Modern Raman Spectroscopy: 
Has the sleeping giant finally awoken?*

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thanks to: Bonner Denton*
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Andrew Whitley
Stated differently: Has Raman spectroscopy made the transition from research tool to widely used routine analytical technique?

To get your attention:

1985: Raman sales ~ $5 million/year          FTIR: ~$400 million

2008: Raman ~ 200 million                FTIR: $600 – 800 million

(Note: Vendor names are informational, and do not imply an endorsement or “rating”)
Rayleigh scattering, no frequency change. Intensity proportional to $\nu^4$.

Cyclohexane

488 nm laser

Raman scattering, at longer wavelength (lower frequency) than input light

488 nm rejection filter in front of camera
Raman spectroscopy in 1985:

- double monochromator
- single channel (PMT)
- high f/#
- tricky alignment required

Problems:

- low sensitivity
- slow (~20 min/spectrum)
- often high background
- intensities strongly dependent on alignment and focusing

Main vendors:

- Spex
- ISA/Jobin-Yvon
- Dilor
- Jasco

Sales: ~$5 million/year, compared to ~$400 million/year for FTIR
Non-research applications: negligible
Some factors underlying Raman growth:

1983: Fiber optic Raman for remote sampling

1986: FT-Raman at 1064 nm greatly reduced background

1989: Diode laser/ CCD Raman at 785 nm

1990-92: Holographic laser rejection filters

1995: Low f/#, holographic spectrometer and integrated fiber optic sampling

1996: ASTM Raman shift standards

1994-98: Low f/# imaging spectrographs with CCD detectors

1997: Luminescent intensity standards

2000-: Automatic Raman shift calibration

2002: NIST Luminescence standards

2004: Hand-held portable spectrometer
1983: Fiber optic Raman for remote sampling (McCreery, Hendra, Fleischmann)

Commercial examples of fiber optic probes:

Horiba-JY:

BW Tek:

Kaiser Optical:

Bruker:
Fluorescence was a big problem for practical samples:

Even a very low concentration of a fluorescer can overwhelm Raman scattering, due to much greater cross section

488 nm laser, with 488 rejection filter preceding camera
1986: FT-Raman at 1064 nm greatly reduced background (Chase, Hirschfeld)

Raman signal
\[
\text{S/N ratio} = \frac{\text{Raman signal}}{(\text{Raman} + \text{“fluorescence”} + \text{dark signal})^{1/2}}
\]

Good news: fluorescence usually much smaller at 1064 nm than with 400-633 nm lasers

Bad news: dark signal higher for NIR detectors, multiplex “disadvantage” and weaker Raman scattering at 1064 nm

Important practical consequences:

• broadened utility of Raman to many commercially important samples (impure organics, polymers, pharma)

• added significantly to vendors and sales (Bio-Rad, Bruker, Nicolet, Perkin Elmer, Varian)
1989: Diode laser/ CCD Raman at 785 nm (Williamson, Bowling, McCreery)

• 785 nm lasers enable much of the reduction in fluorescence available with FT Raman, but retain the advantages of CCD detectors

• diode lasers are also compact, with low power and cooling demand

• CCD’s are OUTSTANDING Raman detectors:

  • multichannel (512 - 2000 in parallel)
  • very low dark signal (< 0.001 e⁻/sec)
  • sensitive (QE> 95% in visible)
  • 2D imaging possible
1990-92: Holographic laser rejection filters (Carrabba, Owen)

1995: Low f/# spectrometers and integrated fiber optic sampling (Owen, Battey, Pelletier, Kaiser, ISA, Chromex, Andor, …)
<table>
<thead>
<tr>
<th></th>
<th>1985 (PMT/Double)</th>
<th>2008 (CCD/Single)</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantum efficiency</td>
<td>0.15</td>
<td>0.95</td>
<td>6.3 X</td>
</tr>
<tr>
<td>Collection ($A_D\Omega$)</td>
<td>$4 \times 10^{-4}$</td>
<td>$5 \times 10^{-4}$</td>
<td>1.2</td>
</tr>
<tr>
<td>Transmission</td>
<td>0.1</td>
<td>0.6</td>
<td>6</td>
</tr>
<tr>
<td># Channels</td>
<td>1</td>
<td>1600</td>
<td>1600</td>
</tr>
</tbody>
</table>

Total signal gain (same acquisition time) 72,000
Scanning/PMT
20 minutes
SNR ~ 28

CCD multichannel
5 seconds
SNR ~ 280

SNR improvement for same acquisition time: 100-500 X
Decrease in acquisition time for same SNR: $10^3$ to $10^4$

Comparable to or greater improvement than that for FT-NMR and FTIR
1996: ASTM Raman shift standards (Carrabba, McCreery, 7 labs for input)

2000: Automatic Raman shift calibration (Allen, Zhou, US pat. 6,141,095)

Automatic Raman Shift calibration:

Bruker “Sure-Cal”

Zhao, Carrabba, Allen, Applied Spectroscopy 2002, 56, 834

Tylenol, intentionally unstable diode laser at 785 nm

standard deviation of Raman shift = 0.066 cm\(^{-1}\) over 20 days

(Data from Jun Zhao)
1997: Luminescent intensity standards (Ray, Frost, McCreery)

2002- NIST Luminescence standards (Choquette, Etz, Hurst, Blackburn)

The problem:

- true relative intensities usually unknown
- uncorrected libraries are instrument dependent
- validation of regulatory data (e.g. pharma)

The consequences:

(spectra from Steve Choquette)
NIST standard reference material luminescent standards

**Cr-doped glass with calibrated luminescent output in response to Raman laser**


Standard is run like any other sample, then software mathematically corrects spectrum.

>230 sold so far, mostly for 785 nm
Uncorrected SRM 2241 on 4 commercial Systems.

Instrument response function significantly distorts relative intensities

(spectra from Steve Choquette)
(much of remaining differences due to $v^4$ factor)
Major progress toward widespread Raman use, 1985-2005:

- $10^4$ to $10^5$ sensitivity increase, 100-500 X in SNR
- Compact, low power, integrated systems available
- Much broader applicability
- Standards for frequency and intensity, automatic shift calibration
- Variety of sampling modes: fiber optic, through glass, in-vivo
- Proven industrial applications in process control and QC

HOWEVER:

- Spectrometer prices bottomed out at ~ $50K due to laser and CCD costs
- Not yet suitable for field applications, not really portable
2004-08 Hand-held portable spectrometer (Carron, DeltaNu, Ahura)

• 785 nm laser
• < 1 – 5 lbs weight
• > 4 hrs battery life
• built-in library for rapid ID
• portable and shock tolerant
• vials, non-contact, through-bag
• $15,000 - $35,000
DeltaNu/Intevac Photonics

remote observation to 3 meters
Ahura Scientific

toluene + acetonitrile

(slide from Chris Brown)
Has the “giant” woken up?

1985: ISA/Horiba
     Spex
     Dilor

~ $5 million sales
(~$400 million for FTIR)

2008:

Vendors*:

Ahura Scientific
Bruker Optics
B&W Tek
Centice
DeltaNu
Foster&Freeman
Horiba/ISA
Jasco
Kaiser Optical
Ocean Optics
Perkin Elmer
PI/Acton
Renishaw
River Diagnostics
SEKI Technotron
Thermo
Varian

Some APPROXIMATE sales numbers:

2008 Raman sales: $201 million  (>40 X since 1985, CPI was 2X)

2008 FTIR sales: $600-800 million  (slow growth since 1985)

• largest segment in dollar value is microscopes with dispersive spectrometers

• portable systems dominate in terms of number of systems (> 2000 since 2006)

• 10-15% annual growth for all but FT-Raman, much higher for portable

• 785 nm most popular laser

• still looking for “killer” application, although fairly wide use in QC, pharma, polymers, drug and hazmat ID, forensics

A final, and persistent question:

Why don’t we do dispersive Raman with a 1064 nm laser, to obtain the same fluorescence reduction as in FT-Raman?
Silicon detectors (i.e. CCDs) are not sensitive to light beyond ~1100 nm, where nearly all of the Raman scattering exists from 1064 nm lasers.
Combine a 1064 nm laser with a dispersive spectrograph and specialized InGaAs array detector (DeltaNu/Intevac)

Captain Morgan Rum

FT-Raman, 1064 nm

Dispersive Raman, 1064 nm

(slide from Keith Carron)