Application of Near –Infrared (NIR) and Raman Spectroscopy for Rapid and Non-Destructive Drug Identification

Dr.Leila Masoumi

some of the greatest dangers and threats encountered by the pharmaceutical industry globally are issues of falsification, counterfeiting, adulteration, incapability and fraudulence.

These issues have a negative impact on patients and are not beneficial for curing the target disease due to their reduced efficiency.

This threat causes a loss in confidence in pharmaceutical products, health care providers and the health system in general.

Botox-A Popular Example of Drug Counterfeiting

Applications in Pharmaceuticals

- ✓ Identification and authentication of Active Pharmaceutical Ingredients (APIs)
- ✓ Detection of counterfeit or substandard medicines
- ✓ Uniformity testing of tablets and content analysis
- ✓ Monitoring the coating thickness and distribution in tablets
- ✓ Real-time Process Analytical Technology (PAT) integration

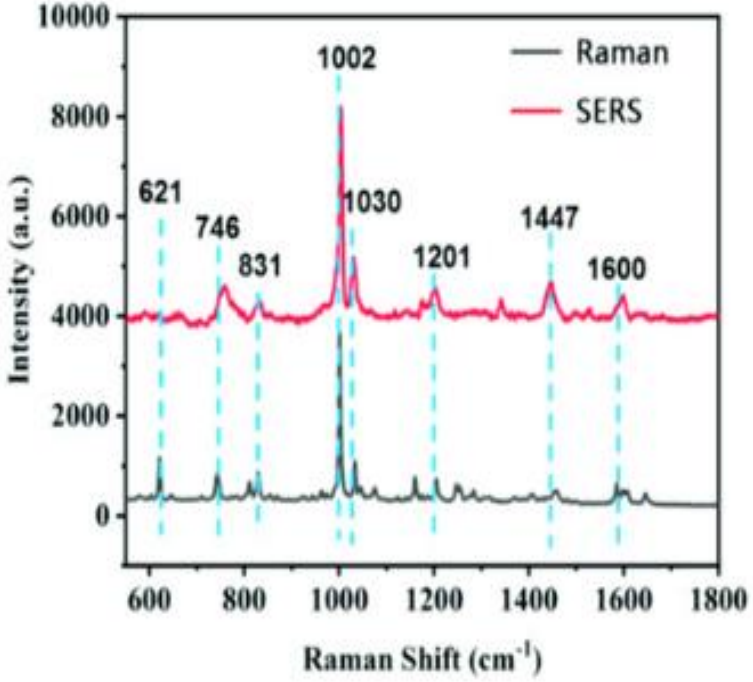
Why Non-Destructive and Rapid Drug Analysis ?

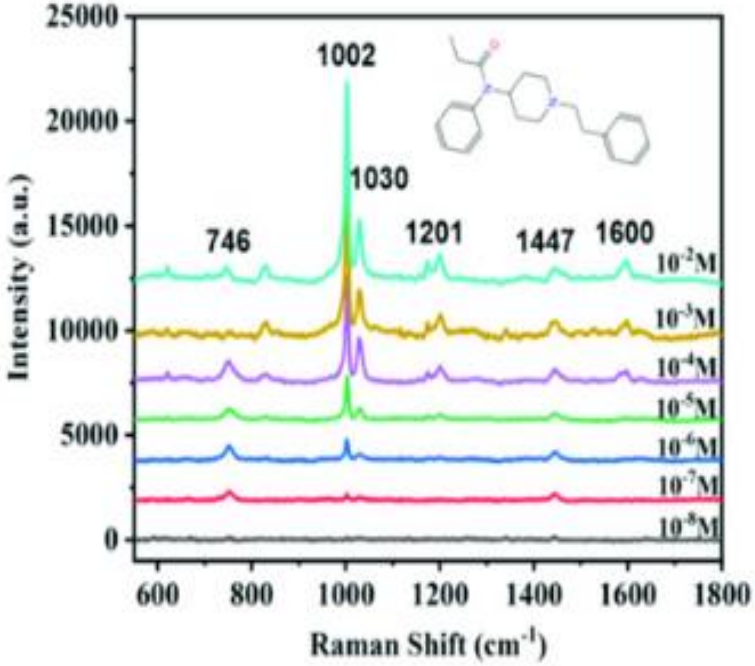
- Non-destructive methods preserve the sample, which is valuable for rare or expensive drugs.
- They offer real-time results, critical for inline process control.
- These techniques eliminate the need for sample preparation, reducing analysis time and costs.
- They allow testing without opening the packaging, which is essential in tamper-evidence and counterfeit detection.

Raw material identification

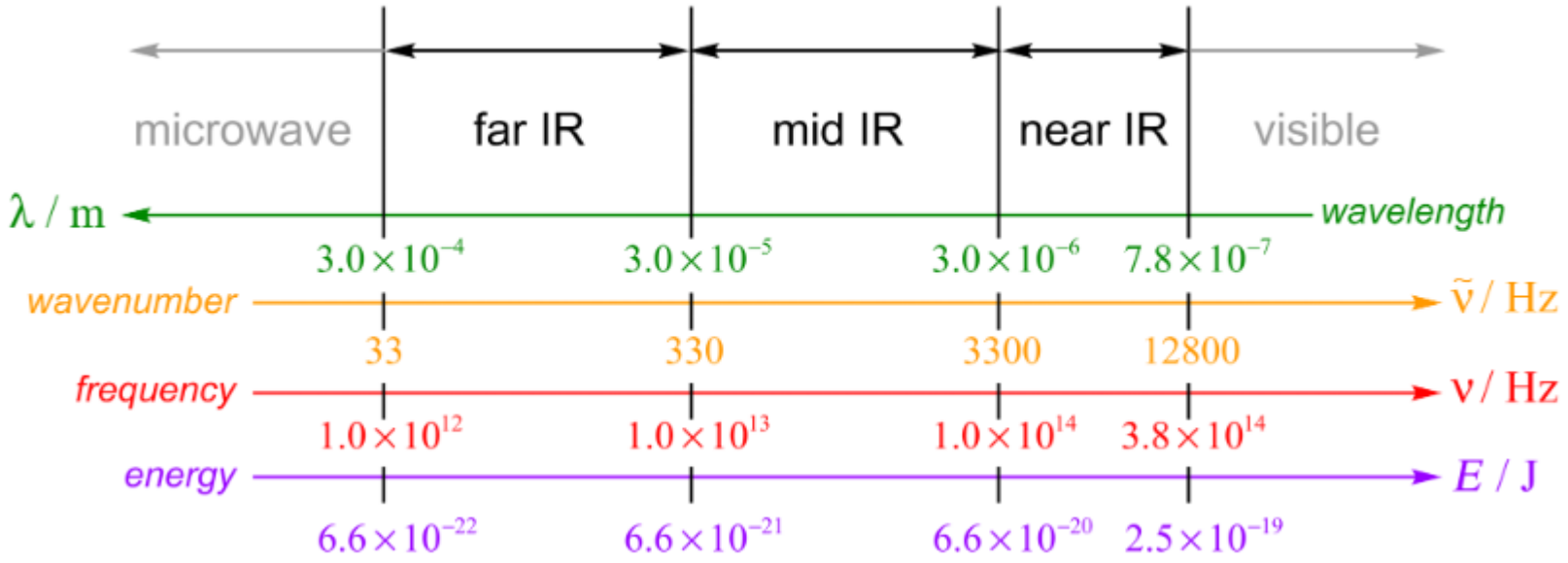
In the pharmaceutical industry, raw materials are the starting point of every processing or manufacturing campaign. The incoming materials are first stocked in a quarantine area for approval before processing. Acceptance of the materials then requires conducting several analytical tests in respect of the recommendations given by pharmacopoeia monographs. These (often destructive) analytical tests are performed in QC laboratories (sometimes located far from the manufacturing plant) .

Fentanyl

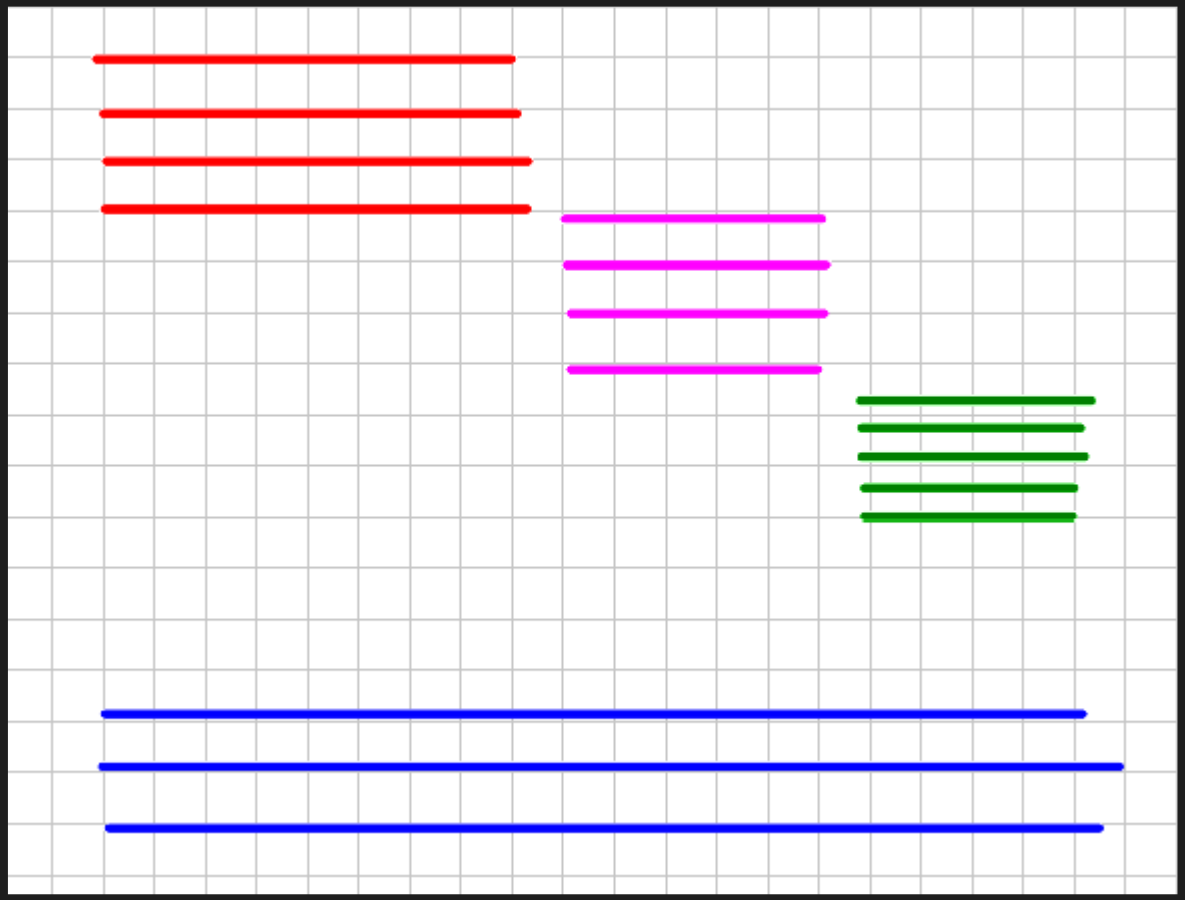

Raman
SERS
1002
621
746
831
1030
1201
1447
1600
Intensity (a.u.)
Raman Shift (cm-1)


1002
1030
746
1201
1447
1600
10-2M
10-3M
10-4M
10-5M
10-6M
10-7M
10-8M
Intensity (a.u.)
Raman Shift (cm-1)

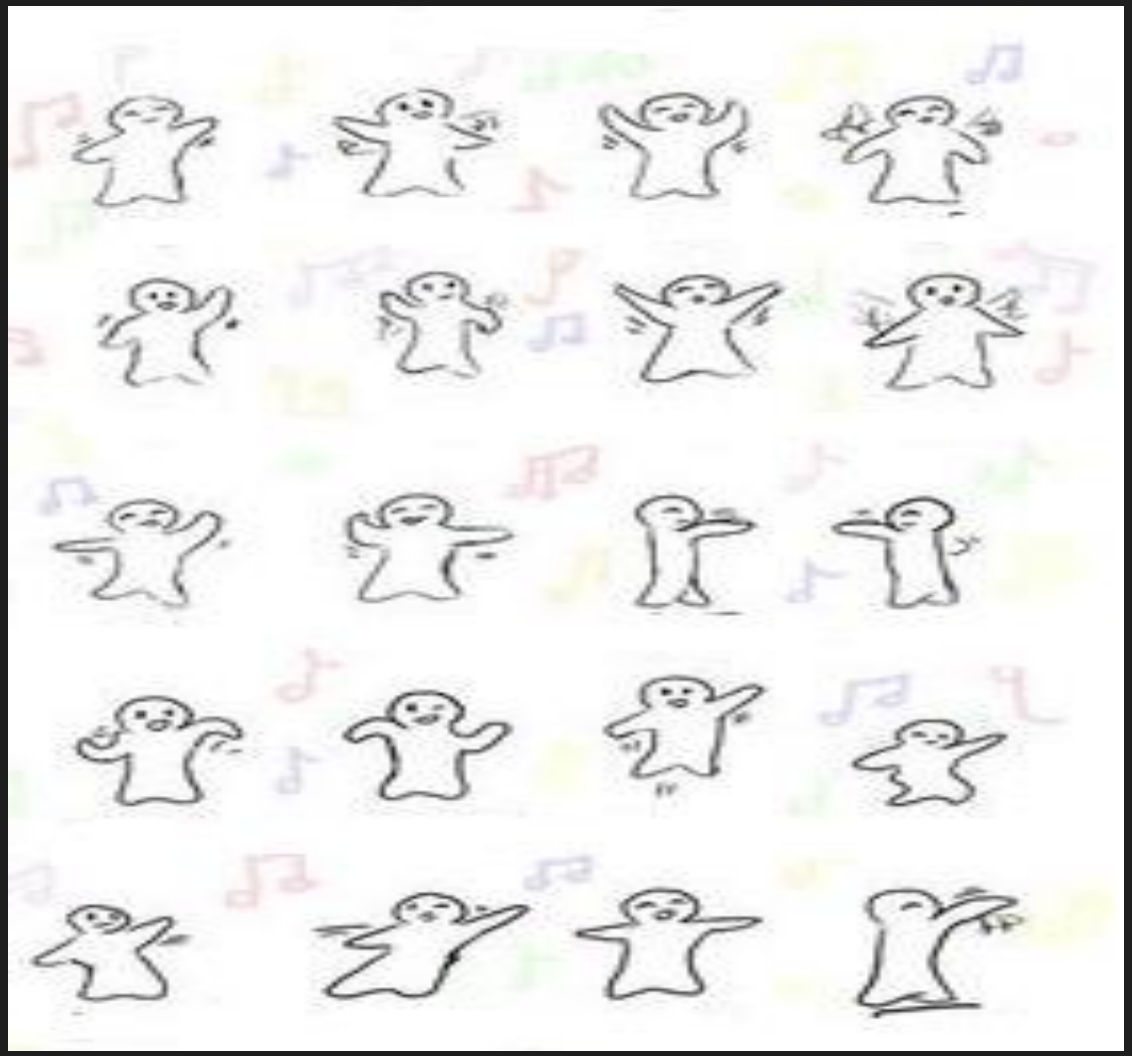
Introduction to NIR and Raman


microwave
far IR
mid IR
near IR
visible
λ / m
wavelength
3.0×10⁻⁴
3.0×10⁻⁵
3.0×10⁻⁶
7.8×10⁻⁷
wavenumber
ν̃ / Hz
33
330
3300
12800
frequency
ν / Hz
1.0×10¹²
1.0×10¹³
1.0×10¹⁴
3.8×10¹⁴
energy
E / J
6.6×10⁻²²
6.6×10⁻²¹
6.6×10⁻²⁰
2.5×10⁻¹⁹

Basics of NIR Spectroscopy



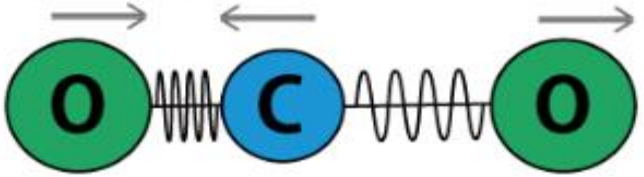
Molecular Vibrations and Absorption



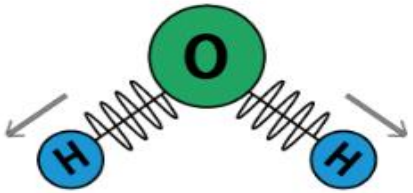
Instrumentation in NIR

- *Symmetric stretching "IR-inactive" vibration*

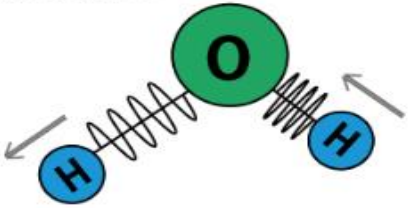
- *Anti-symmetric stretching vibration at 2349 cm-1*



- *Symmetric stretching vibration at 3652 cm-1*



- *Anti-symmetric stretching vibration at 2349 cm-1*



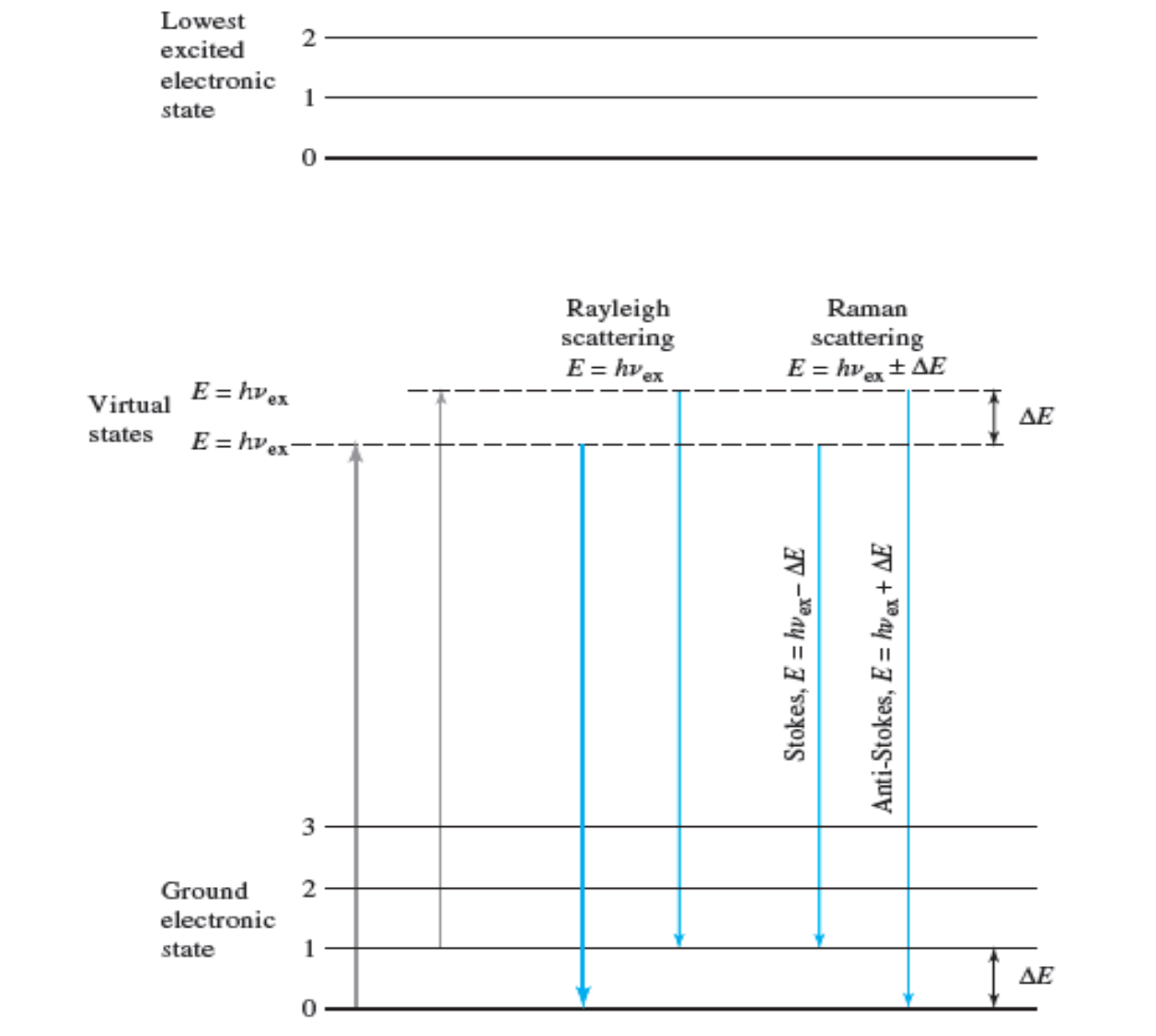
Advantages of NIR Spectroscopy

Quantitative Precision: NIR Spectroscopy is distinguished by its capability to quantify specific substances with exceptional precision. This includes the quantification of substances like heroin, THC/CBD, and MDMA, showcasing its versatility in various fields.

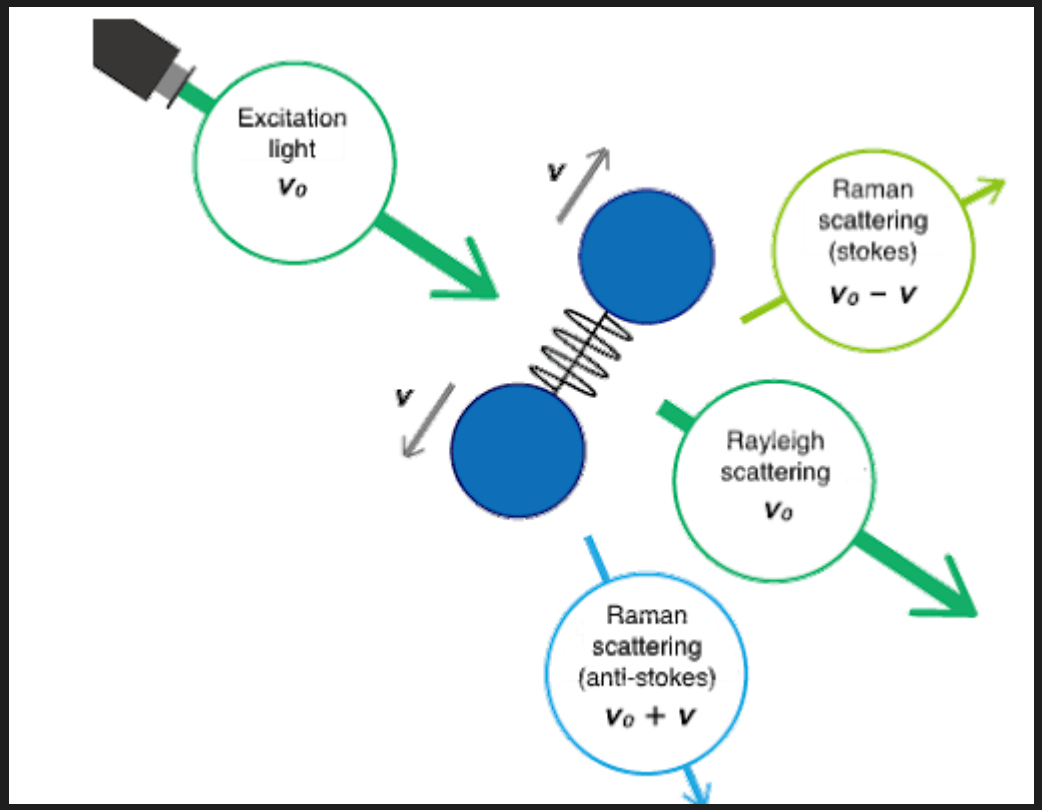
Safety First: The use of low-energy radiation eliminates safety concerns for both operators and samples. This safety feature makes NIR Spectroscopy an attractive option, especially in environments where minimizing risks is paramount.

Many physicochemical parameters of pharmaceutical products can be analyzed quantitatively using NIR spectroscopy such as particle size, hardness, dissolution rate compaction force and water content among others

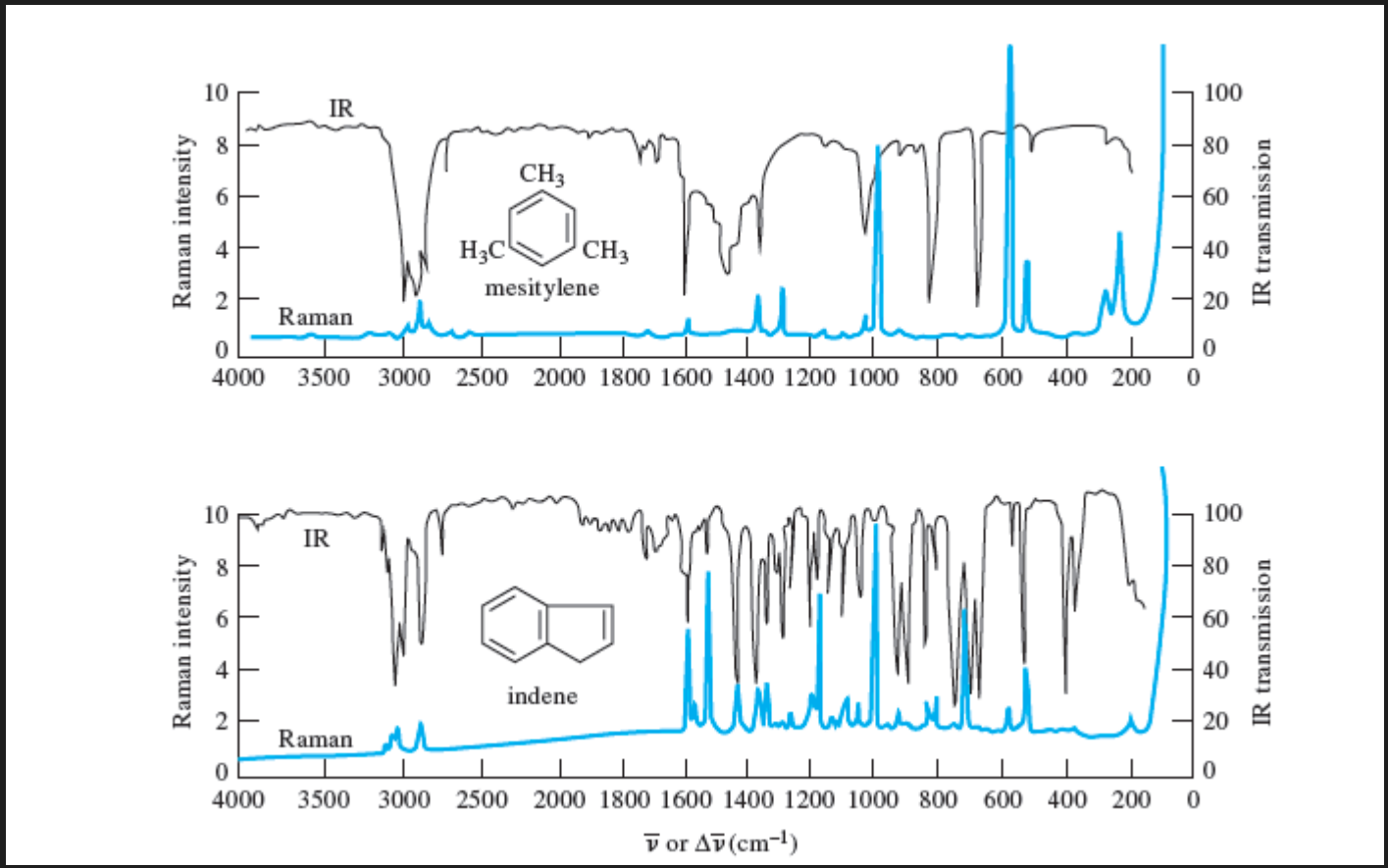
Basics of Raman Spectroscopy



Raman Scattering Explained

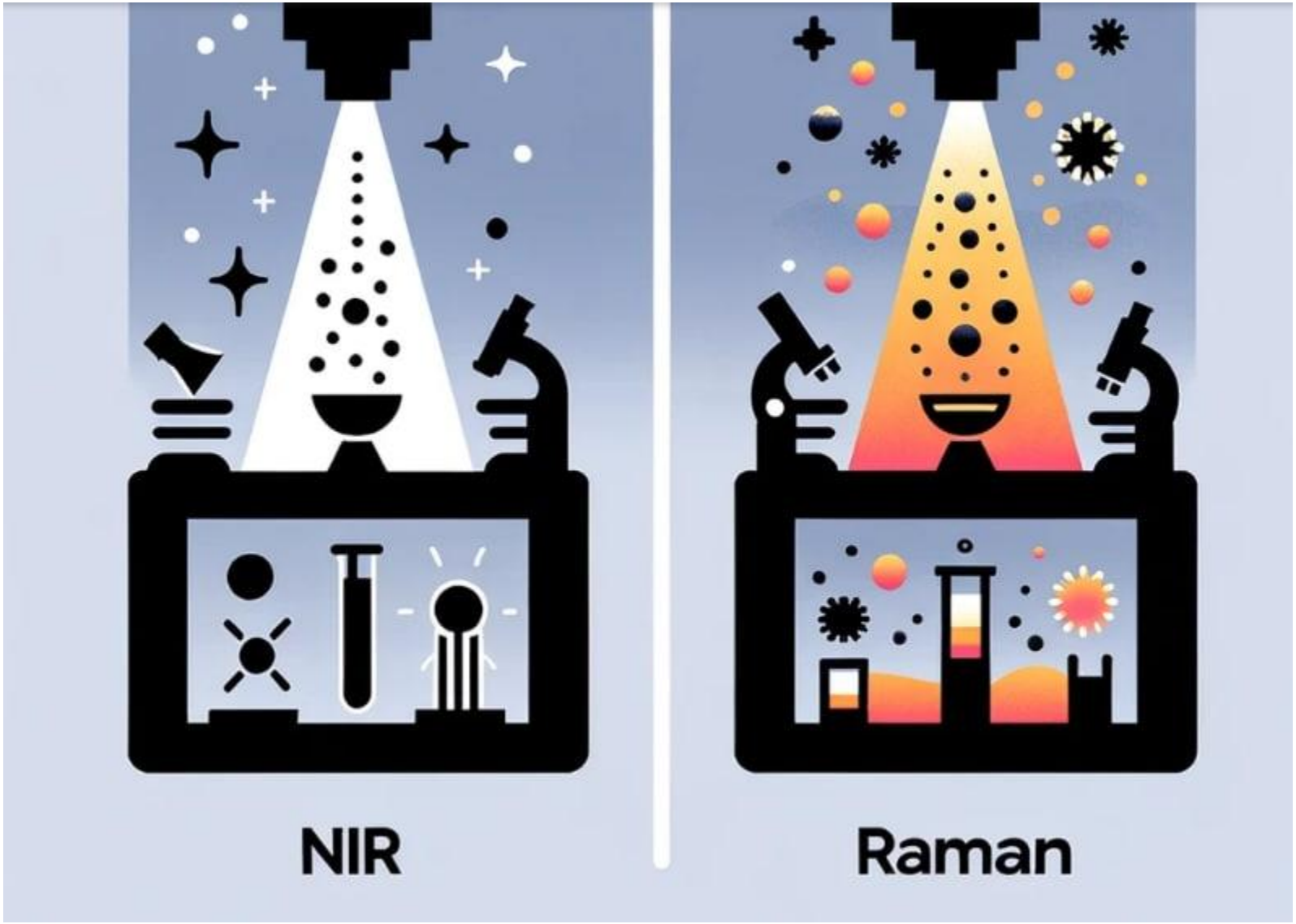


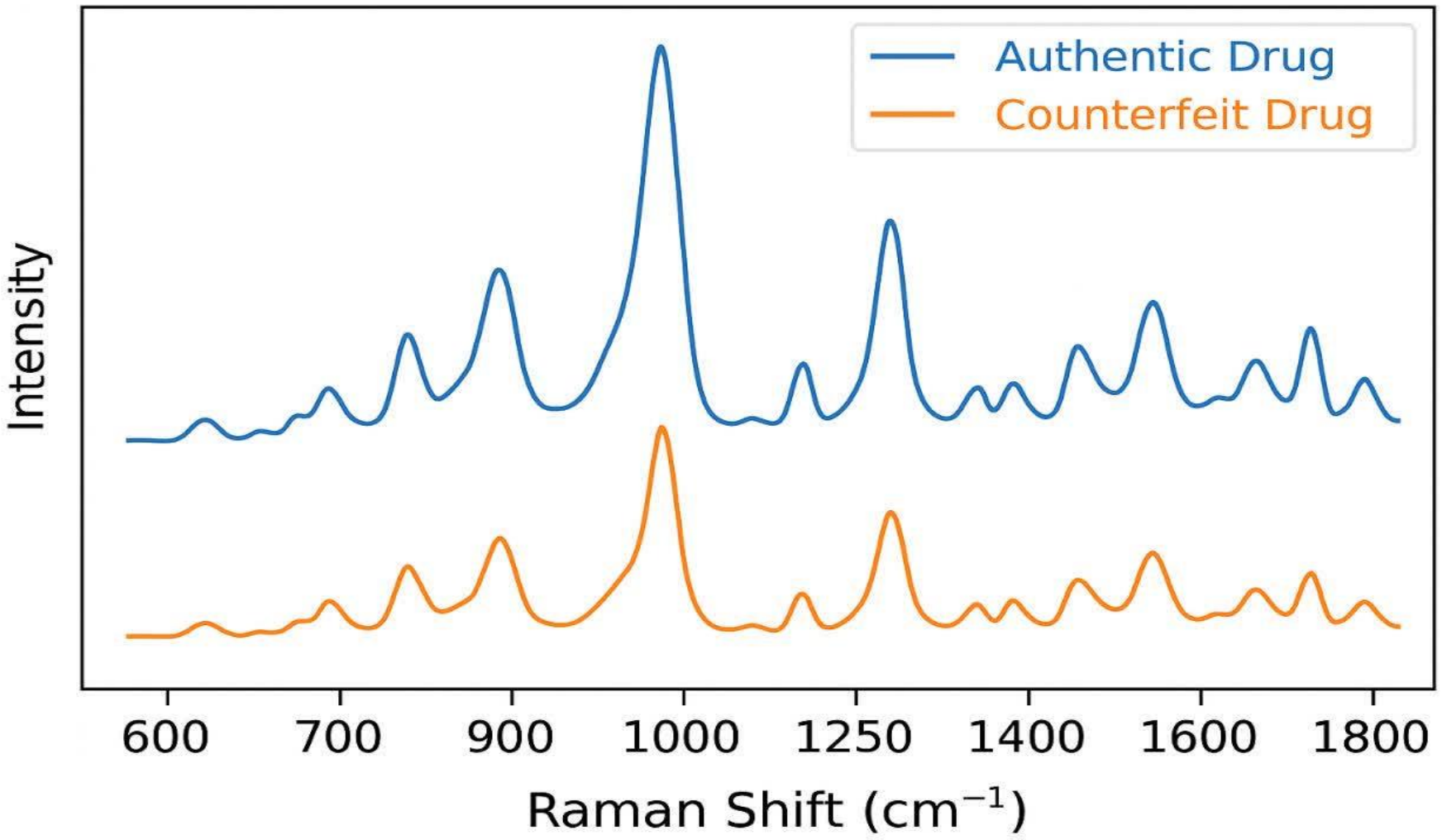
Comparison of NIR vs Raman



Comparison between Raman and Infrared (FT-IR and NIR) spectroscopies

RAMAN Spectroscopy	**Infrared Spectroscopy**
It is due to the scattering of light by the vibrating molecules	It is the result of absorption of light by vibrating molecules
The vibration is Raman active if it causes a change in polarizability	Vibration is IR active if there is change in dipole moment
The molecule doesn't have to posses a permanent dipole moment	The vibration concerned should have a change in dipole moment due to that vibration
Water can be used as a solvent	Water can't be used in IR due to its high intense absorption in IR
Sample preparation is not very elaborate it can be in any state	Sample preparation is elaborate gaseous samples can rarely be used
Gives an indication of covalent character in the molecule	Gives an indication of ionic character in the molecule
Cost of instrumentation is very high	Comparatively inexpensive


NIR
Raman


Authentic Drug
Counterfeit Drug
Intensity
600
700
900
1000
1250
1400
1600
1800
Raman Shift (cm^{-1})

Advantages Over Traditional Techniques

- No sample destruction or chemical reagents needed
- Portable and handheld devices are available
- Quick results (often within seconds)
- Easy to automate and integrate with manufacturing lines

Challenges in Implementation

Despite their strengths, both techniques have limitations:

NIR: Susceptible to moisture interference.

Raman: Affected by fluorescence in some compounds.

Both require chemometric calibration and reference libraries for accuracy.

Future Trends

Handheld NIR/Raman devices will be standard tools in pharmaceutical manufacturing.

Cloud-based data sharing and AI-driven pattern recognition will enhance real-time decision-making.

These techniques will enable personalized medicine, tailoring drug dosages to individual needs.

Conclusion

NIR and Raman spectroscopy are not only transforming quality control but also providing a pathway to smarter, faster, and safer drug manufacturing. Their non-destructive nature, speed, and flexibility make them ideal tools for modern pharmaceutical challenges.

1. Galli, V. et al. (2024). Near-infrared spectroscopy in pharmaceutical quality control. Journal of Pharmaceutical Analysis.

2. Skidmore, M. et al. (2024). Detection of Fentanyl and Analogues Using Portable Raman Spectroscopy. MediresOnline.

3. Burns, D.A. & Ciurczak, E.W. (Eds.). Handbook of Near-Infrared Analysis.

4. ICH Q8-Q11 Guidelines for PAT (Process Analytical Technology)

THE END