



Handheld Raman for quality control

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Outline

- Definitions
- Design of handheld Raman system
- Spectral processing
- Specific cases

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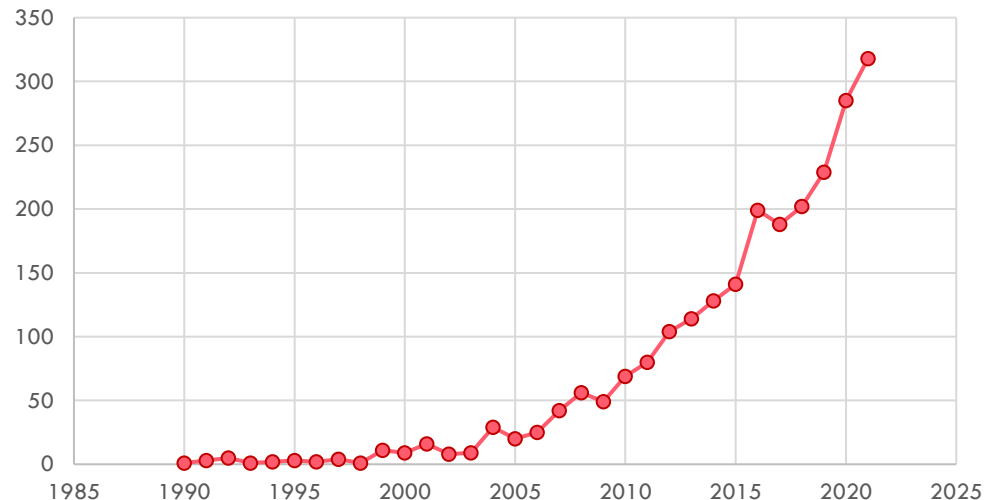
- **Definitions**
- Design of handheld Raman system
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- Specific cases

Portable spectroscopy

Developments mainly driven by safety, security, terrorism, and military concerns

- Significant market presence after 9/11 attacks
 - screening and detection of explosives, chemical threats, etc...

Scientific papers 1990 - 2021
(handheld or portable) and Raman



SOURCE: SCOPUS



Nomenclature

- **Portable**
 - 3 – 20 kg, may be moved from a location to another
 - Hard waterproof case + laptop + optical fiber probes
- **Handheld**
 - 0.5 – 3 kg
 - All-in-one systems battery powered
- **Miniature**
 - <0.5 kg



SOURCE: TSI



SOURCE: BRUKER



Source: Hamamatsu

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Design of handheld Raman

- Design driven by the **intended application**
 - Qualitative vs quantitative
- General principle of “**good enough**”
 - Accurate answer with the required confidence level
 - Smallest measurement time
 - Lowest cost
 - Lowest power draw
 - Minimal inter-equipment variation

➔ compromises have to be made

Design of handheld Raman

- **Indoor and outdoor operations:**
 - Temperature
 - Shocks and vibrations
 - Humidity
 - Dust
 - Stray light mitigation
- **Users:**
 - Non expert spectroscopists (vs laboratory equipment)

Handheld Raman spectrometer

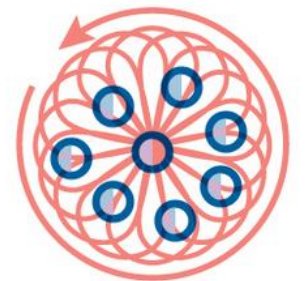
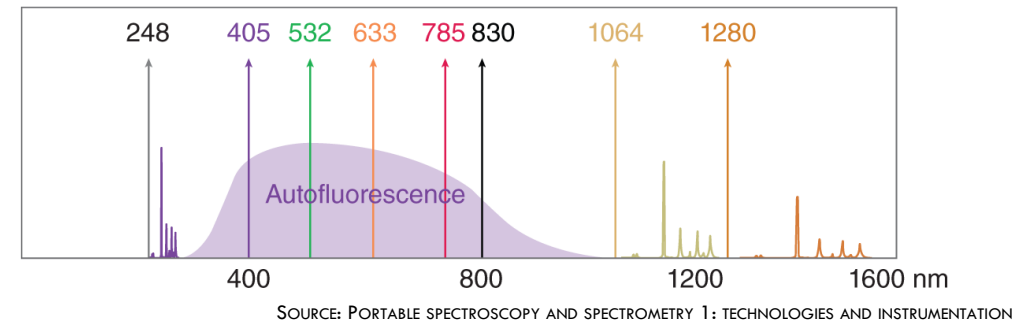
Composed of **4 main parts**:

- Laser source
- Spectrometer
- Sample interface
- User interface

Laser source

Development of **diode lasers** → key enabling technology

- Short warmup times
- May be switched on and off
- Power of 5 – 500 mW
 - May be adjusted (→ analysis of explosives)
- Small spot size
 - May be rastered → improve representativity and less local heating



Source: Metrohm

Spectrometer

Usually a **trade-off** has to be found between:

- Spectral range
 - 200-2400 cm^{-1}
- Optical resolution
 - $< 15 \text{ cm}^{-1}$ FWHM
- Analysis throughput
 - $< 5 \text{ sec}$ / analysis

Minimal performances described in:

- Ph. Eur. 2.2.48
- USP $<1858>$ and $<858>$

Sample interface

- Usually **point-and-shoot** configuration (180° backscattering)
- Analyse of samples in their **original container**
 - Should be translucent (plastic bags, blister packs, bottles/vials)
- ➔ Less manipulation
 - ↗ throughput
 - ↘ risk for analyst (e.g. high potent chemicals)
 - ↘ risk of sample contamination



Source: Metrohm

User interface

The interface should be **application dedicated**

- ➔ short training
- ➔ higher throughput



Source: Metrohm

- **Integrated module** with embedded computer + screen
- **Physically separated module**
 - Necessitates a smartphone / tablet / laptop



Source: Hamamatsu

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Spectral processing

- **Data collection settings**
 - Exposure time, co-adds, ...
- **Automatically selected** for the user
- Based on **general settings** (e.g. sufficient SNR)
 - May depend on the environmental conditions (e.g. amount and nature of stray light)
- Based on **previously acquired data**

Spectral processing

- **Conditioning of spectra**
- Make data “robust” to measurement conditions
 - Subtraction of ambient signal
 - Correction of dead pixels / spikes
 - Intensity correction
 - Raman shift calibration
- Preprocessing of spectra (derivative, baseline correction, ...)

Spectral processing

- **Qualitative objective**
 - Identification
 - Confirmation
 - ➔ One-class modelling
 - ➔ Multi-class modelling
- **Quantitative objective**
 - Mixture analysis
 - Multivariate regression analysis

Spectral processing

- **Cached library** stored in device
 - Commercial or third party
 - User-defined library
- **Cloud-based services**
 - Up-to-date
 - Deployable
 - IT vulnerabilities
 - Needs network
 - Security issues

Spectral processing

- **Display of results**
 - **User inference**
 - Rank ordered list of items with metric values
- **Statistical inference**
 - Classification of results (pass/marginal/fail)
 - Hypothesis testing
 - Definition of threshold



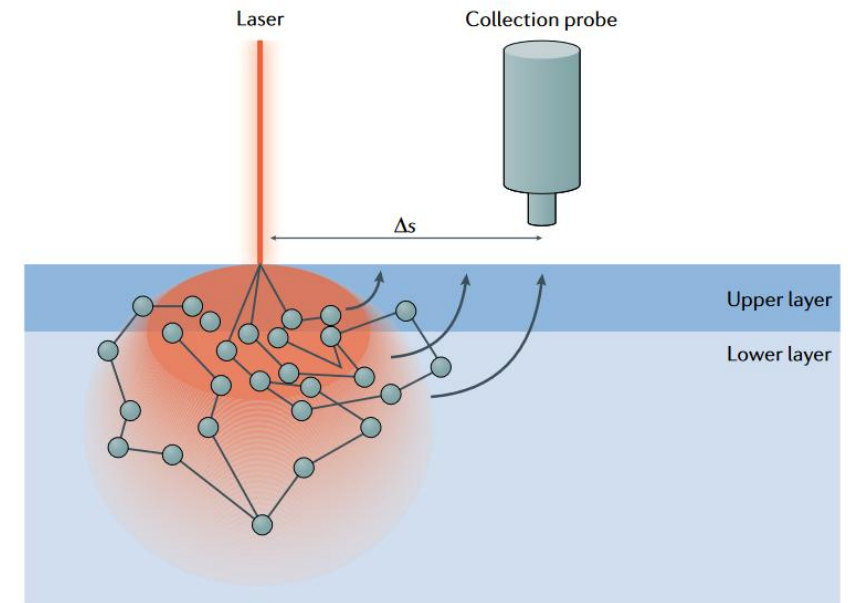
Source: Metrohm

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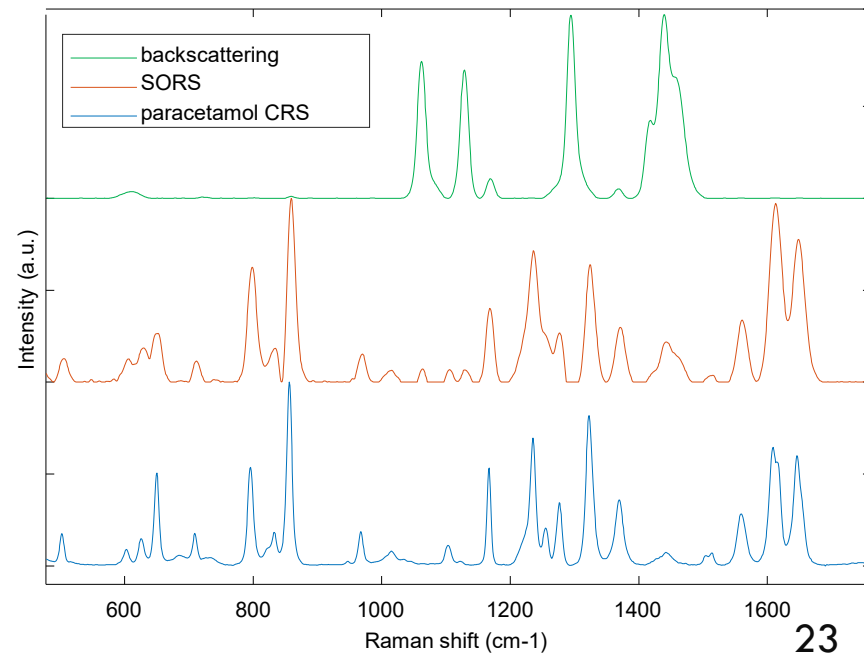
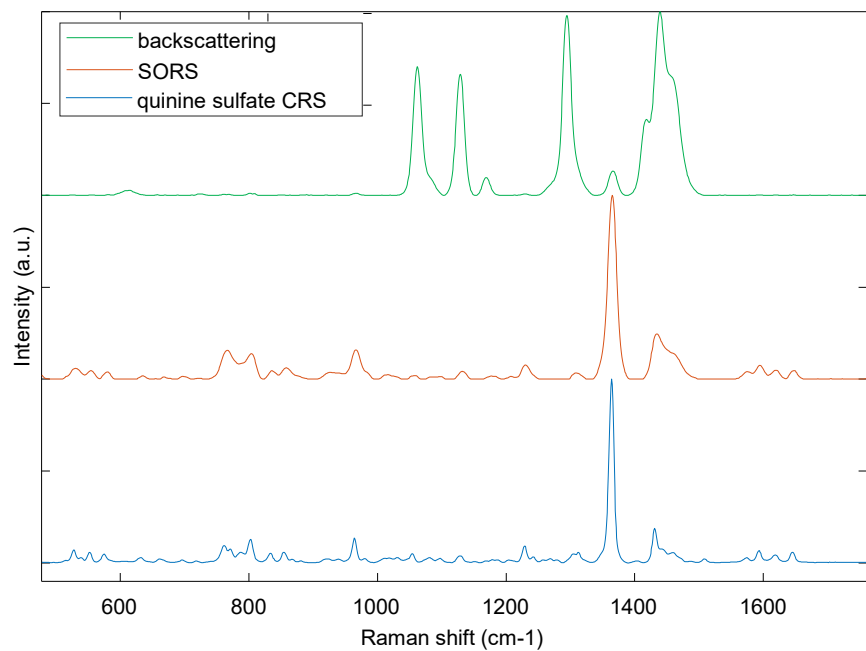
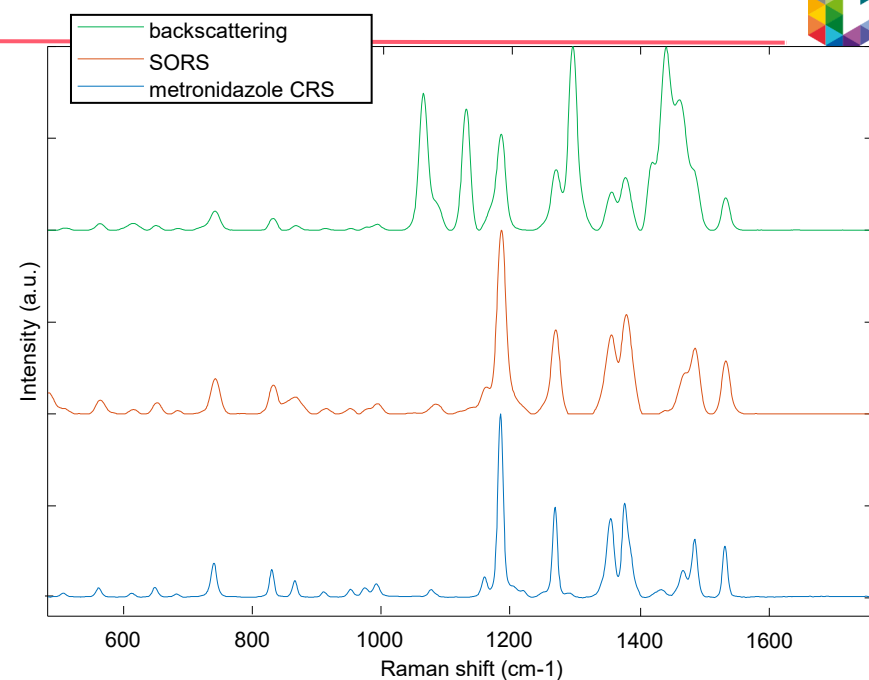
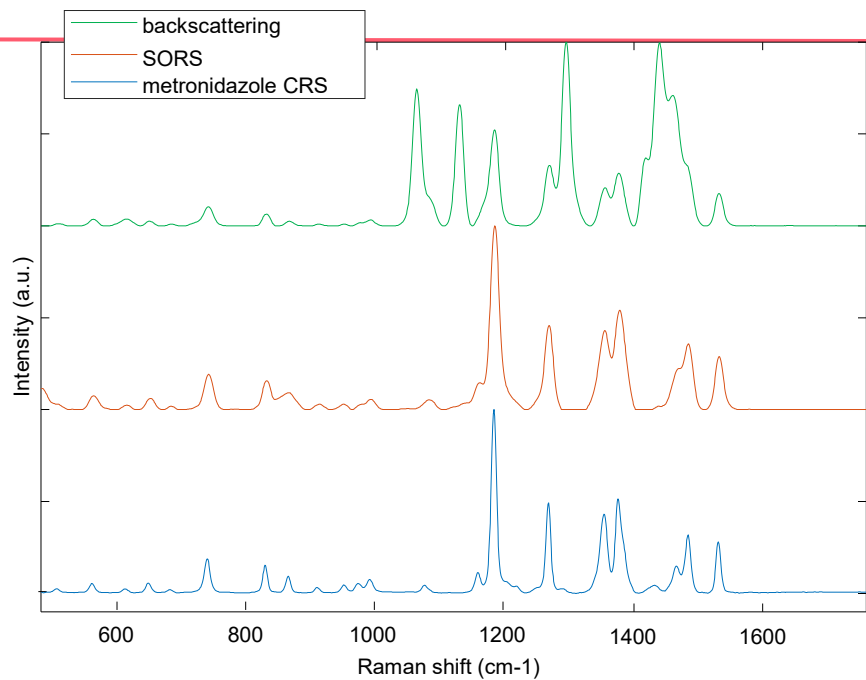
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Specific cases

- **Through Barrier analysis**
 - Defocused lenses
 - 180° backscattering measurement
 - 1064 nm laser compatible
- **Spatially offset Raman spectroscopy**
 - 830 nm laser
 - Limitations for some containers
(e.g. cardboards)







Specific cases

- **Fluorescence mitigation**

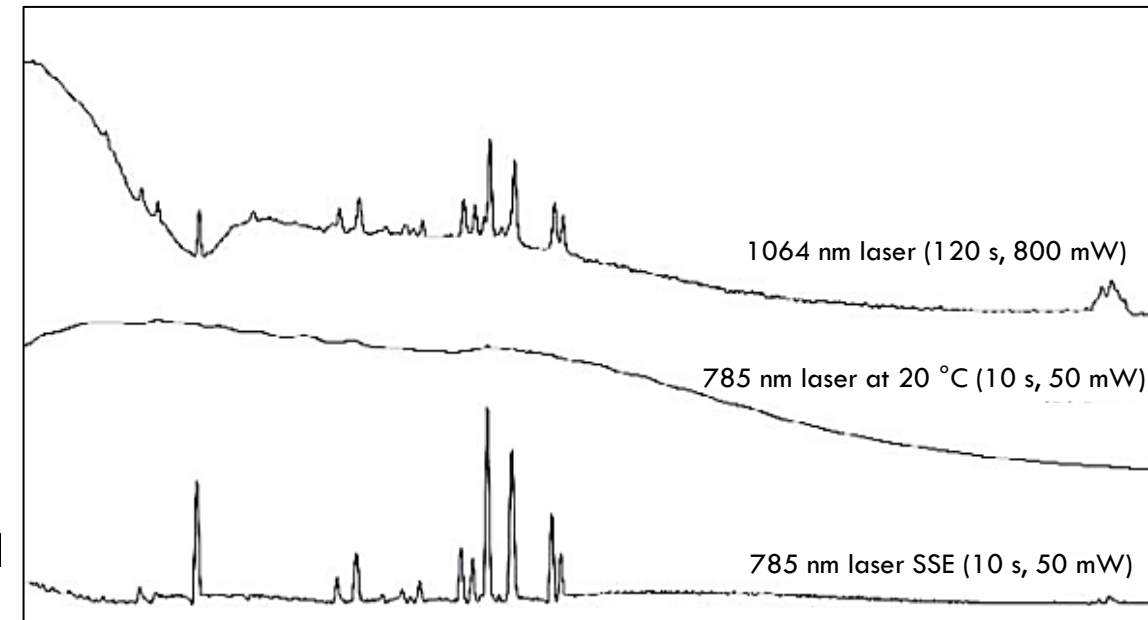
- Choice of laser wavelength (e.g. 1064 nm)
 - But $1/\lambda^4$ signal intensity $\rightarrow$ longer acquisition time, more power needed, risk of burning

- SERDS

- Sequentially shifted excitation (SSE)

- SORS

- OK if fluorescence of packaging
- NOK if fluorescence of investigated material



Source: Cooper et al. doi:10.1177/0003702817724164

Specific cases

- **Stand off measurements:**
 - Max 2 meters distance
 - Can be combined with SERDS and raster scanning



Source: Pendar



Source: Metrohm

Specific cases

- **Surface Enhanced Raman Spectroscopy (SERS):**
 - Enhancement of Raman signal with metallic nanostructures (Au or Ag)
 - Increasing factor up to 10^6
 - Exist as solid substrates or colloidal nanoparticles
 - Issues regarding reproducibility and stability
- ➔ for qualitative analyses



Source: Metrohm



Source: Hamamatsu



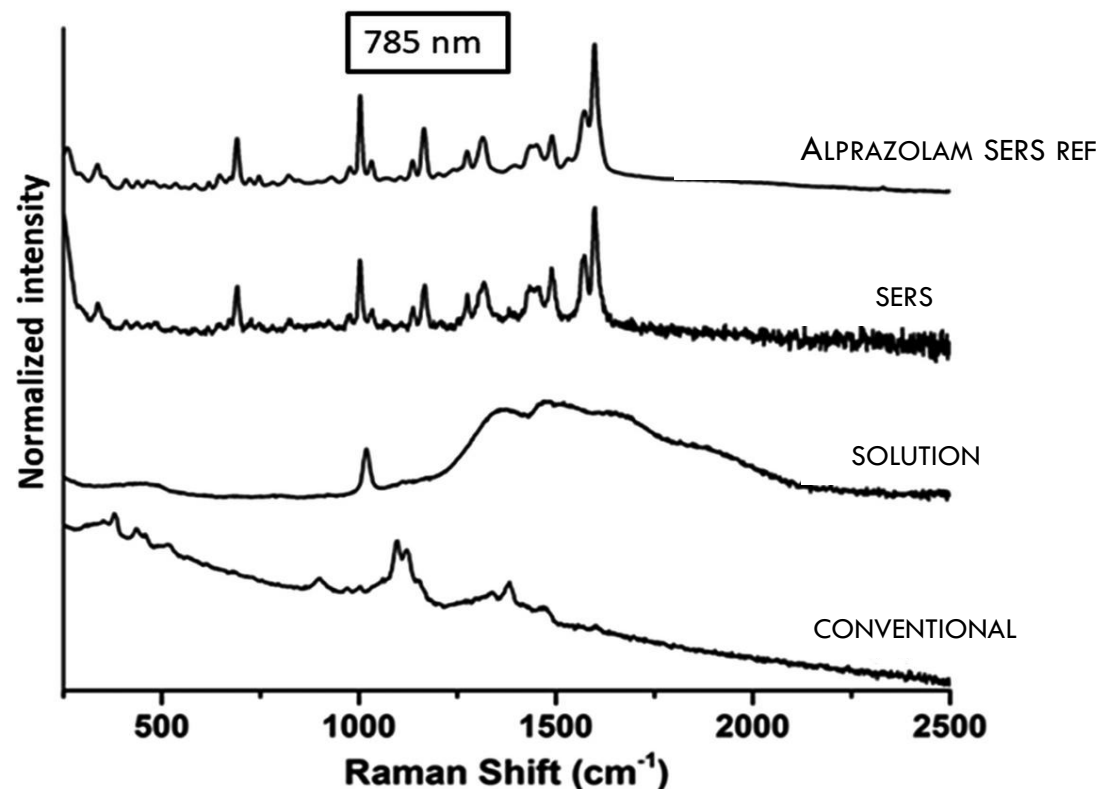
Source: Metrohm

Specific cases

SERS detection of low-dosed APIs in suspect samples (1 – 2 mg / tablet)

$C_{\min}$ ref: 0.5 $\mu\text{g}/\text{ml}$

$C_{\min}$ sample: 1 $\mu\text{g}/\text{tablet}$



Source: Kimani et al. DOI: 10.1111/1556-4029.14797

Conclusion

- Recent technology (~20 years)
- Many applications → many designs and possibilities
- **Perspectives**
 - Hyphenation of techniques (MIR, NIR, XRF, LIBS)
 - Miniaturization, portability, cost
 - Algorithms, databases, calibrations



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