Application Note AN-RS-034

Orbital Raster Scan (ORSTM)

Safer, more representative sampling with 785 nm Raman

The ability of an optical system to efficiently collect light is known as its throughput or etendue. In an ideal world of homogeneous samples, a Raman spectroscopic system would need only a small laser spot with a similar-sized aperture to collect high resolution spectra. However, the world is more complicated than this. Identification of all the components in a heterogeneous sample requires a larger area of interrogation. To accomplish this, the laser spot size could be increased to cover more area. Unfortunately, high resolution requires a small aperture which reduces the amount of Raman light a system can collect, and thus sacrifices sensitivity. Alternatively, a small aperture could be used while quickly moving (rastering) a tightly focused laser over the sample to collect information from a large area of the sample. This is the principle behind the patented Orbital Raster Scanning (ORS™) method developed by Metrohm Raman.

ORS technology is Metrohm Raman's proprietary way of overcoming low resolution, poor sensitivity, and sample degradation while still interrogating a large sample area. This is illustrated in a variety of applications detailed within this Application Note.

INTRODUCTION

Figure 1 shows a graphical representation of Orbital Raster Scanning, which is defined as quickly moving a tightly focused laser beam over a large area.

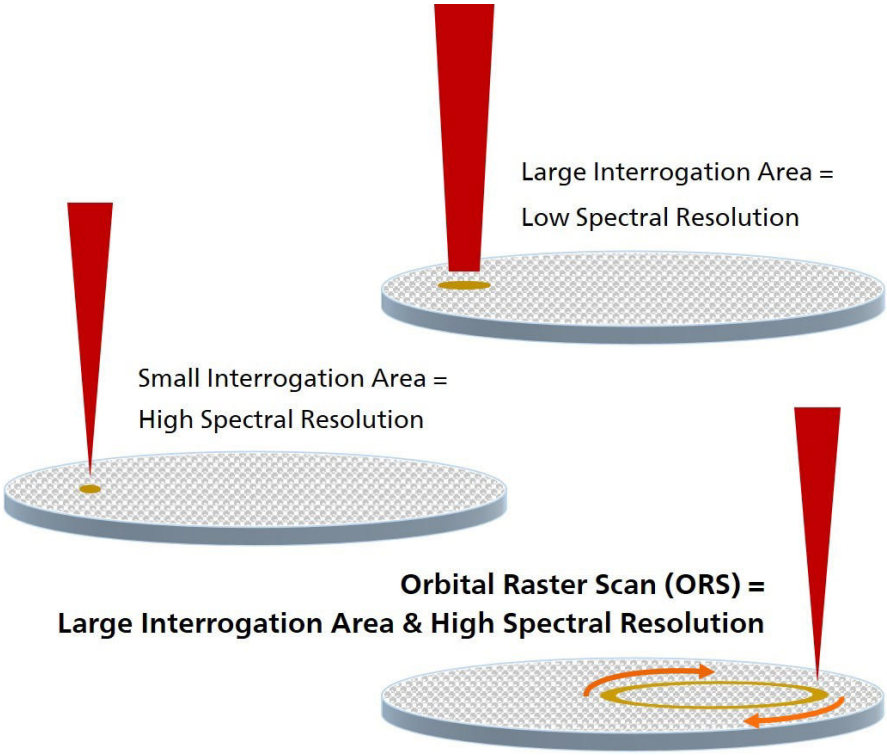


Figure 1. ORS quickly collects the most representative, highest quality information about any sample.

Raman spectroscopy is used in many different applications and industries where high-quality data is essential. The abilities of Metrohm Raman's MIRA (Metrohm Instant Raman Analyzer) and MISA (Metrohm Instant SERS Analyzer) systems with ORS are highlighted in three different applications below: pharmaceutical regulation, material identification, and sampling of SERS (Surface Enhanced Raman Scattering) substrates.

ORS AND REPRESENTATIVE SAMPLING IN PHARMACEUTICALS

The European Pharmacopoeia (Ph. Eur, or EP) is a complete standard for the production of medicines, quality control of medicines and raw materials, and the instruments used to perform such tests. Raman spectrometers are increasingly used for quality control of medicines because they are user-friendly, flexible, and provide fast, non-destructive measurements. A newly revised chapter, Ph. Eur. 2.2.48 Raman Spectroscopy, focuses on aspects that enhance the reliability of results, and it specifically mentions ORS [1].

«When using Raman spectroscopy [...] care must be

taken to ensure that the measurement is representative. This can be achieved by, for example rotation of the sample, performing multiple measurements on different preparations of the sample, using orbital raster scanning (ORS) [...]» [1]

Pharmaceuticals are mixtures of excipients and active pharmaceutical ingredients (APIs) in carefully controlled proportions. Representative sampling can be an issue with the small beam diameter of most Raman systems (40–200 µm) and the small particle size (averaging 36–39 µm) in tablets [2]. MIRA and MISA spectrometers with ORS raster the laser around a 2000 µm diameter circle to interrogate a large area in a very short time and capture all of the ingredients in a single scan.

ORS AND SAMPLE PRESERVATION

All MIRA and MISA systems use low laser power to collect high resolution spectra. This results from the combination of 785 nm laser excitation and a patented high etendue «free space» spectrograph design. For example, ≤50 mW lasers are sufficient for good Raman signal acquisition at 785 nm in MIRA and MISA systems, while 1064 nm systems must employ 420 ± 30 mW lasers to compensate for poor signal-to-noise and reduced Raman scattering exhibited at longer wavelengths. The combination of low laser power and ORS is ideal for interrogation of sensitive materials, such as highly colored and volatile substances.

Raman Identification of Polystyrene

A comparison between conventional 1064 nm and MIRA XTR DS 785 nm Raman systems in the interrogation of the plastic barrel of a ballpoint pen clearly shows the benefit of combining low laser power and ORS (Figure 2).

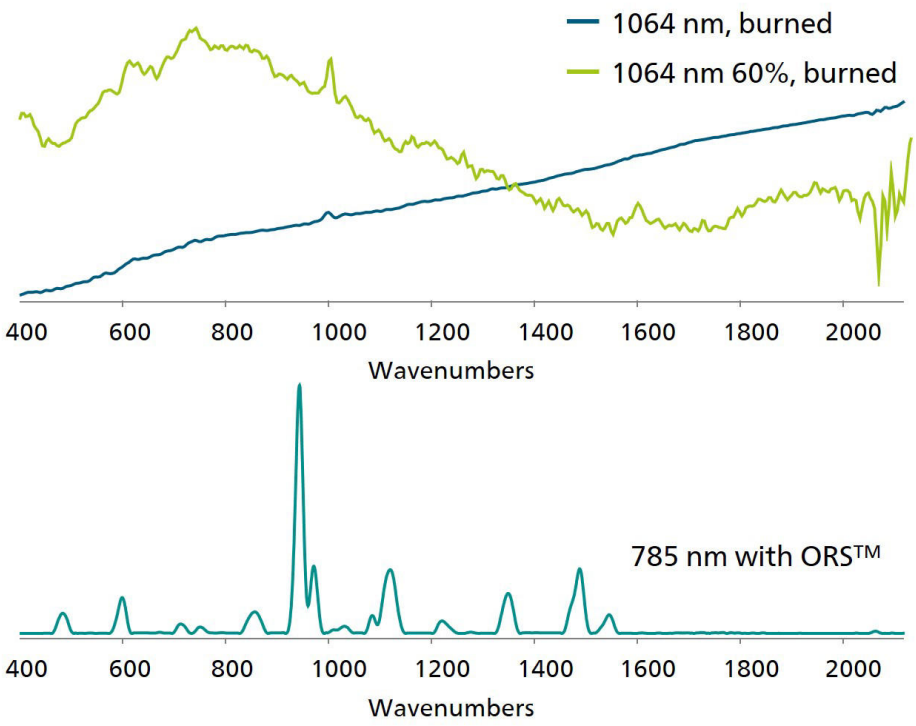


Figure 2. A comparison of Raman spectra collected from a grey plastic pen, with 1064 nm and 785 nm systems.

The crater on the left in Figure 3 was created when a fixed-laser 1064 nm system at 100% power burned the sample. The second test at 60% laser power gave the same result (Figure 3, right) and both tests failed to identify the material.

Figure 3. Grey plastic pen, burned with a 1064 nm system and identified as polystyrene with MIRA XTR DS.

MIRA XTR DS collected high quality data with no sample damage and identified the plastic as polystyrene, with a Hit Quality Index (HQI) of 0.91. This indicates high correlation between the sample spectrum and a library spectrum.

Raman Identification of Polyphenylene Ether (PPE)

A second example of non-destructive sampling and positive material identification with a MIRA system can be seen in Figure 4.

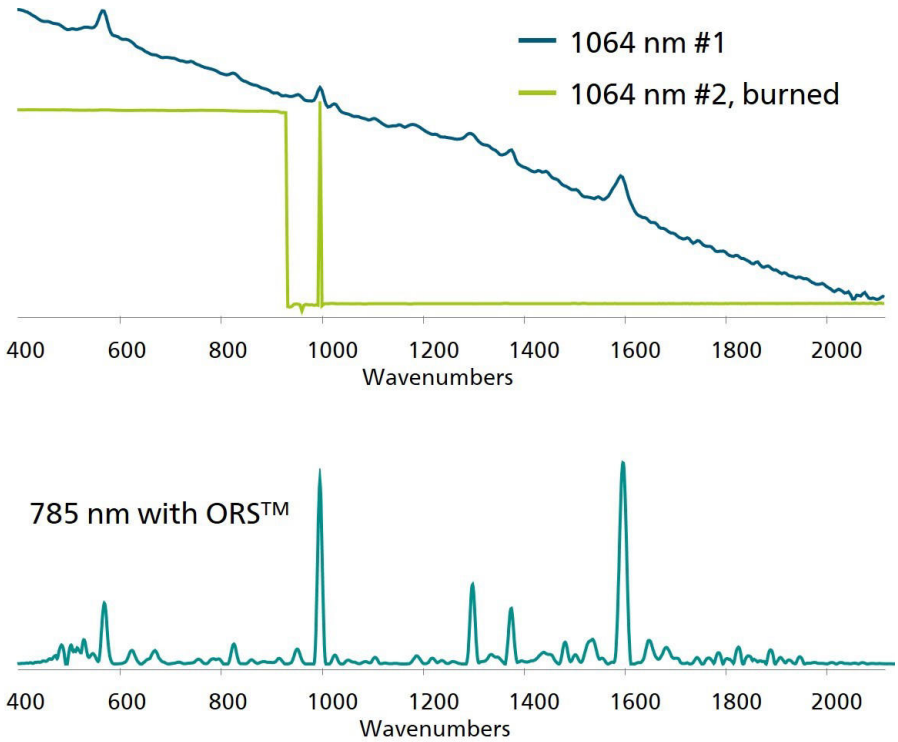


Figure 4. A comparison of Raman spectra collected from a colored material with 1064 nm and 785 nm systems.

The first test with the fixed-laser 1064 nm system produced a low-resolution spectrum, albeit one with some identifiable Raman peaks. The second test burned the material (Figure 5) and yielded no useful information.

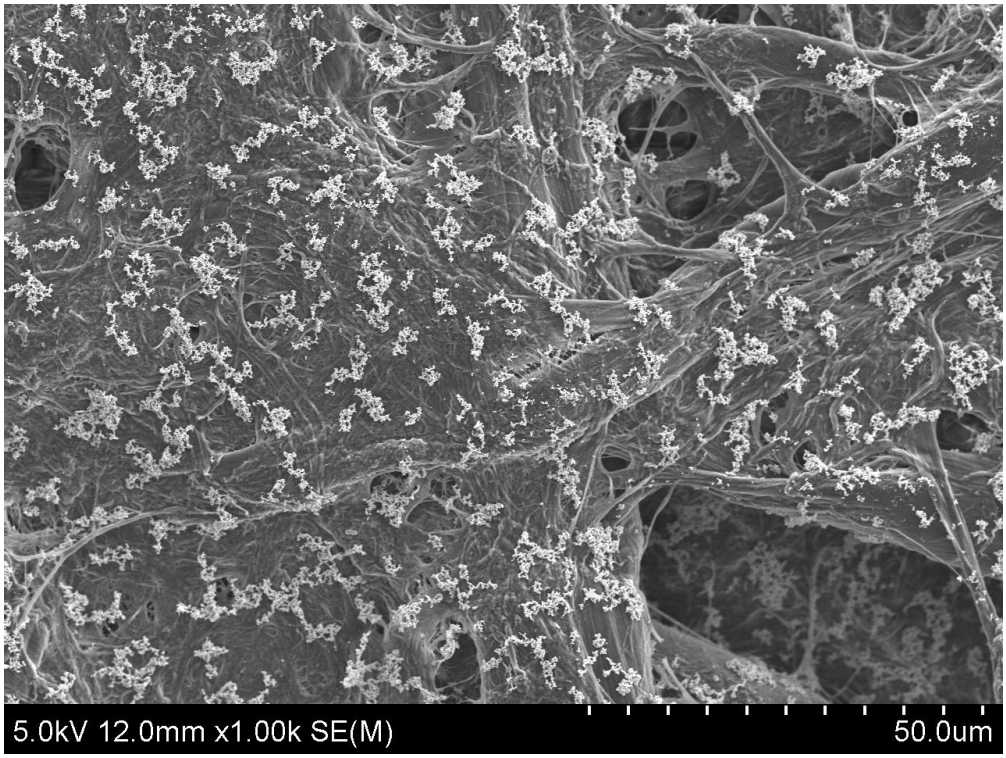
Figure 5. Example of sample burning with a 1064 nm system. This material was identified as polyphenylene ether (PPE) with MIRA XTR DS.

Again, MIRA XTR DS easily identified this material, giving a positive identification of PPE with HQI = 0.91. It must be acknowledged that these results may be successful because of a combination of factors: low power 785 nm lasers *and* ORS. The following application will focus entirely on the power of ORS to improve results for heterogeneous materials.

ORS AND SAMPLING OF P-SERS SUBSTRATES

P-SERS are paper-based substrates embedded with nanoparticles which enhance the Raman signal and permit very sensitive detection of trace analytes with SERS. P-SERS are used with MISA, a portable 785 nm Raman system equipped with ORS.

Inks prepared from silver and gold colloids are used to print P-SERS substrates, resulting in a heterogeneous distribution of nanoparticles on paper fibers [3]. This can be seen in the SEM images below (Figure 6).



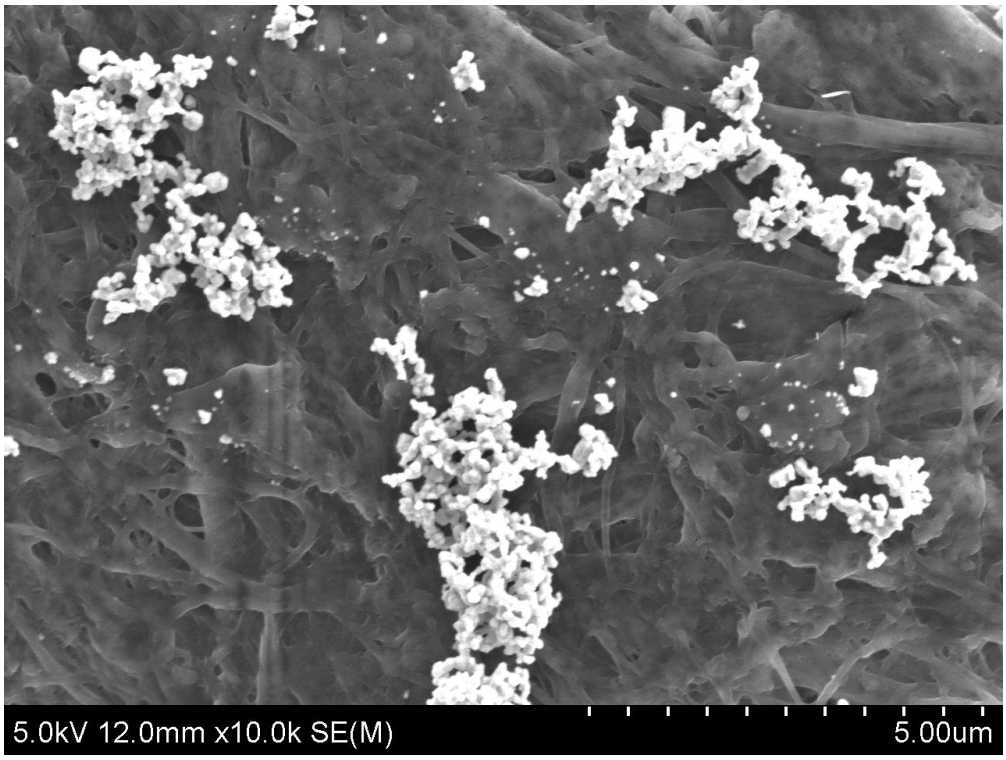


Figure 6. Silver nanoparticle distribution on P-SERS substrates.

Scanning a standard on P-SERS with the raster OFF and contrasting this with raster ON data is a perfect demonstration of the ORS advantage. BPE [1,2-Bis(4-pyridyl) ethylene] was solvated and dropped directly onto the printed portion of a P-SERS strip. This strip was analyzed with MISA using constant acquisition parameters but with raster ON and OFF (Figure 7).

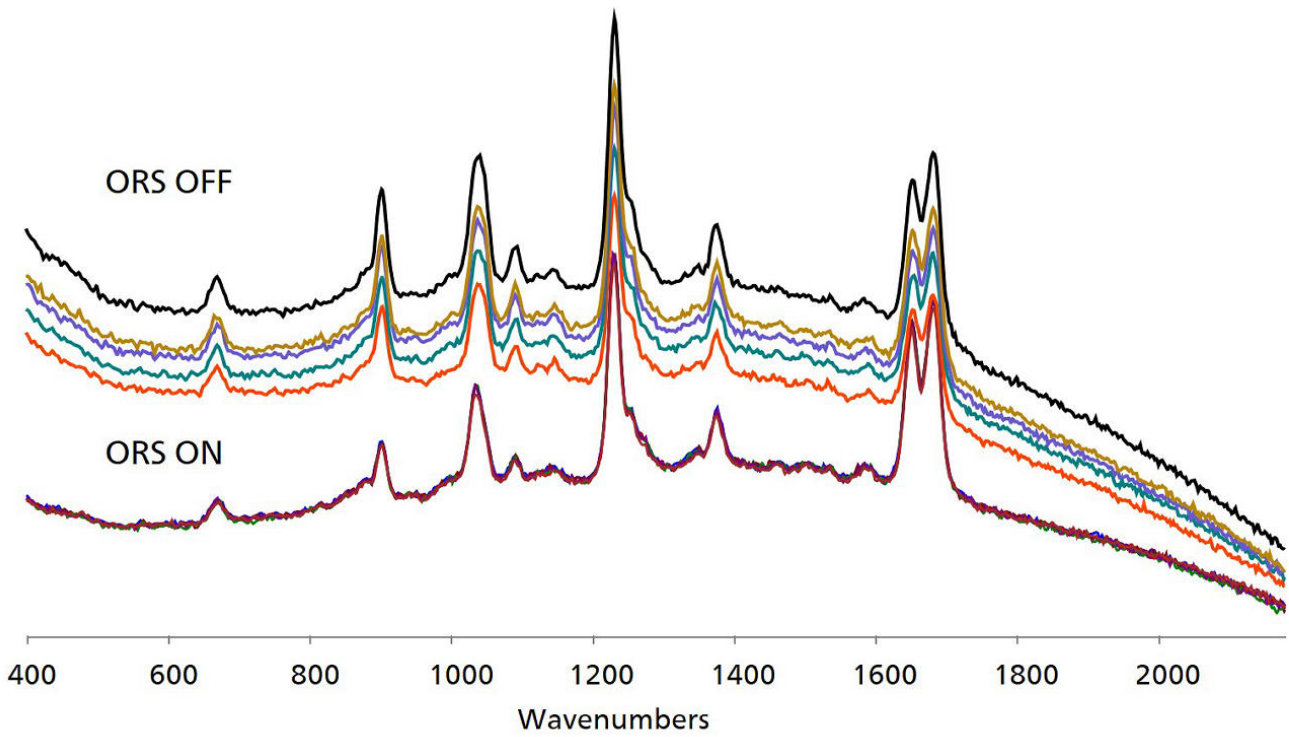


Figure 7. SERS data acquired with the raster ON (bottom) and OFF (top).

Each set of five spectra in Figure 7, ORS either OFF or ON, contains the same signature peaks for BPE. However, spectral consistency is ideal with the raster ON. Each spectrum is the averaged data from a large number of signal-producing hotspots collected during a single ORS scan. The result is a better representation of the heterogeneous surface. The variability of SERS signal intensity (standard deviation over a set of five spectra = 1.4%) with ORS ON is significantly lower than with ORS OFF (SD = 10%.) This confirms the strength of ORS in obtaining consistent data from a sample.

CONCLUSION

All systems from Metrohm Raman feature ORS, which has three significant benefits over stationary-beam systems:

1. Confidence in sample preservation, because the laser spot does not remain in the same location and there is very low risk of sample burning.
2. Data consistency, even for heterogeneous samples. The rastered beam collects data over a larger area of the sample, increasing reproducibility.
3. Best quality data collection. ORS covers a large sample area without losing resolution.

REFERENCES

[1] European Pharmacopoeia (Ph. Eur.) 10th Edition | EDQM - European Directorate for the Quality of Medicines https://pheur.edqm.eu/home (accessed 2021-11-08). [2] Smith, C. J.; Stephens, J. D.; Hancock, B. C.; Vahdat, A. S.; Cetinkaya, C. Acoustic Assessment of Mean Grain Size in Pharmaceutical Compacts. *Int. J. Pharm.* **2011**, *419* (1–2), 137–146. https://doi.org/10.1016/j.ijpharm.2011.07.032 [3] Yu, W. W.; White, I. M. Inkjet Printed Surface Enhanced Raman Spectroscopy Array on Cellulose Paper. *Anal. Chem.* **2010**, *82* (23), 9626–9630. https://doi.org/10.1021/ac102475k

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CONFIGURATION

MIRA P Advanced

The Metrohm Instant Raman Analyzer (MIRA) P is a high-performance, handheld Raman spectrometer used for rapid, nondestructive determination and verification of different material types, such as Pharmaceutical APIs and excipients. Despite the small size of the instrument, the MIRA P has a ruggedized design and features a high-efficiency spectrograph design equipped with our unique Orbital-Raster-Scan (ORS) technology. The MIRA P is fully compliant with FDA 21 CFR Part 11 regulations.

The Advanced Package includes an attachment lens for analyzing materials directly or through containers (laser class 3b), as well as a vial holder attachment for analyzing samples contained in glass vials (laser class 1).

MISA Advanced

Metrohm Instant SERS Analyzer (MISA) is a high performance, portable analyzer system used for rapid, trace level detection / identification of illicit materials, food additives and food contaminants. MISA features a high-efficiency spectrograph equipped with Metrohm's unique Orbital-Raster-Scan (ORS) technology. It has a minimal footprint and extended battery life, perfect for on-site testing or mobile laboratory applications. MISA offers various Laser Class 1 attachments for flexible sampling options. Analyzer operation is available through BlueTooth or USB connectivity.

The MISA Advanced package is a complete package that allows the user to perform SERS analyses using Metrohm's nanoparticle solutions and P-SERS strips.

The MISA Advanced package includes a MISA Vial Attachment, a P-SERS Attachment, a ASTM Calibration Standard, a USB Mini Cable, a USB Power Supply and MISA Cal software for operating the MISA instrument. A ruggedized protective case is also provided to securely store the instrument and accessories.