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

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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

Multiplex/Broadband vs Narrowband CARS

- Narrowband CARS
  - High speed ~ 6.4 μs
- Narrowband

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

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

Evans C L, et al. PNAS, 2005
Phase-controlled pulse for CARS excitation

Femtosecond pulse

Picosecond pulse

\( E_p(t) e^{-i\omega_p t} \)

\( E_p(t) e^{-i\omega_p t - \alpha t^2} \)

Second-order phase control

Chirp by glass rod

Sellmeier dispersion formula

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

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

Chirp by grating pairs

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

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Spectral focusing CARS

- Two broadband femtosecond pulses
- Same chirp

*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


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Spectral focusing CARS

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UTS Motorized Linear Stages, Newport

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Broadband CARS spectra of olive oil

- Travel Range 2 mm
- Maximum Speed 20 mm/s
- Measurement time >100 ms/pixel
From mechanical scanning to optical scanning

◆ Mechanical motion

<table>
<thead>
<tr>
<th></th>
<th>Mechanical</th>
<th>Optical</th>
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<tbody>
<tr>
<td>Scanning speed</td>
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<td>Scanning stability</td>
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<td>Enable dynamics analysis</td>
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</table>

◆ Dual-comb optical scanning

\[
\text{Comb1 } f_{\text{rep}}
\]

\[
\text{Comb2 } f_{\text{rep}} + \delta f_{\text{rep}}
\]

Dual-comb asynchronous optical sampling
Principle of phase-controlled dual-comb CARS

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

Yb-dope fiber
Comb 1 $f_r$
100 MHz

Yb-dope fiber
Comb 2 $f_r+\Delta f$
100 MHz-1kHz

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

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Dual-comb CARS experimental system

- The amount of Chirp: 52000 fs$^2$
- Chirp parameter: $3.03 \times 10^{-6}$ 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

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Dual-comb CARS experimental system

◆ Dual-comb Source

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

Rubidium atomic clock

Frequency standard source

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Dual-comb CARS experimental system

- Generation of Stokes Beam
Dual-comb CARS experimental system

Data acquisition and processing

\[ \delta f_r = 100 \text{Hz} \]

Retinoic acid (RA)

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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 x 100 μm x 21 μm
- Pixel size: 1 μm x 1 μm x 1 μm

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Performance of spectral focusing dual-comb CARS microscopy
Performance of spectral focusing dual-comb CARS microscopy

- Repetition frequency difference $\delta f_r$
- Refresh rate $\delta f_r$
- Delay time step $\Delta \tau = \frac{\delta f_r}{f_r^2}$
- Real delay time $\tau_{real} = \frac{1}{f_r}$
- Effect delay time $\tau_{eff} = \tau_{pump} + \tau_{Stokes}$
- Effect measurement time $t_{eff} = \frac{\tau_{eff}}{\Delta \tau} \cdot \frac{1}{f_r} = \tau_{eff} \frac{f_r}{\delta f_r}$
- Spectral step $\Delta \Omega = \Delta \tau \cdot \alpha = \frac{\delta f_r}{f_r^2} \cdot \alpha$
- Duty cycle $dc = \frac{t_{eff}}{t_{real}} = \tau_{eff} \cdot f_r$

Experiment results

Simulated results

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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 ($\delta f_r$) 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 $\sim 6 \times 10^{-4}$
  - Low pulse energy utilization
Acknowledgement

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Thanks for listening!