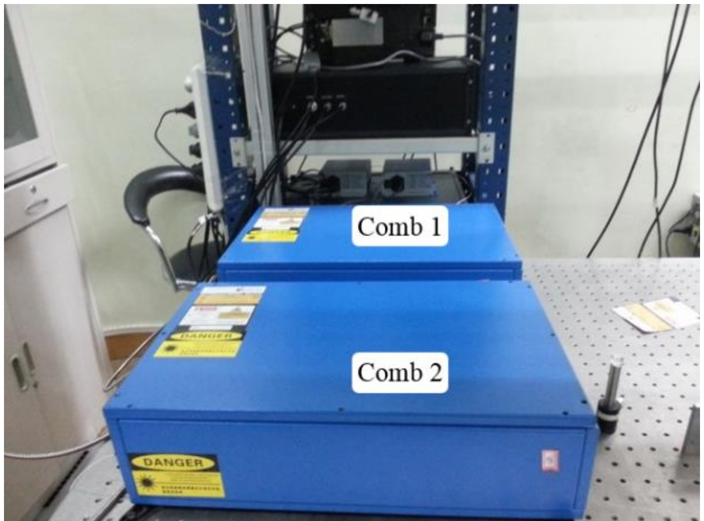
- The amount of Chirp: 52000 fs^2
- Chirp parameter: 3.03×10^{-6} fs^{-2}
- Pump pulse: (43 fs) 4.01 ps
- Stokes pulse: (79 fs) 2.21 ps



K. Chen, T. Wu, T. Chen, HY. Wei and *et al.*, Optics Letters, 42(18), 2017

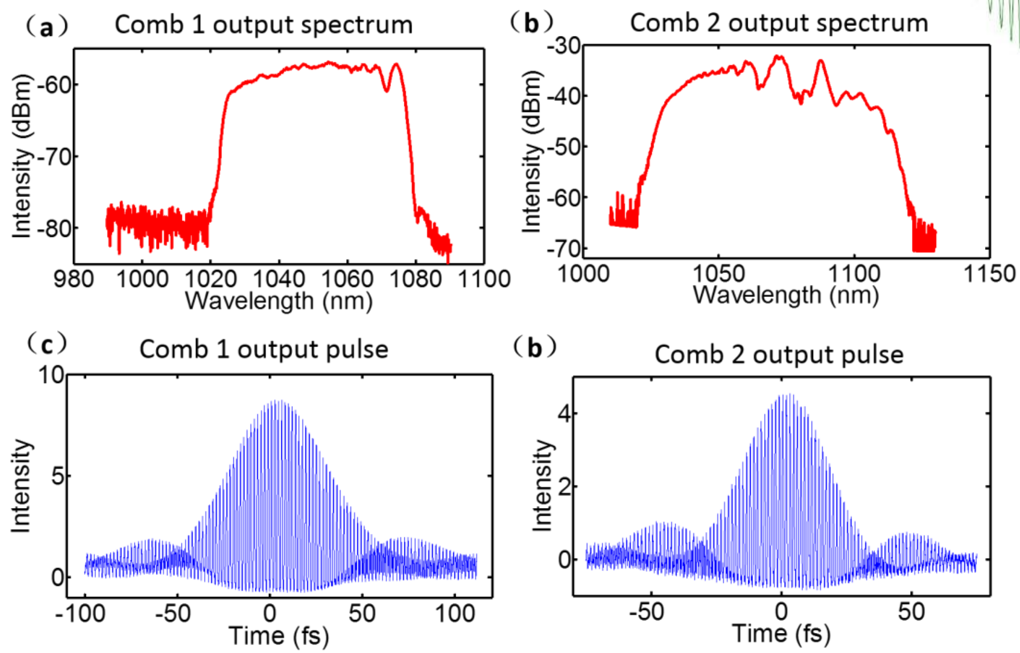
Dual-comb CARS experimental system

◆ **Dual-comb Source**



Frequency standard source

Rubidium atomic clock

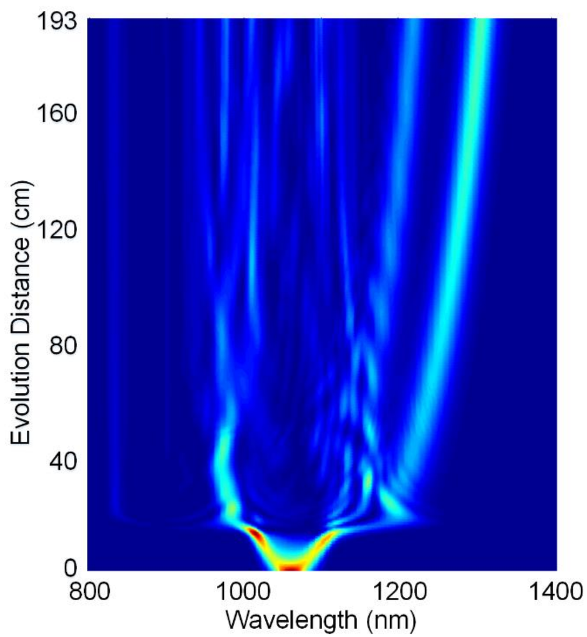


Comb 1: frep~100 MHz±100kHz
center wavelength ~1050 nm
pulse width ~65 fs

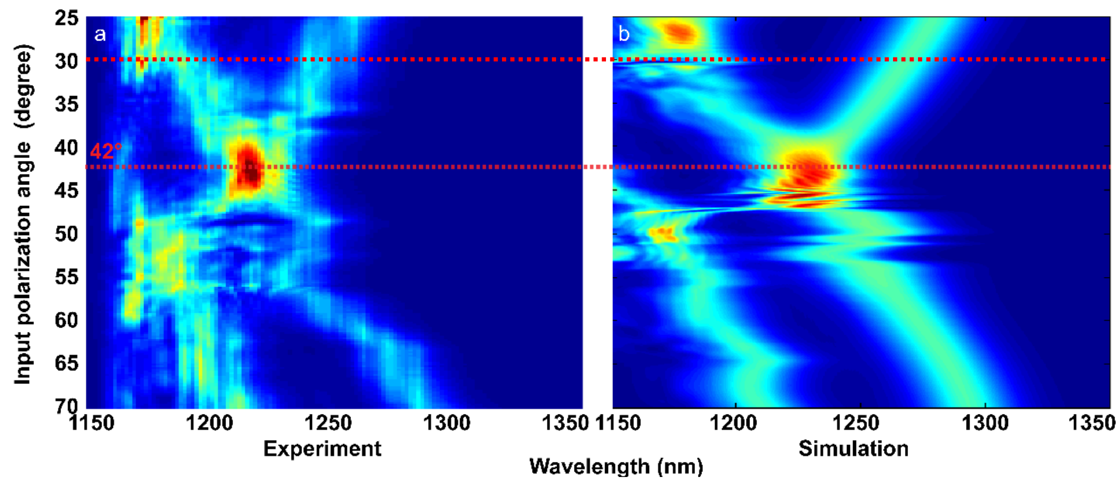
Comb 2: frep~100 MHz±100kHz
center wavelength ~1060 nm
pulse width ~43 fs

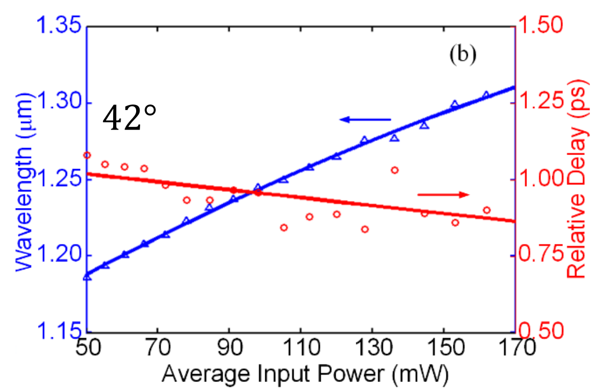
Dual-comb CARS experimental system

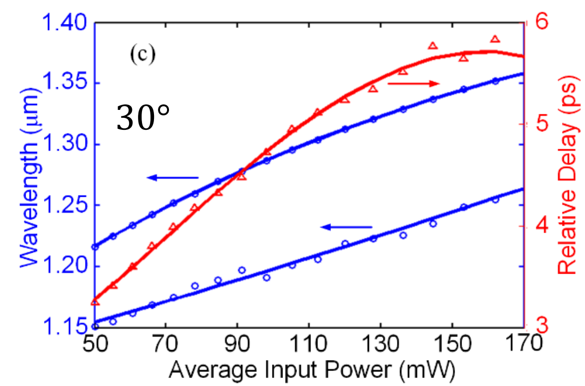
◆ Generation of Stokes Beam



NKT Photonics

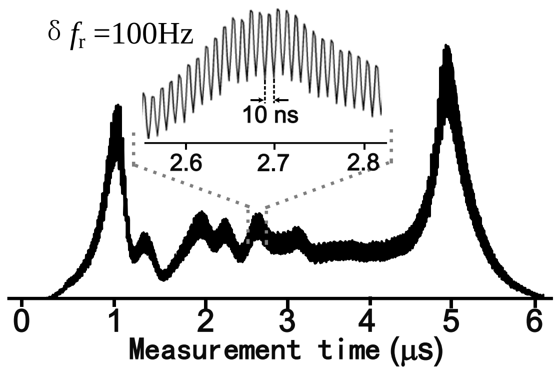


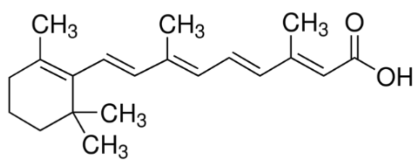




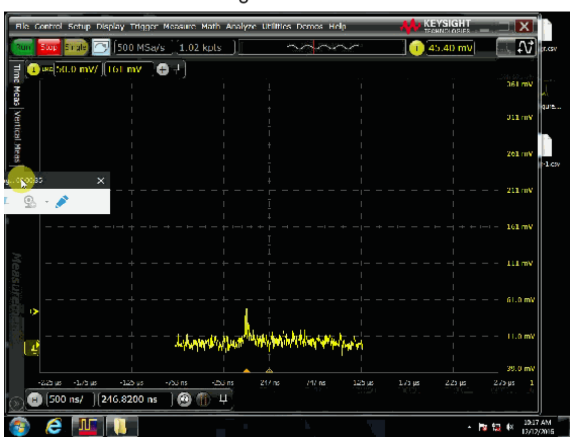
Dual-comb CARS experimental system

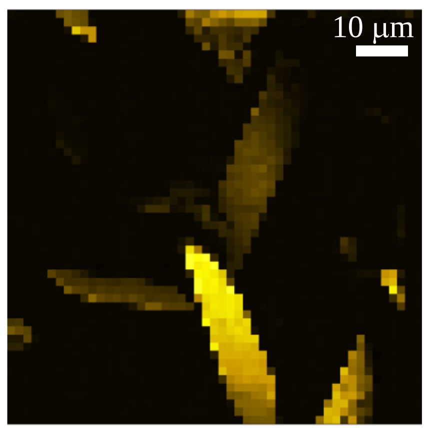
◆ Data acquisition and processing

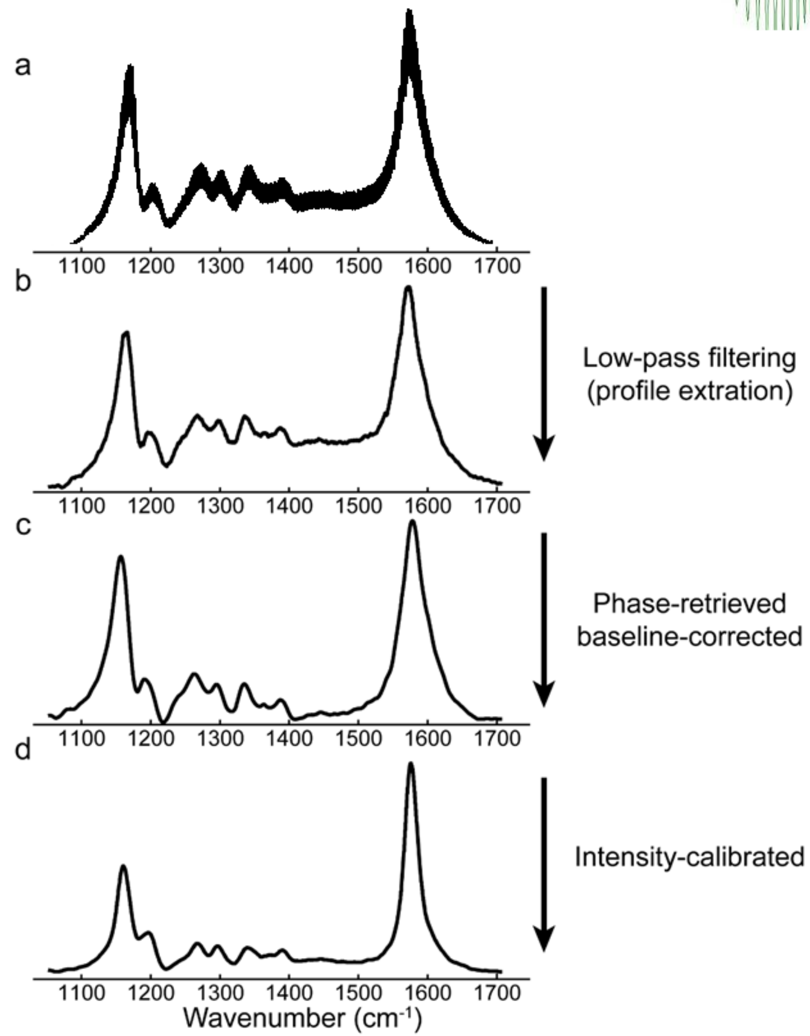




Retinoic acid (RA)







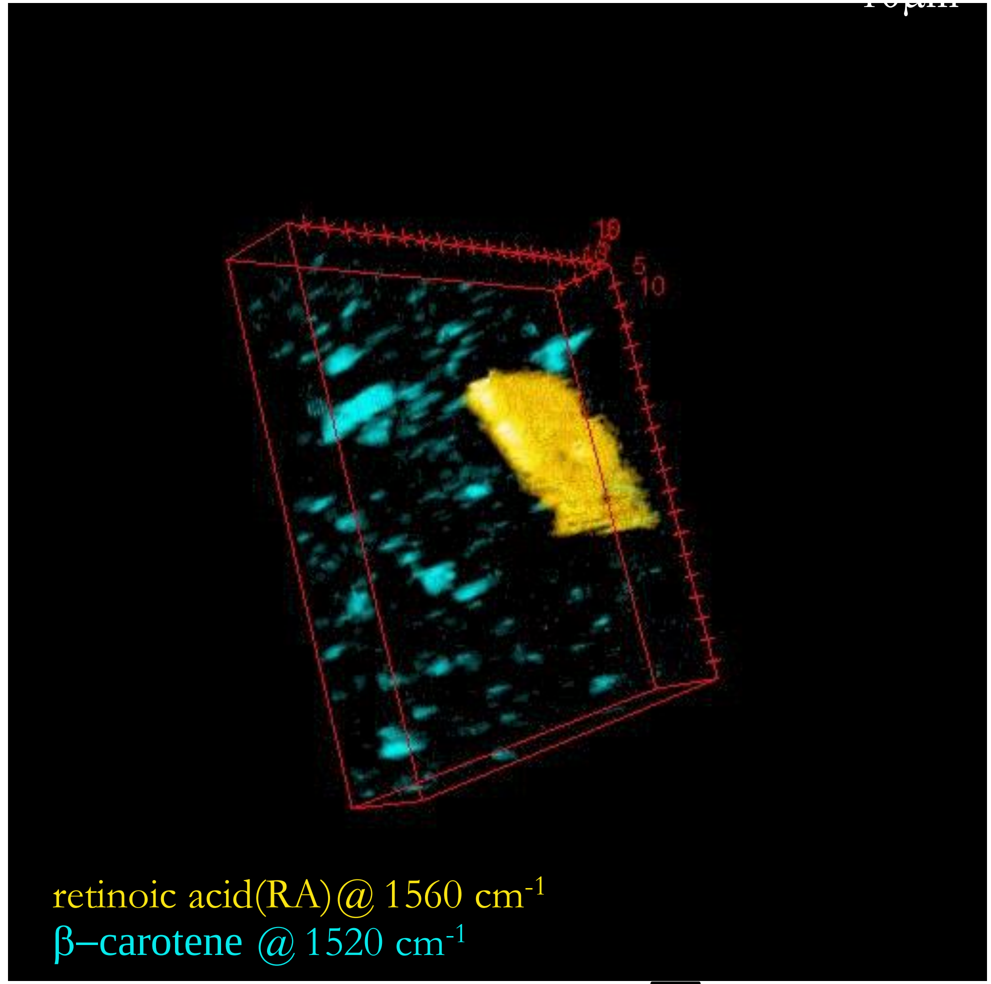
Dual-comb CARS microscopy

◆ High-speed broadband CARS microscopy

CARS 3D imaging for mixture of β-carotene and retinoic acid (RA)

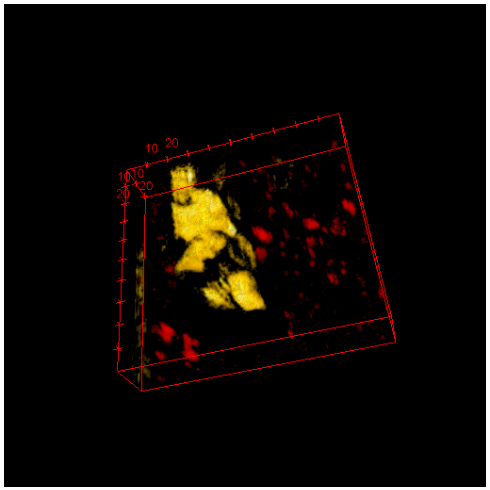
- Imaging size:
  100 μm × 100 μm× 20 μm
- Pixel size :
  1 μm × 1 μm× 1 μm

- Spectral span:1100-1700 cm^{-1}
- Spectral measurement time: 0.5 ms
- Spectral resolution: 12 cm^{-1}
- Pixel refresh rate: 1200 Hz
- Imaging speed: 8.3 s/frame



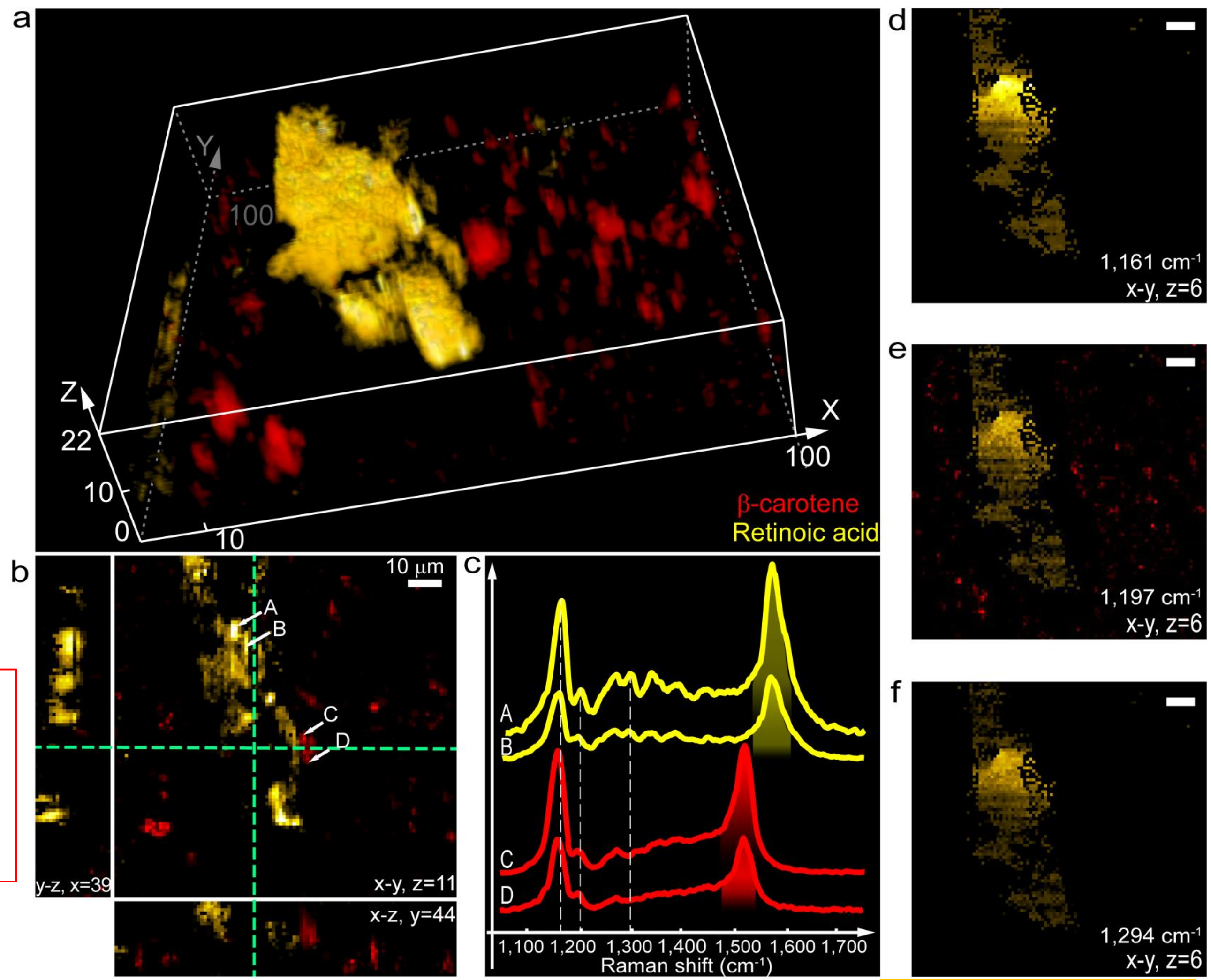
Dual-comb CARS microscopy

◆ High-speed broadband CARS microscopy

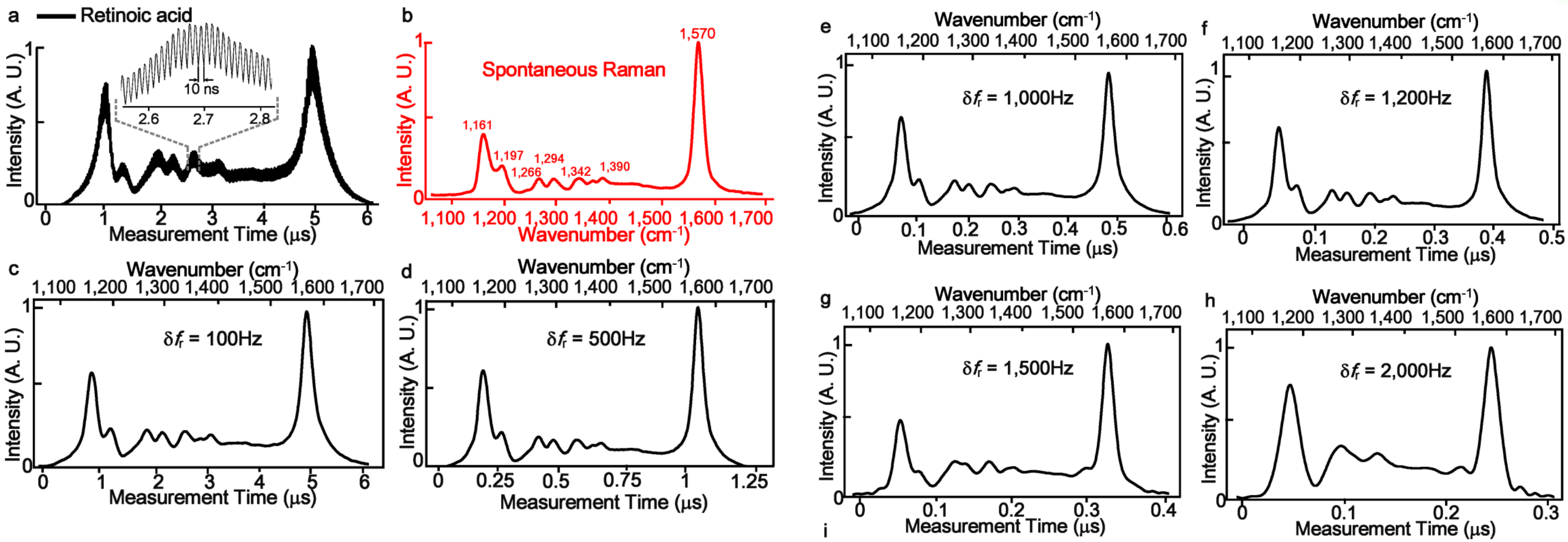


CARS 3D imaging for mixture of β-carotene and retinoic acid (RA)

- Imaging size:
  100 μm × 100 μm× 21 μm
- Pixel size：
  1 μm × 1 μm× 1 μm



Performance of spectral focusing dual-comb CARS microscopy



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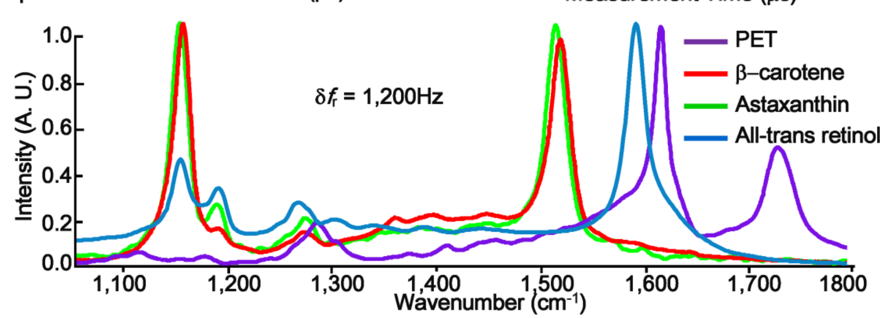
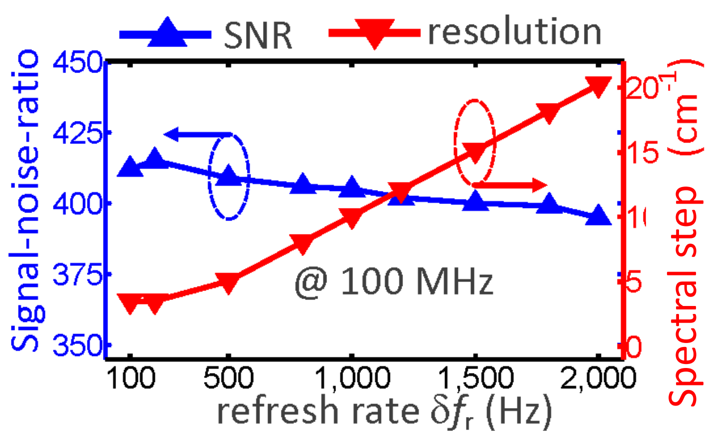




Performance of spectral focusing dual-comb CARS microscopy

Repetition frequency difference δf_r

Refresh rate δf_r

Delay time step $\Delta\tau = \dfrac{\delta f_r}{f_r^2}$

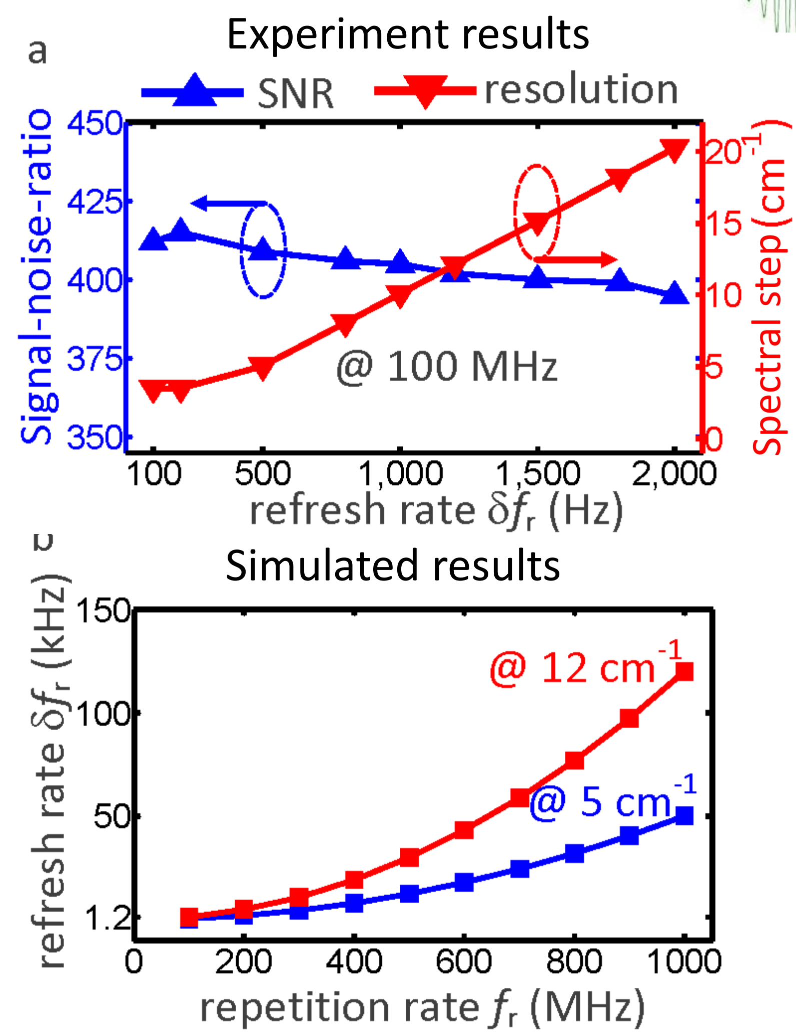
Real delay time $\tau_{real} = \dfrac{1}{f_r}$

Effect delay time $\tau_{eff} = \tau_{pump} + \tau_{Stokes}$

Effect measurement time $t_{eff} = \dfrac{\tau_{eff}}{\Delta\tau} \cdot \dfrac{1}{f_r} = \tau_{eff} \dfrac{f_r}{\delta f_r}$

Spectral step $\Delta\Omega = \Delta\tau \cdot \alpha = \dfrac{\delta f_r}{f_r^2} \cdot \alpha$

Duty cycle $dc = \dfrac{t_{eff}}{t_{real}} = \tau_{eff} \cdot f_r$



Conclusion

The proposed dual-comb CARS technique enables high speed and broadband measurement

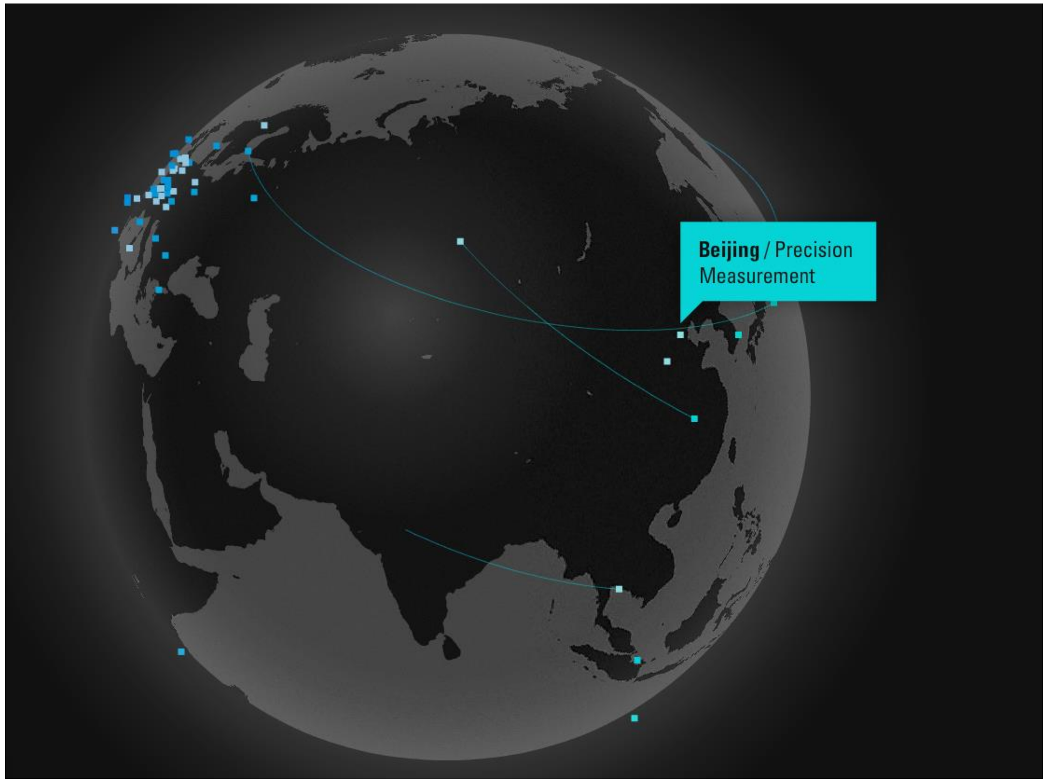
- **Advantages**
  - ☺ High-speed and Multiplex nature
  - ☺ Motionless and Synchronization-free
  - ☺ The SNR of CARS spectrum is not significantly decreased when increase refresh rate
  - ☺ Refresh rate (δf_r) is proportional to the square of repetition frequency (f_r)

  ——1GHz combs may achieve up to **hundreds of kHz refresh rate**

  while the resolution and SNR remain the same in theory

- **Disadvantages**
  - ☹ Low duty cycle ~6×10^{-4}
  - ☹ Low pulse energy utilization

Acknowledgement



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Thanks for listening!