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

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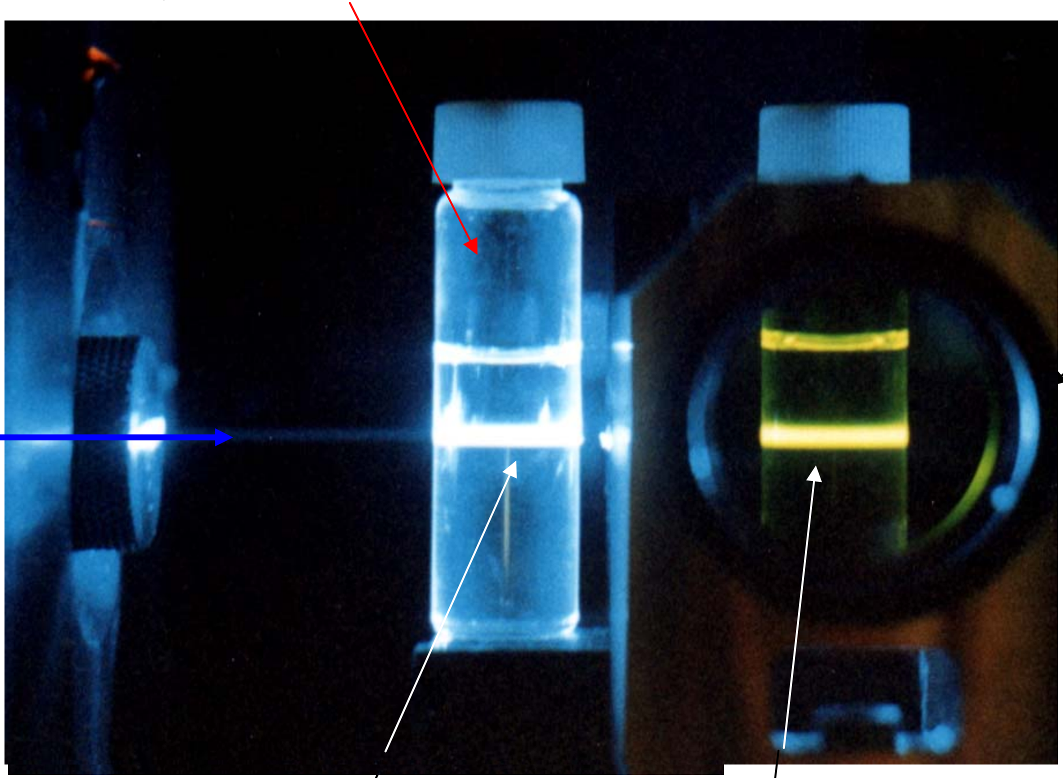
Stated differently: Has Raman spectroscopy made the transition from research tool to widely used routine analytical technique?

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”)



cyclohexane

488 nm rejection filter in front of camera

488 nm laser

Rayleigh scattering, no frequency change. Intensity proportional to ν^4

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

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

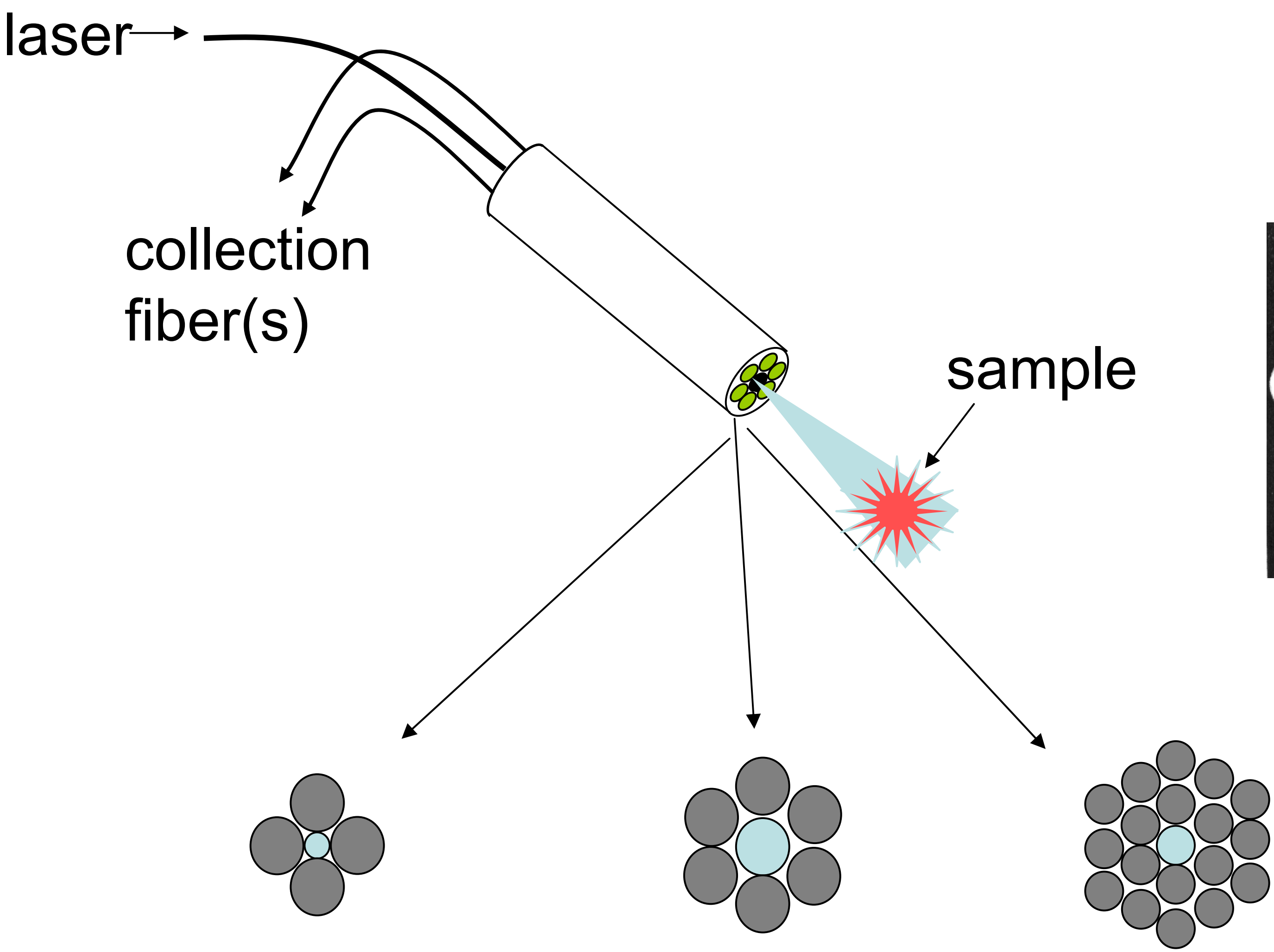
1997: Luminescent intensity standards

2000- Automatic Raman shift calibration

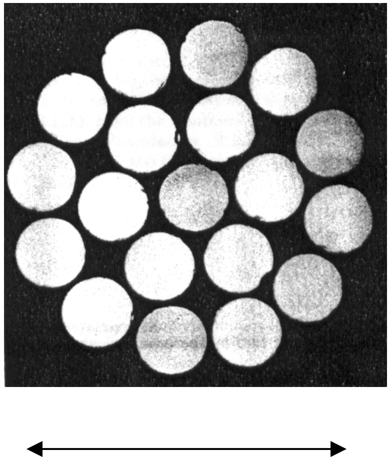
2002- NIST Luminescence standards

2004- Hand-held portable spectrometer

1983: Fiber optic Raman for remote sampling (McCreery, Hendra, Fleischmann)



18 around 1 photo

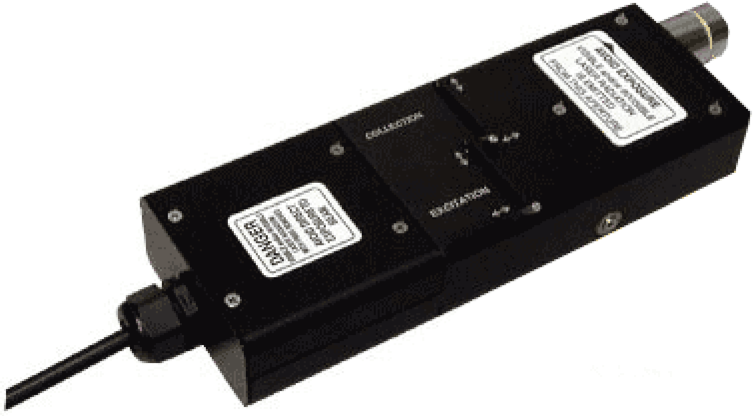


McCreery, Hendra, Fleischmann, *Anal. Chem.* **1983**, *55*, 146.
Schwab, McCreery, *Anal. Chem.* **1984**, *56*, 2199.

Commercial examples of fiber optic probes:

Horiba-JY:

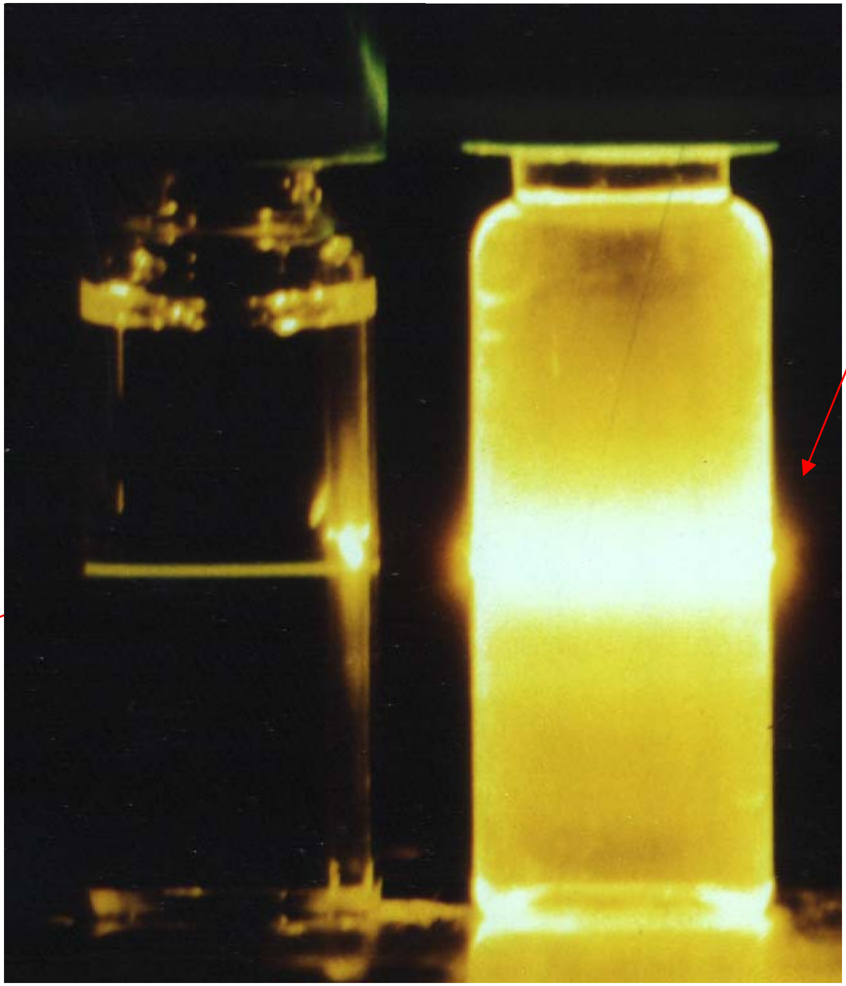
Kaiser Optical:



BW Tek:

Bruker:

Fluorescence was a big problem for practical samples:



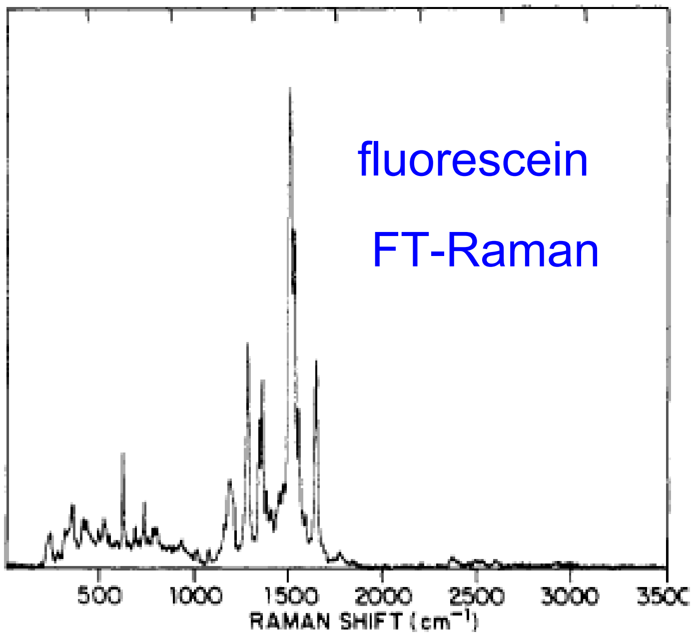
fluorescein fluorescence
(10^{-5} M)

cyclohexane
Raman
(9 M)

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

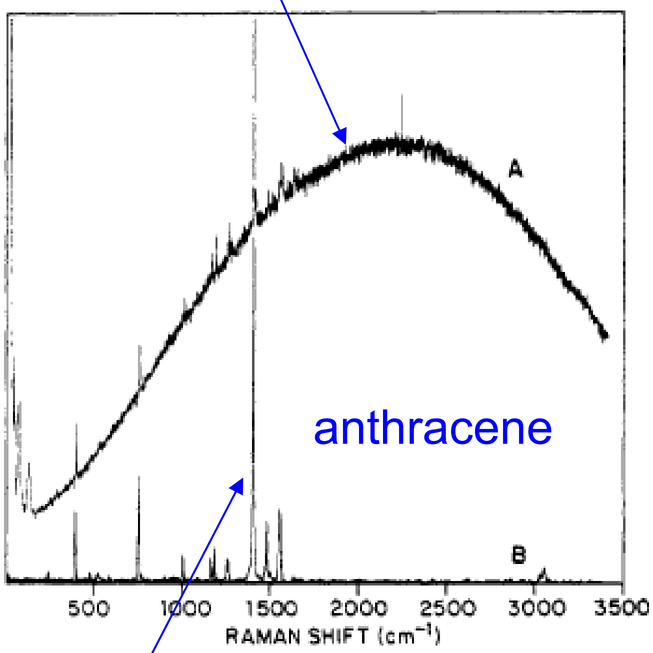
1986: FT-Raman at 1064 nm greatly reduced background (Chase, Hirschfeld)



fluorescein

FT-Raman

514.5 nm dispersive



anthracene

1064 nm FT-Raman

Chase, D. B.; Fourier transform Raman spectroscopy; *JACS* **1986**, *108*, 7485.
Hirschfeld, T.; Chase, B.; *Applied Spectroscopy* **1986**, *40*, 133.

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

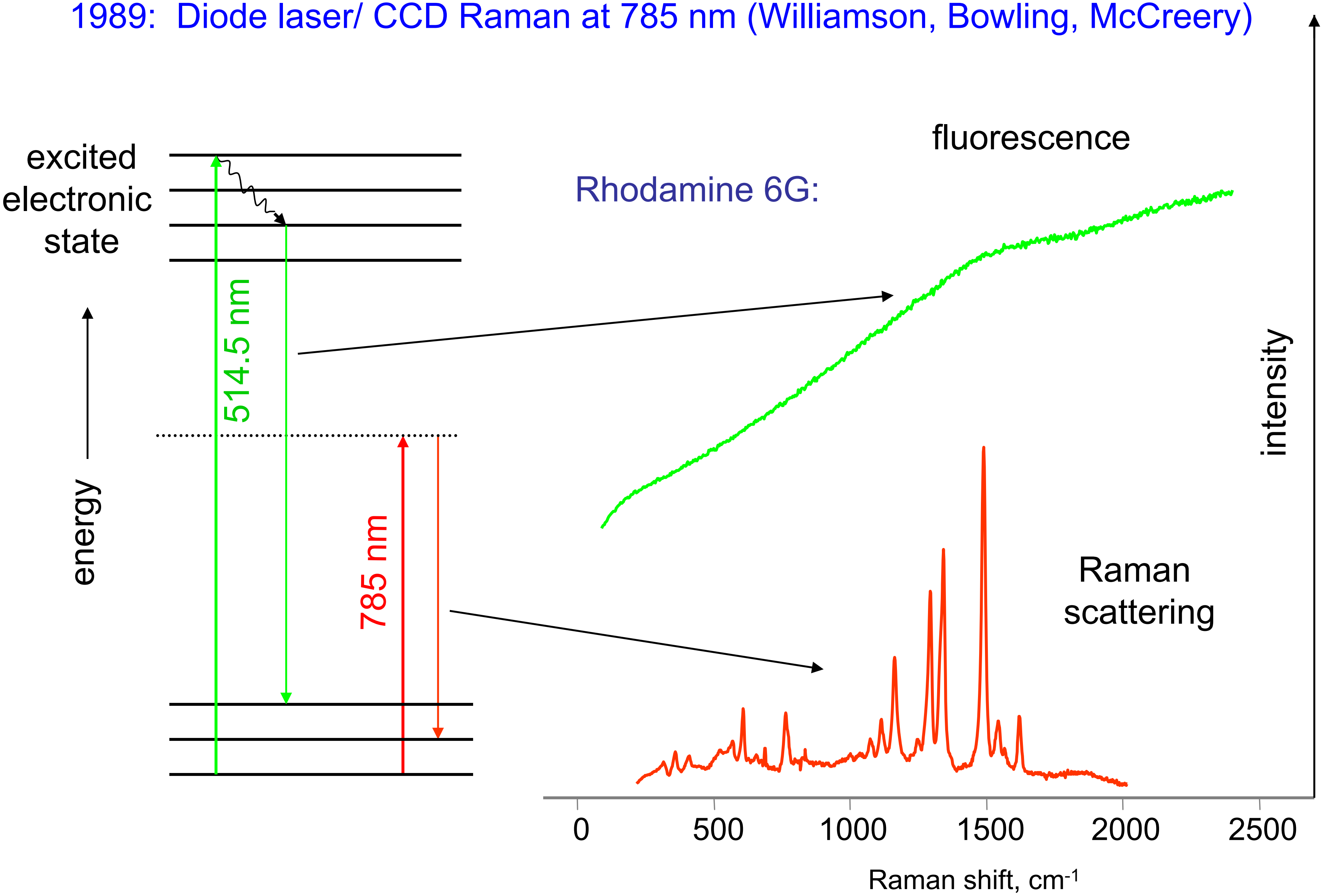
Good news: fluorescence usually much smaller at 1064 nm
than with 400-633 nm lasers

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

Important practical consequences:

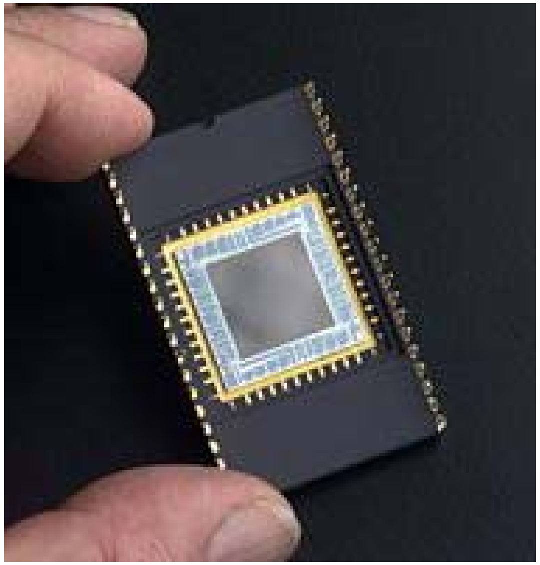
- broadened utility of Raman to many commercially important samples
(impure organics, polymers, pharma)
- added significantly to vendors and sales
(Bio-Rad, Bruker, Nicolet, Perkin Elmer, Varian)

1989: Diode laser/ CCD Raman at 785 nm (Williamson, Bowling, McCreery)



Williamson, Bowling, McCreery, ; *Applied Spectros.* **1989**, *43*, 372
Allred, McCreery, *Applied Spectroscopy* **1990**, *44*, 1229.
.

- 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



- 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

1990-92: Holographic laser rejection filters (Carrabba, Owen)

1995: Low f/# spectrometers and integrated fiber optic sampling
(Owen, Battey, Pelletier, Kaiser, ISA, Chromex, Andor,…)

	1985 (PMT/Double)	2008 (CCD/Single)	Improvement
Quantum efficiency	0.15	0.95	6.3 X
Collection ($A_D\Omega$)	4×10^{-4}	5×10^{-4}	1.2
Transmission	0.1	0.6	6
# Channels	1	1600	1600

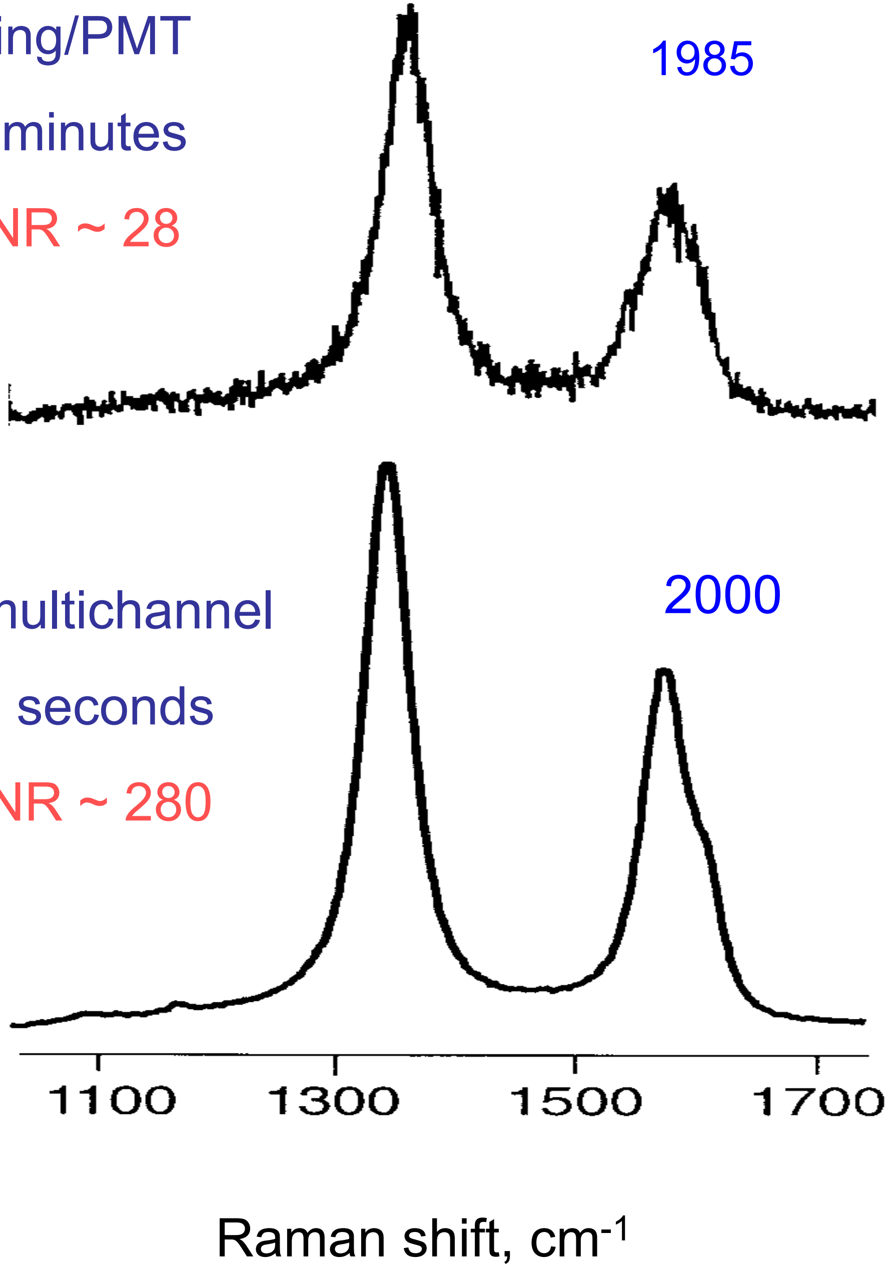
Total signal gain 72,000
(same acquisition time)

Scanning/PMT

20 minutes

SNR ~ 28

1985



CCD multichannel

5 seconds

SNR ~ 280

2000

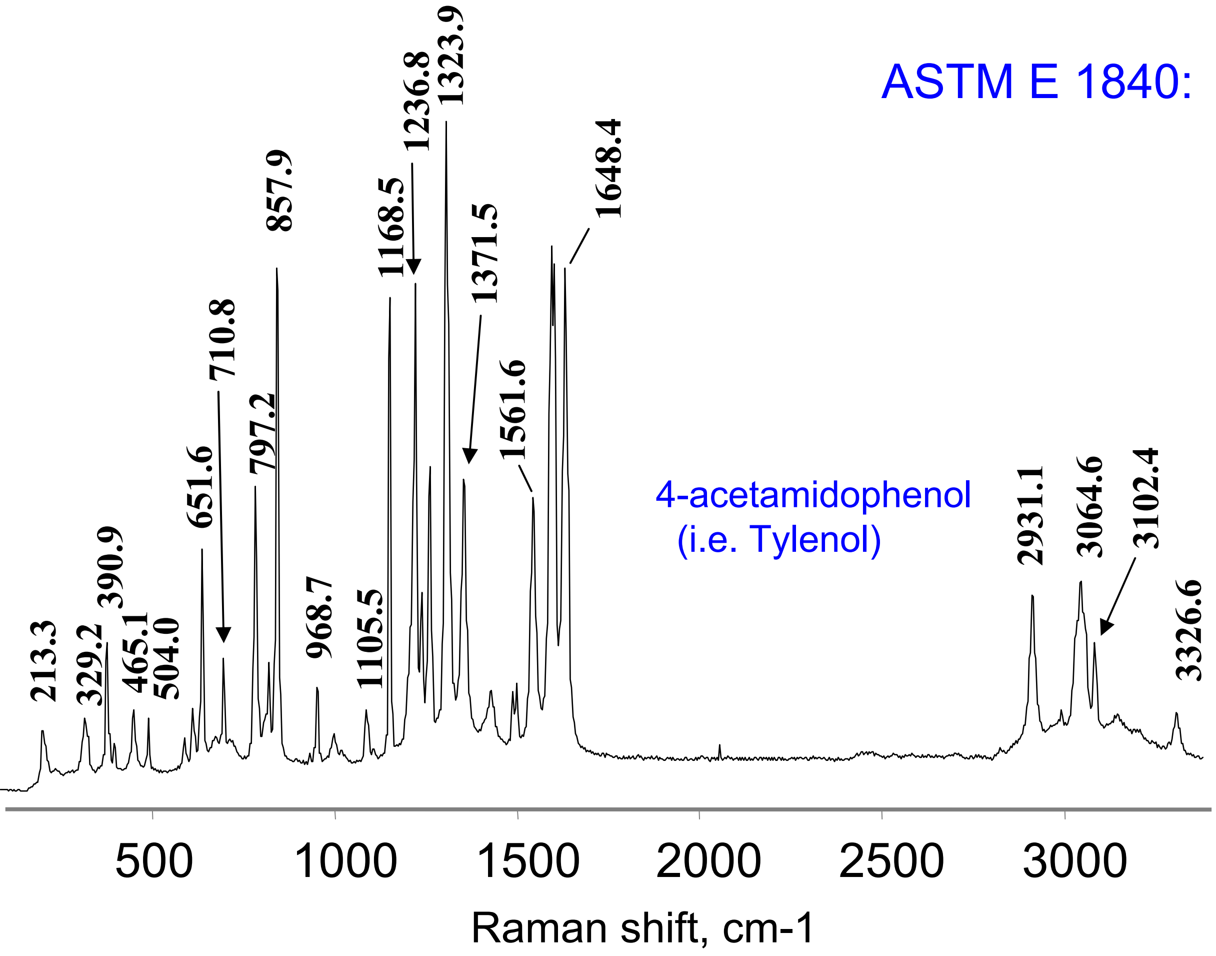
SNR improvement for same acquisition time: 100- 500 X

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)



ASTM E 1840:

4-acetamidophenol
cyclohexane
naphthalene
toluene/acetonitrile
sulfur
bis-methylstyrylbenzene
benzonitrile
indene
polystyrene

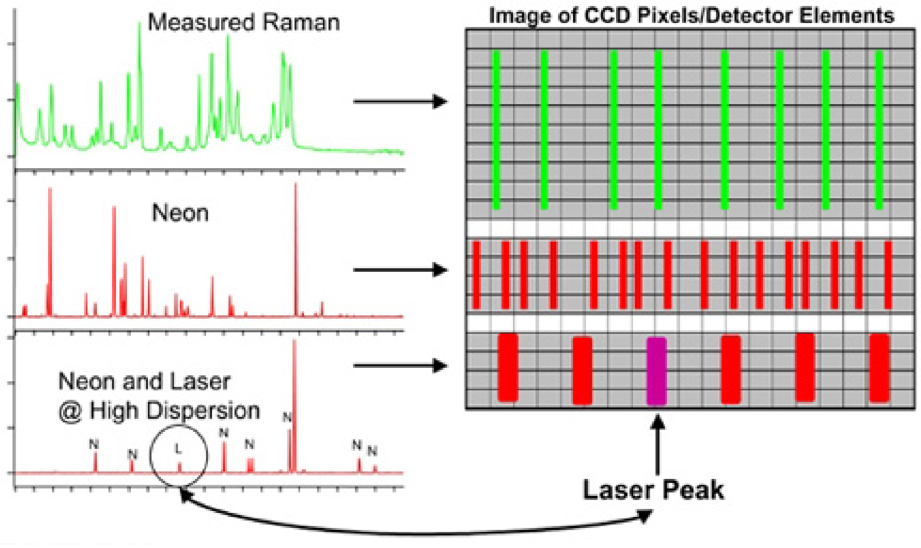
Raman shifts from 7 labs, all with standard deviation < 0.5 cm^{-1}

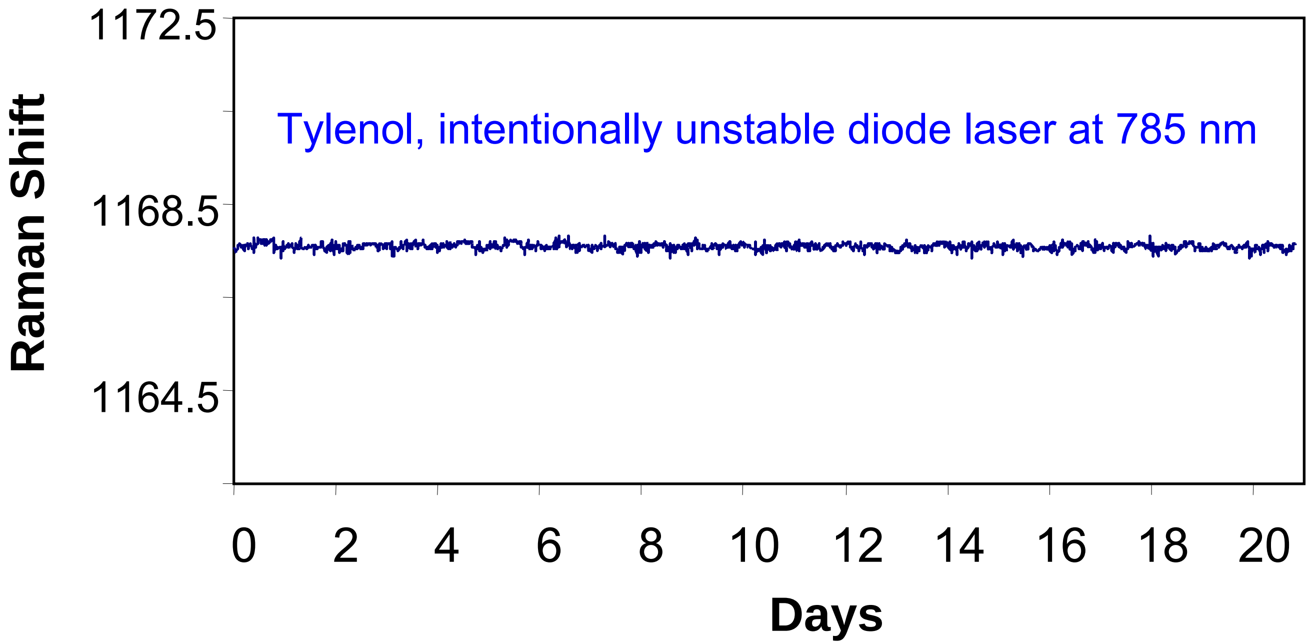
ASTM E 1840 Standard Guide for Raman Shift Standards for Spectrometer Calibration

Automatic Raman Shift calibration:

Bruker "Sure-Cal"

Allen, Zhou, US patent 6,141,095 (2000)
Zhao, Carrabba, Allen, *Applied Spectroscopy* **2002**, *56*, 834





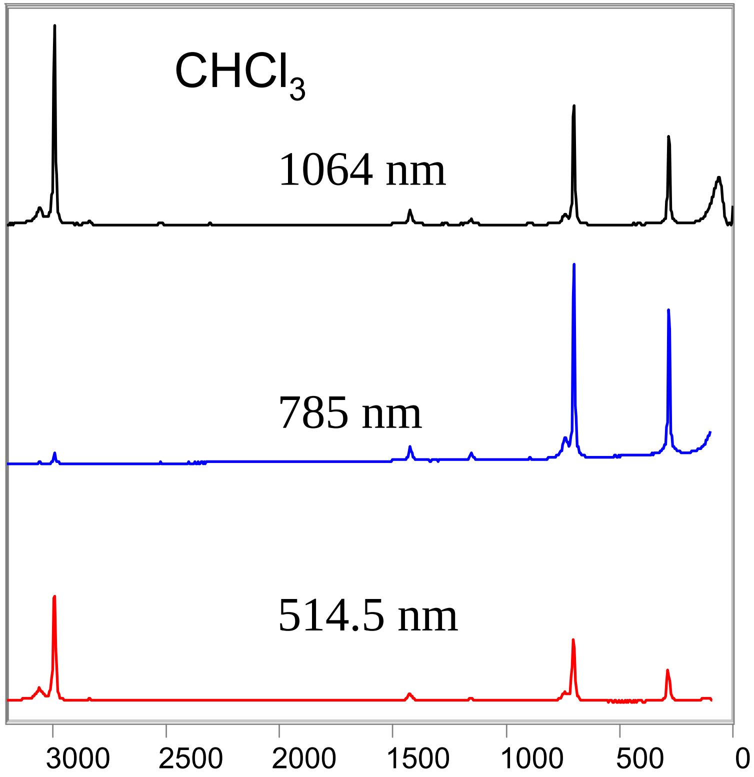
standard deviation of Raman shift = 0.066 cm^{-1} over 20 days

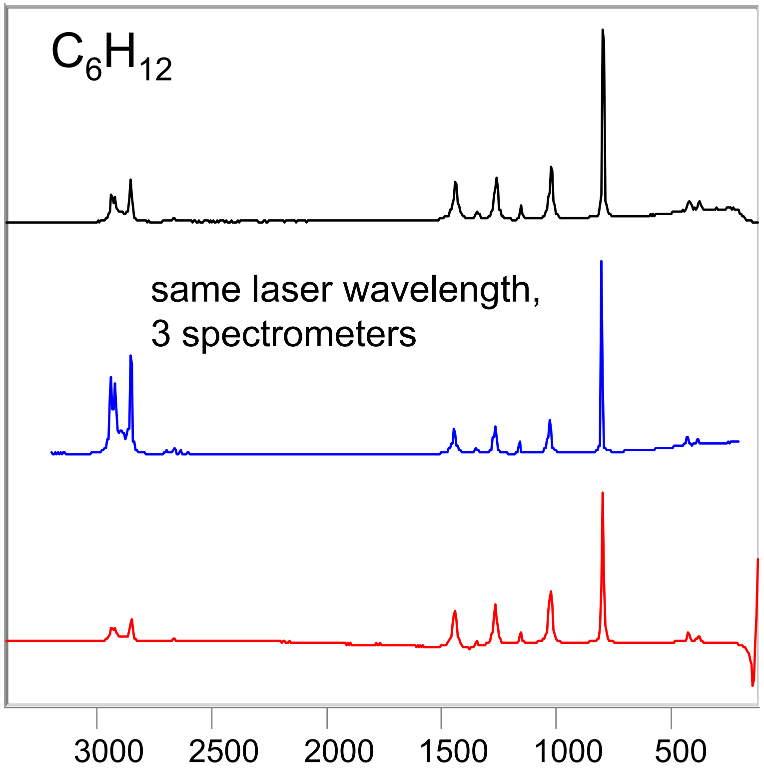
(Data from Jun Zhao)

1997: Luminescent intensity standards (Ray, Frost, McCreery)

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

The problem:





same laser wavelength,
3 spectrometers

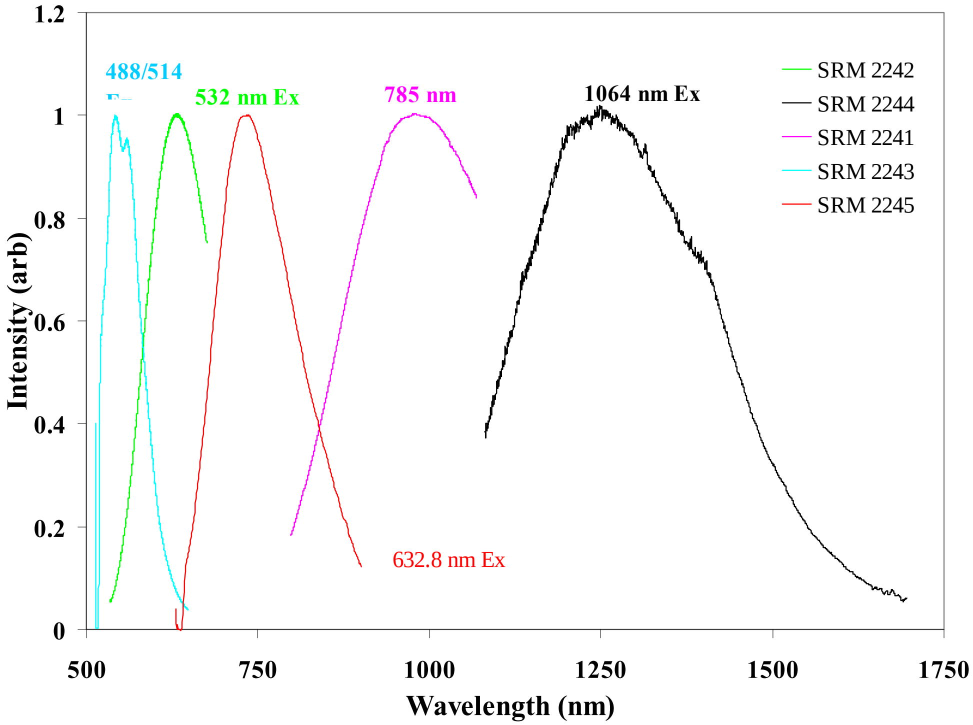
The consequences:

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

(spectra from Steve Choquette)

NIST standard reference material luminescent standards

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



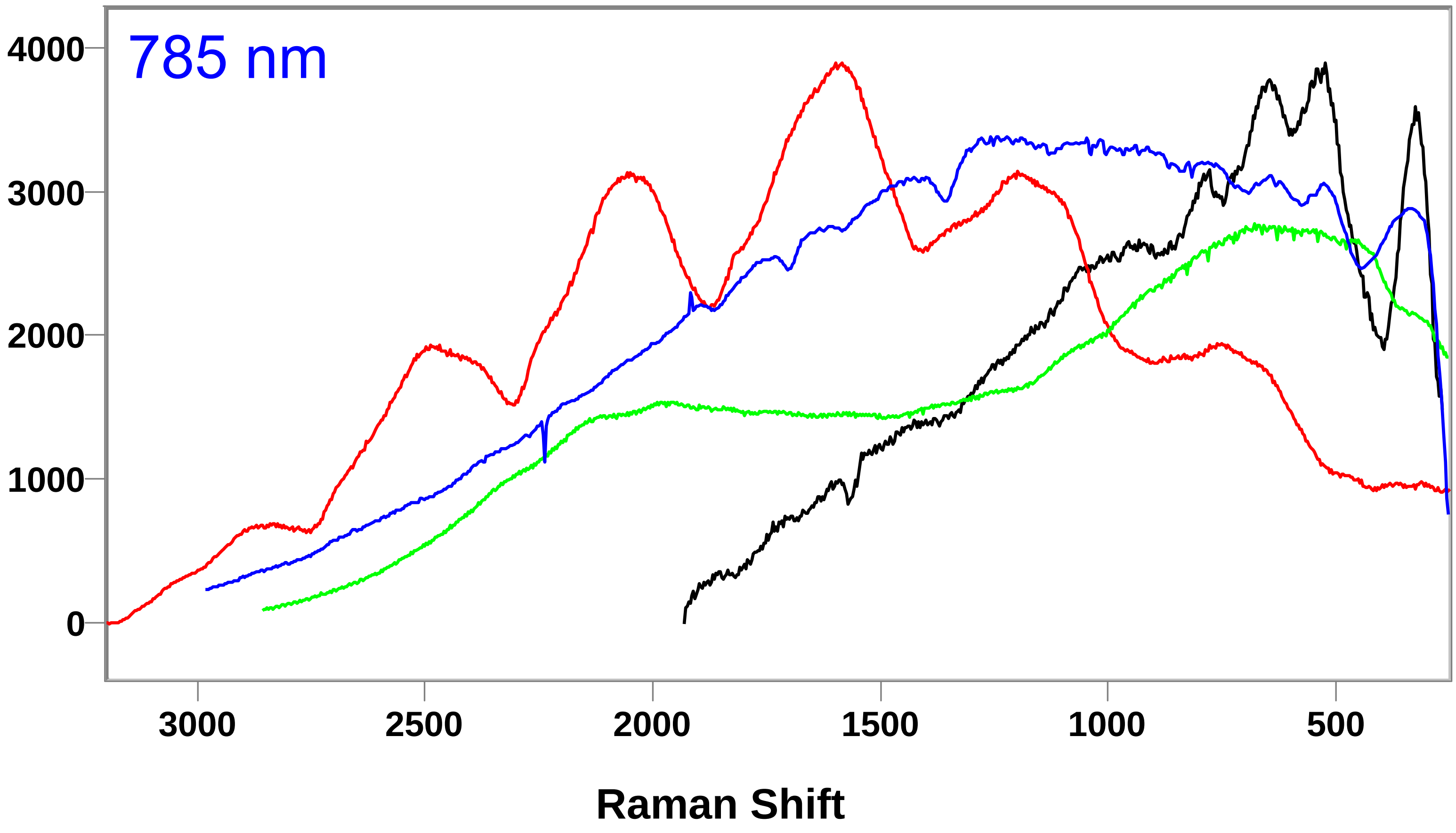
Standard is run like any other sample, then software mathematically corrects spectrum.

>230 sold so far, mostly for 785 nm

Hurst, Choquette, Etz, *Applied Spectroscopy* **2007**, *61*, 694.
Choquette, Etz, Hurst, Blackburn, Leigh, *Applied Spectroscopy* **2007**, *61*, 117.

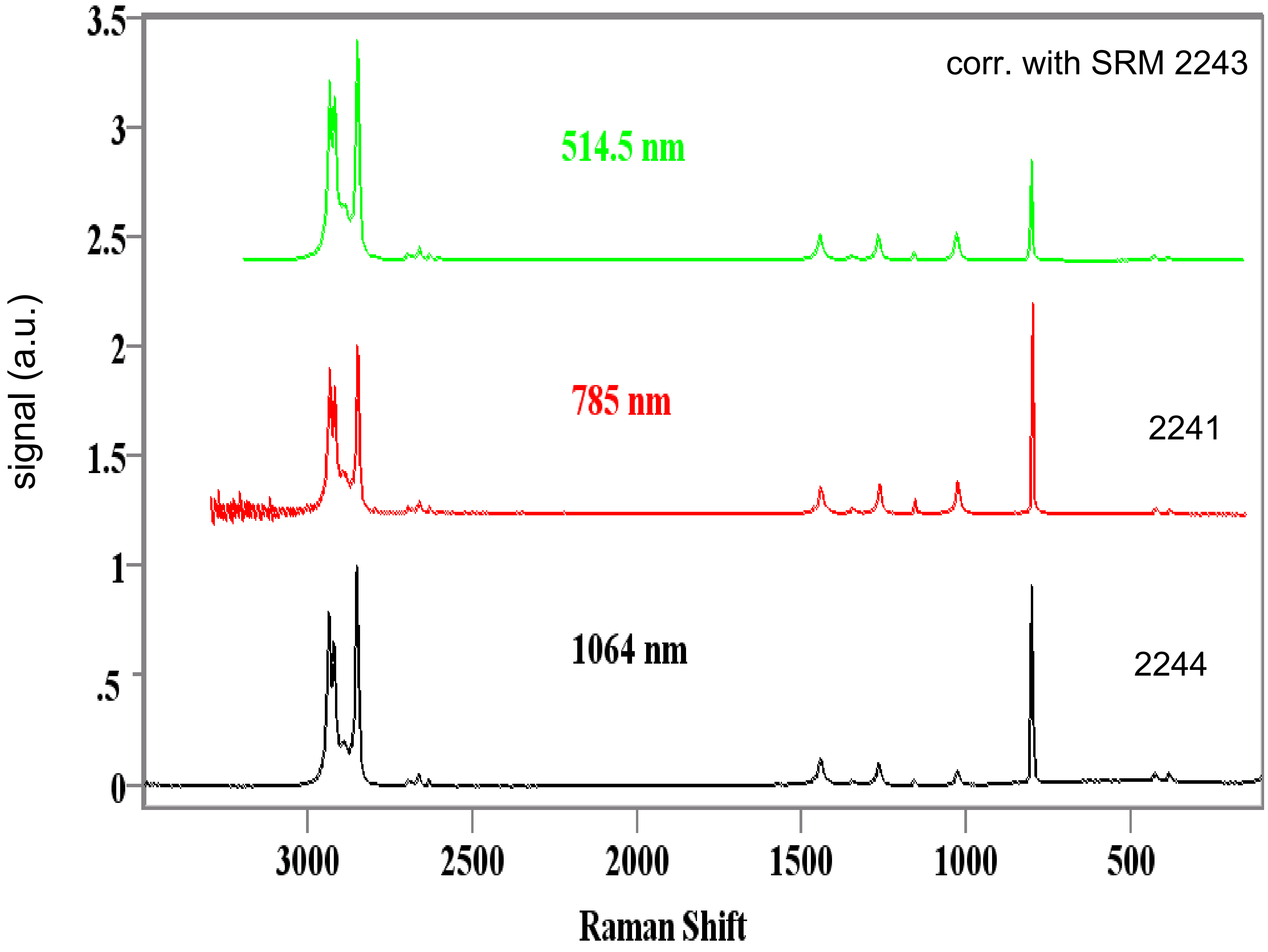
(spectra from Steve Choquette)

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)

(spectra from Steve Choquette)

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

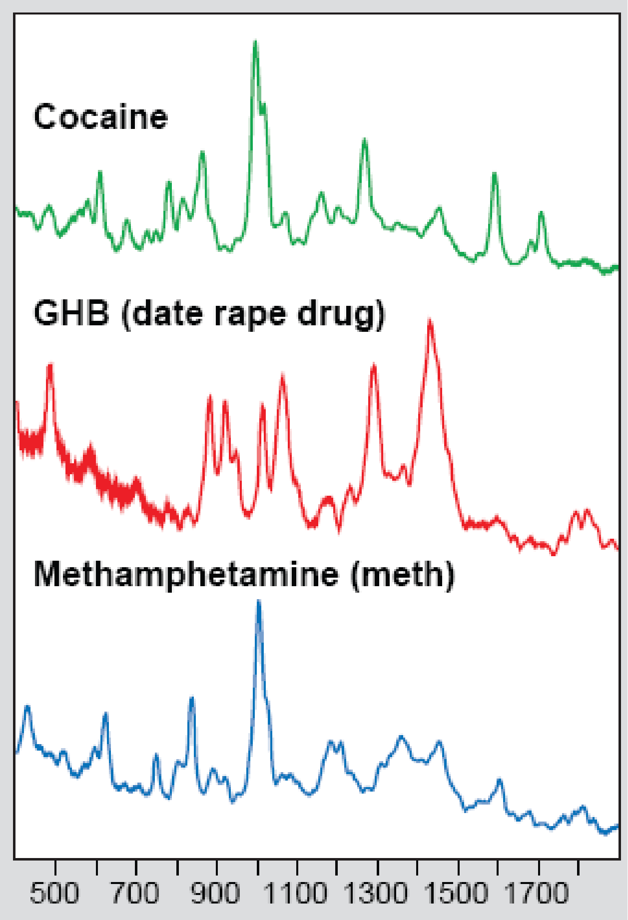
HOWEVER:

- 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)

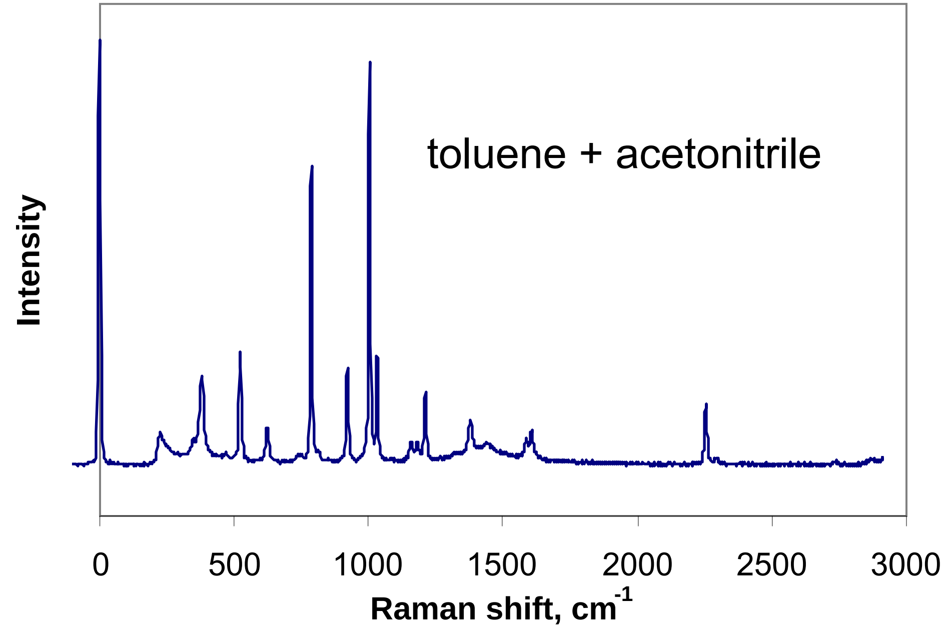
- 785 nm laser
- < 1 – 5 lbs weight
- > 4 hrs battery life
- built-in library for rapid ID
- portable and shock tolerant
- vials, non-contact, through-bag
- $15,000 - $35,000

DeltaNu/Intevac Photonics



remote observation to 3 meters

Ahura Scientific



(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

*Mukhopadhyay, Analyt. Chem. product review, May 2007 (in part)

Some APPROXIMATE sales numbers:

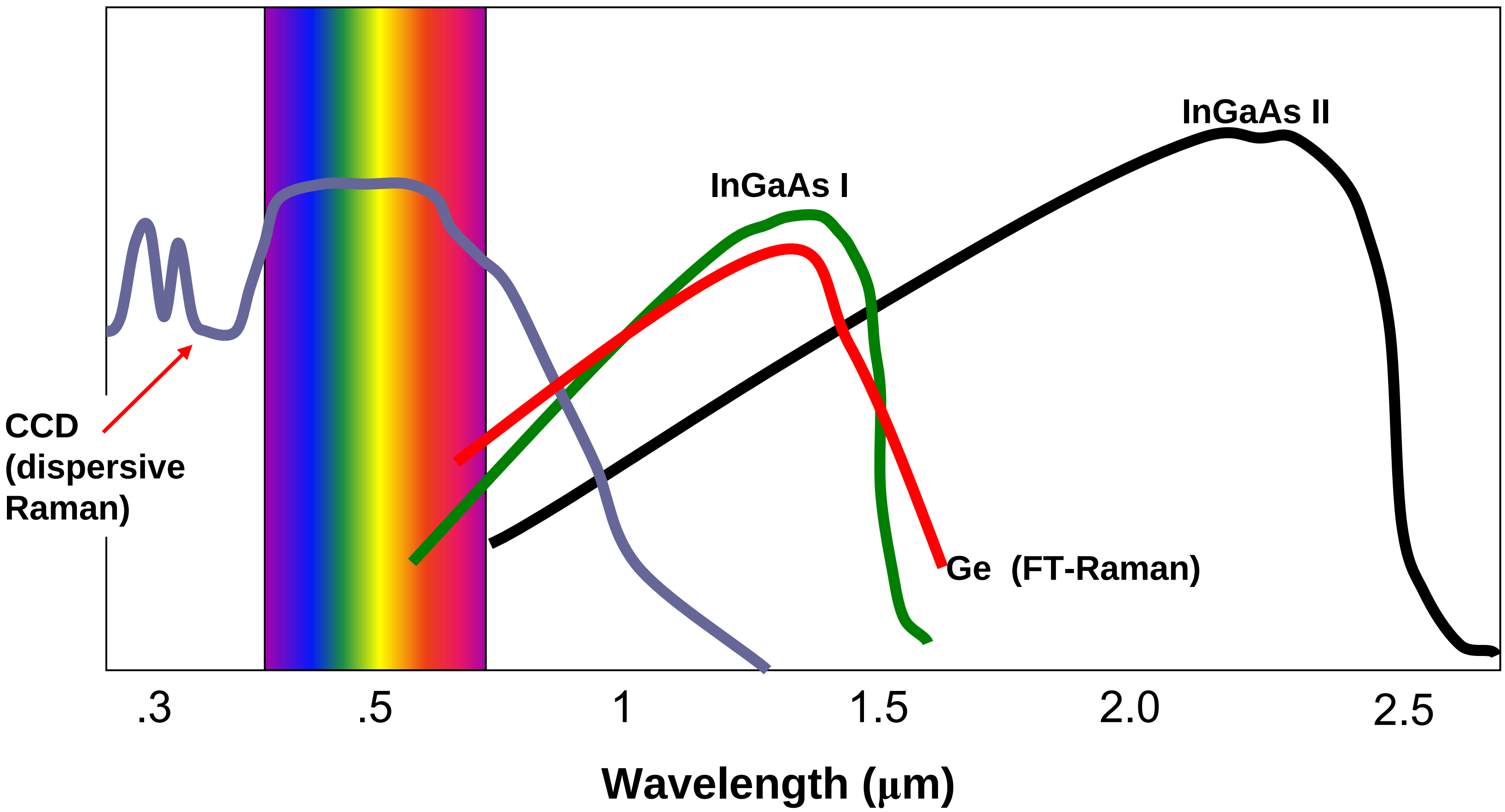
2008 Raman sales:	$201 million	(>40 X since 1985, CPI was 2X)
2008 FTIR sales:	$600-800 million	(slow growth since 1985)

- 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?

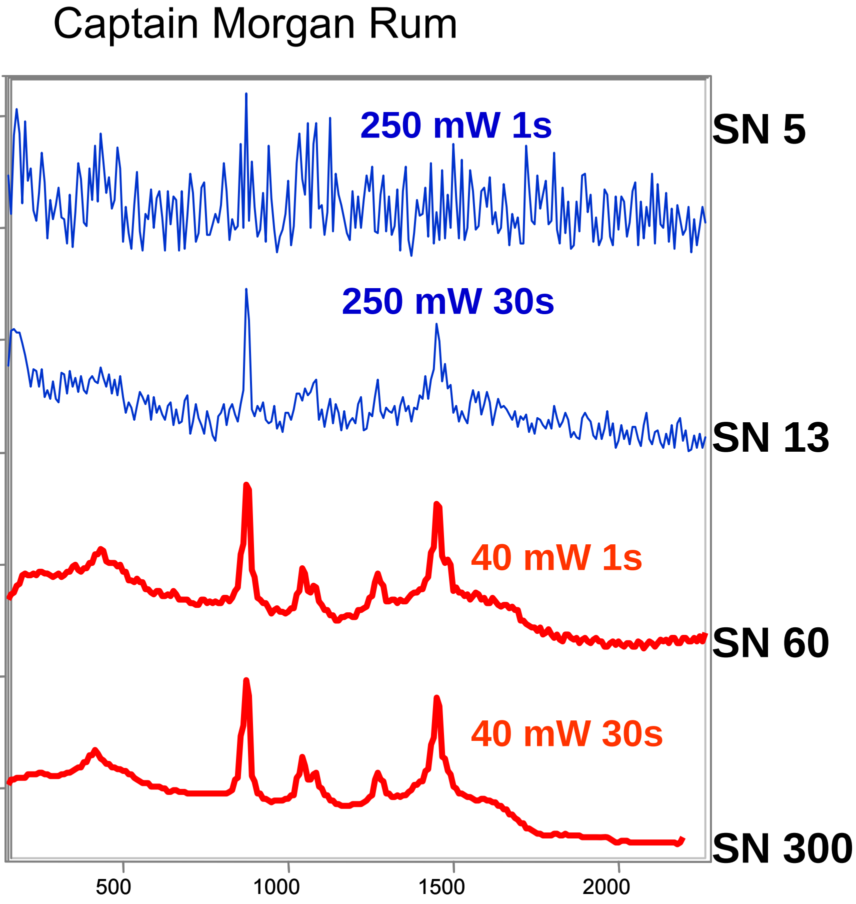
Detector Spectral Response Curves



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

(slide from Keith Carron)

Combine a 1064 nm laser with a dispersive spectrograph and specialized InGaAs array detector (DeltaNu/Intevac)



FT-Raman, 1064 nm

Dispersive Raman, 1064 nm

(slide from Keith Carron)