

# The Renishaw Biological Analyser



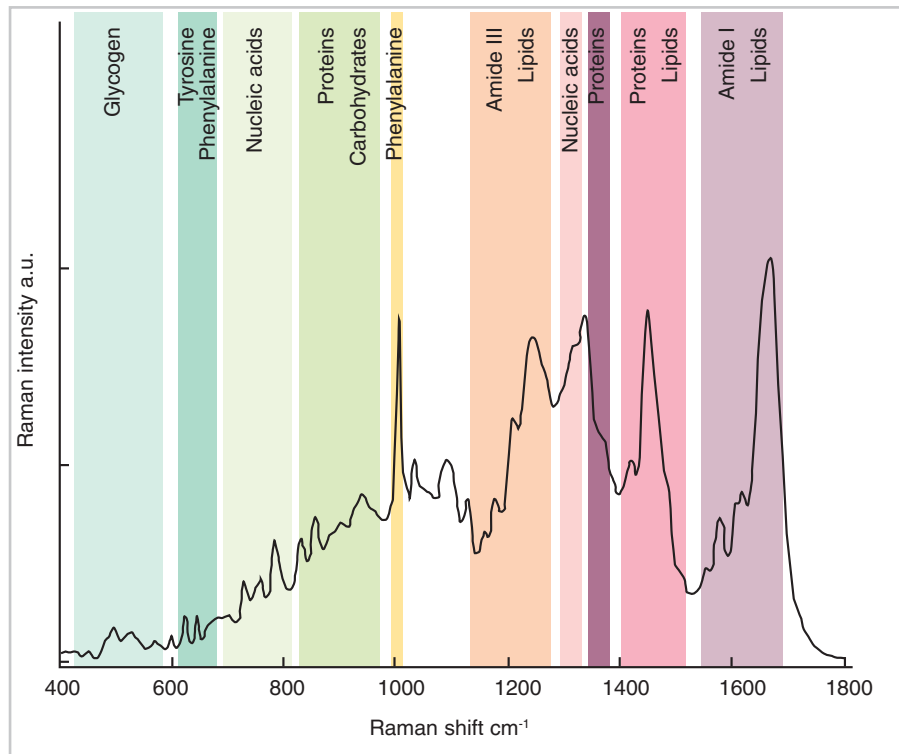
## The Renishaw Biological Analyser - RA816

The Renishaw Biological Analyser is a compact benchtop Raman imaging system that redefines tissue and biofluid analysis. It is easy to use, yet gives rich biochemical information about the biological samples being analysed.

Designed exclusively for the biological community, the system rapidly obtains detailed information on the distribution and amount of biochemical species within biological samples including tissue biopsies, tissue sections and biofluids.

The Renishaw Biological Analyser brings together the chemical analysis power of Raman spectroscopy (a light scattering technique) and advanced optical and spectroscopic imaging technologies in a simple, robust system. It produces outstanding results, quickly and easily.

Detailed biochemical information is revealed from biological samples. From the distribution of exogenous and endogenous compounds within tissue, to the detection of protein secondary structure changes due to drug interaction and tissue injury.



Typical biological tissue Raman spectrum demonstrating the wealth of information obtained from a single measurement

Raman spectroscopy provides many benefits for the study of biological materials:

- Non-invasive optical technique (retains sample integrity)
- Measures multiple molecular constituents in biological samples at once (saves cost and time)
- No sample staining or labelling required
- High specificity: aids in discovery and validation of early onset disease markers
- The generated high-resolution Raman images provide biomolecular information but also retain the spatial morphology

## Bringing Raman into the Clinic

The Renishaw Biological Analyser has a range of features making it the ideal tool for clinical research.

### Easy to use

- Easy to use software with simple concept and workflow: making Raman spectroscopy accessible to all users, without compromising performance
- Macro and high magnification modes, with digital zooming for a range of sample sizes
- Reflection or transmission illumination for best image contrast
- Image tiling for large area coverage

Compact, robust and transportable

- Small footprint - ideal for a space conscious laboratory environment
- System can be easily moved between lab and clinic with inbuilt performance checking to ensure accurate operation
- Robust system with no user alignment

### High performance for demanding applications

- Stable and repeatable, with integrated performance qualification (PQ) and alignment
- Post measurement check option to validate performance stability over the measurement period
- High throughput with high signal to noise spectral data and optimised substrates
- LiveTrack™ technology to track sample surface and retain focus
- Streamline™ technology for high speed data collection and image generation, without causing laser sample damage

### Dedicated data acquisition and analysis software

- Experiment templates for different biological sample types to simplify operation
- Model building software for clinical data classification:
  - provides the ability to build and validate pathology and disease models
  - validate the model with new samples enabling the stratification and classification of unknown tissue and biofluid samples
- Optimal system and sample workflow: enables robust, repeatable and reproducible data to be collected and analysed
- Enable configuration of multiple measurements for unattended operation

### The ideal toolkit for translating Raman to the clinic

- Performance standards support data transferability of classification models on additional Renishaw Biological Analyser systems
- Specially designed bio-sample holders and inserts for bio-fluids/liquids and tissue sections
- Bulk tissue biopsy sample holder eliminates the need for tissue sample preparation (e.g. cryosectioning or microtoming)
- Low-cost, ultra-low background disposable mirror slides for enhanced reflection, to increase Raman signal and improve white light contrast



A range of specially designed sample holders

## Powerful software

### Data acquisition

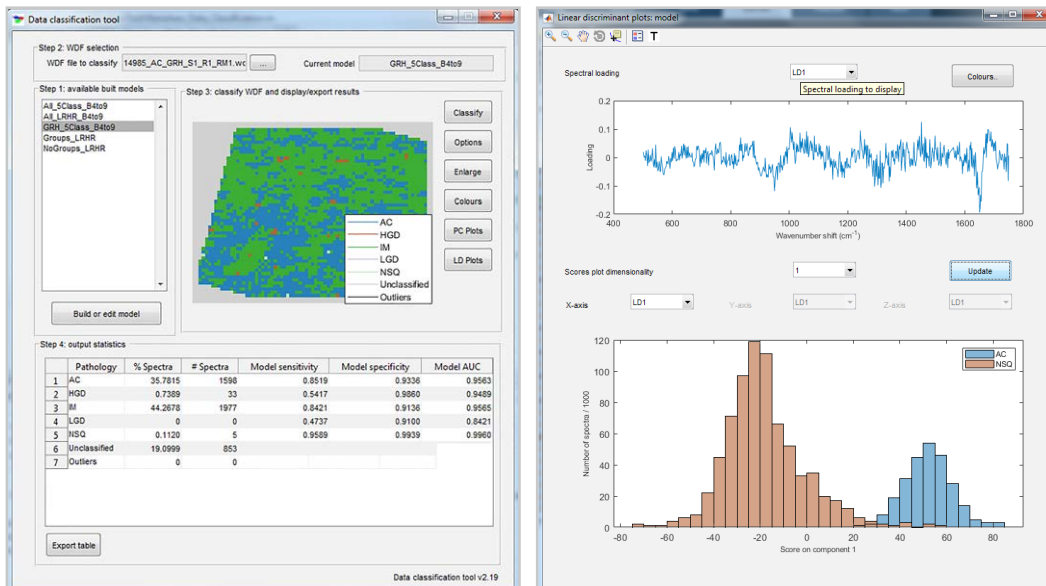
The Renishaw Biological Analyser is entirely computer-controlled. Its software provides a structure for managing every step of the measurement process using pre-defined experiment setups and protocols. The unique macro image provides a comprehensive overview of all subsequent work and enables easy sample navigation and visualisation. The system can acquire data unattended. Its queuing capability enables you to configure measurements and leave the instrument to run them; you can analyse multiple samples on a slide without the need for user intervention.

### Building and validating a classification model

The system includes a software package that enables the user to:

- Data process spectra datasets
- Build, test and validate pathology and disease classification models (using PCA-LDA)
- Minimise instrument and sample quality variations within and between the instruments and sites
- Test and validate classification models with new independent sample data

These tools aid in the discrimination of cancer stages with high sensitivity and specificity, establish early onset disease markers and identify biochemical changes associated with cancer formation and progression.



Renishaw data classification software



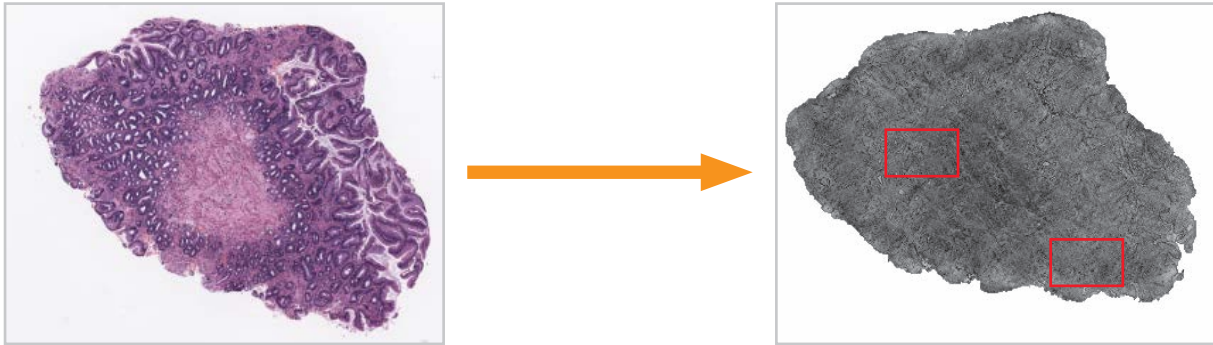
The Renishaw Biological Analyser



## Example workflows for routine operation

Raman tissue imaging with the Renishaw Biological Analyser and correlating results with stained/labelled slides

1. Place your stained/labelled slide in the dedicated holder and select from list of available bio-sample types
2. The system automatically digitises the slide using reflection or transmission white light imaging (macro view or high-resolution tile)
3. Insert and digitise an adjacent unstained tissue section
4. Select the regions or whole sections for Raman analysis on the unstained image based on areas of interest from the stained image



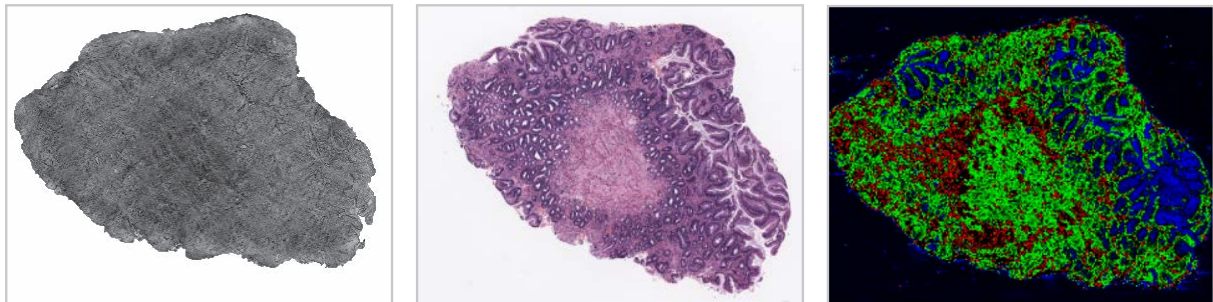
H&E stained image

Correlate H&E and unstained image

Select regions of interest or whole section

5. The system then:

- a) scans the tissue section or selected areas (if necessary, using LiveTrack focus-tracking technology to keep in focus and maintain highest signal quality)
- b) generates biochemical images that reveal chemical and morphological information about your tissue sample



Unstained white light image

H&E stained image

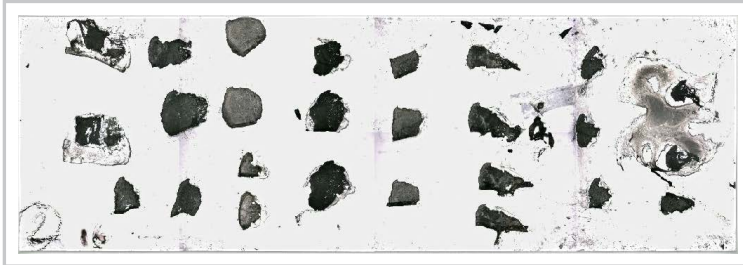
Raman biochemical tissue image



The Renishaw Biological Analyser

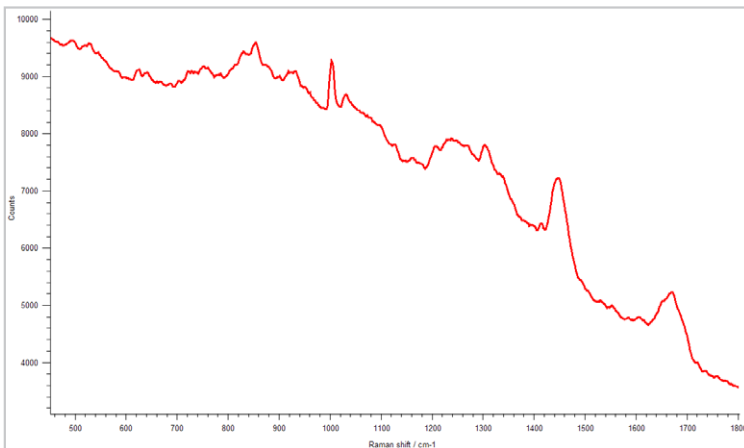
**Raman spectral data collection for disease/pathology classification**

1. Place your tissue or biofluid samples on one of the dedicated sample holders
2. The system automatically generates a macro image of the entire slide (providing an overview of the array of samples)



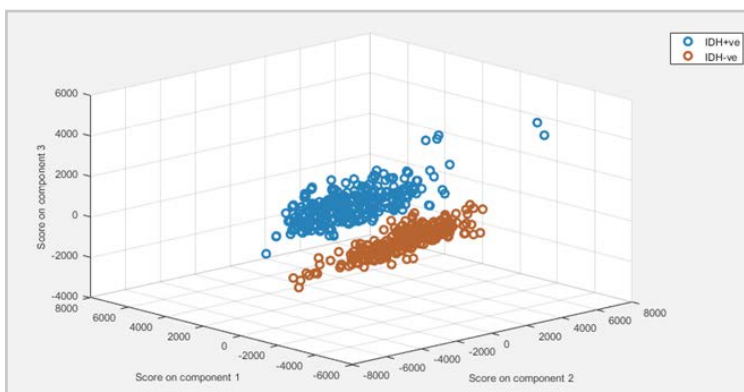
Macro image of slide

3. Generate a high resolution tiled image of the individual tissue sections if necessary
4. Specify the area or points to analyse and start analysis using predefined measurement settings



Mean of example spectral dataset (taken from data measured at 4s time exposure; 1 accumulation; 100% laser power)

5. Perform multivariate analysis using the inbuilt data classification tool to reveal biochemical information about your tissue samples, and generate classification performances of the disease and pathology models



Example Multivariate analysis (PCA) of IDH genomic mutation status of brain glioma

Pathology	Sensitivity	Specificity	AUC
IDH +	1.00	0.99	1.00
IDH -	0.99	1.00	1.00

IDH genomic mutation status classification performance using the Renishaw data classification software\*1

\*1 Livermore *et al.* 2018 manuscript in preparation.

## Specifications - The Renishaw Biological Analyser RA816

Parameter	Value
Laser wavelength	785 nm Integral Renishaw high power near infrared diode laser, 300 mW at 785 nm, air cooled, with integral plasma filter. Laser power: > 150 mW at sample. Innovative StreamLine technology enables higher laser power use without sample damage
Spectral range	100 cm <sup>-1</sup> to 3250 cm <sup>-1</sup> Performed in two separate scan ranges Range 1: 100 cm <sup>-1</sup> to 2000 cm <sup>-1</sup> ; Range 2: 1950 cm <sup>-1</sup> to 3250 cm <sup>-1</sup>
Spectral dispersion	2 cm <sup>-1</sup> pixel <sup>-1</sup>
Data collection speed	Over 1500 spectra/s
Minimum Raman image pixel size	1 µm Spatial resolution 1 µm per pixel
Objective	8.2 mm working distance 0.55 NA 50× long working distance objective Additional macro-view colour video camera
Field of view	Macro 21 mm × 16 mm Micro 330 µm × 250 µm
Maximum tiled image size	Macro 134 mm × 76 mm High magnification 112 mm × 81 mm
White light modes	White light transmission and reflection capability
Focusing	Macro – Manual or pre-defined Micro – Automatic (LiveTrack) or manual Real time automated LiveTrack dynamic focusing for both Raman data acquisition and white light video viewing modes
System calibration and transferability	Self-calibration and auto-align using built in neon and silicon references Automatic PQ data collection – (polystyrene) Optional post measurement check (PMC) for inter-measurement validation
Maximum sample size	~ (110 mm × 90 mm × 25 mm) – fits 96 well plate
Power, voltage	100 – 240 VAC ± 10%, 50/60 Hz, 100 W maximum
Dimensions	720 mm (W) × 502 mm (H) × 535 mm (D)
Mass (not including computer)	54 kg
Laser class	Class 1 laser product complies with IEC60825-1. CE marked

The Renishaw Biological Analyser is designed for research use only (RUO) and is not for use in diagnostic procedures.

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## Renishaw. The Raman innovators

Renishaw manufactures a wide range of high performance optical spectroscopy products, including confocal Raman microscopes with high speed chemical imaging technology, dedicated Raman analysers, interfaces for scanning electron and atomic force microscopes, solid state lasers for spectroscopy and state-of-the-art cooled CCD detectors.

Offering the highest levels of performance, sensitivity and reliability across a diverse range of fields and applications, the instruments are designed to meet your needs, so you can tackle even the most challenging analytical problems with confidence.

A worldwide network of subsidiary companies and distributors provides exceptional service and support for its customers.

**Please visit [www.renishaw.com/Raman](http://www.renishaw.com/Raman) for more information.**

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