Fast, high-definition Raman imaging

Fast Laser Raman Microscope

RAMAN-11
Fast Raman Imaging
A New Generation of Raman Microscope

RAMAN-11 developed by Nanophoton was created by combining confocal laser microscope technology with Raman spectroscopy. Fast, high-definition Raman imaging is only available from Nanophoton through combination of their laser microscopy and Raman spectroscopy expertise.
A New Generation of Fast Raman Imaging

First generation Raman spectroscopy was developed over 30 years ago. Second generation instruments combined a Raman spectrometer with a microscope to enable Raman mapping of a selected micro-region of a sample with stage scan. RAMAN-11, is a third generation tool combining very fast high-definition Raman imaging with excellent spatial resolution.

<table>
<thead>
<tr>
<th>I Generation</th>
<th>II Generation</th>
<th>III Generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser Raman Spectrophotometer</td>
<td>Low speed</td>
<td>Fastest in the world</td>
</tr>
<tr>
<td>Microscope with mapping function</td>
<td>High Definition</td>
<td>Very fast high-definition Raman imaging</td>
</tr>
<tr>
<td>(2D Imaging)</td>
<td></td>
<td>with excellent spatial resolution</td>
</tr>
<tr>
<td>Observation of geometry</td>
<td>Laser Raman Microscope with fast imaging function</td>
<td>RAMAN-11</td>
</tr>
</tbody>
</table>

Fast High-Definition Raman Imaging

RAMAN-11 imaging speed is unsurpassed. RAMAN-11 achieves imaging speeds 300 to 600 times faster than other products. It’s like comparing the time savings of flying across the USA to driving.

RAMAN-11

10,000 pixels (spectra) / minute

Rival product A

32 pixels (spectra) / minute

Rival product B

15 pixels (spectra) / minute

Conditions of the comparison:
The comparison was done using the same exposure amount and included the data transfer time.
Application

Fast Raman imaging observation opens up new applications!
Fast, high-definition Raman imaging capabilities that are now available with the RAMAN-11 enable Raman applications into fields where it had previously been impossible to observe Raman images.

**Distribution of materials**
The left-hand figure shows the distribution of hand lotion on skin. Fast Raman imaging was able to identify lotion distribution by the Raman spectra of lotion constituents. Lotion distribution by optical microscopy is, of course, impossible (the right-hand figure).

**Stress distribution**
The detection of crystalline distortion, such as in silicon, is possible using Raman imaging. The Raman peak of silicon is seen at 520 cm\(^{-1}\). The peak position shifts in response to distortion in the silicon crystal lattice resulting from stress. The figure shows the stress distribution of the silicon crystal obtained by imaging the shift of the peak position. RAMAN-11 enables us to achieve the imaging by detecting just 0.1 cm\(^{-1}\) of the peak shift.

**Crystallinity evaluation**
The observed image shows the crystallinity resulting from ion implantation in a silicon wafer. Crystallinity can be evaluated by peak width analysis because of the correlation that exists between crystallinity and Raman peak width. Better crystallinity gives a narrower peak width.
Depth profile analysis
This is a cross-sectional Raman image of a multi-layer film observed non-destructively. By combining line illumination with confocal optics, the cross-sectional image can be non-destructively observed using depth profile analysis.

Biological samples
Laser scanning eliminated the needs for slow sample stage scanning and the inherent problems associated with mechanical vibration that result from the use of mechanical stage designs. Vibration-free laser scanning enable use to image samples prone to vibration, in this case cells suspended in a culture medium. High speed imaging capabilities of RAMAN-11 also enable observation over time of dynamic processes such as cell division. The figure shows a Raman image of unstained human uterine cervix cancer cells.

Ingredients of a pharmaceutical compound
This Raman image shows the distribution of pharmaceutical ingredients and diluents on the surface of a tablet. The pharmaceutical ingredients exist as various polymorphic crystals. The polymorphs of the pharmaceutical ingredients can be non-destructively analyzed without contact using a small amount of the sample. The distribution of the grain size of each ingredient can also be observed.
Cellular uptake of materials
The figure shows an image of the distribution of an anticancer drug administered to cancer cells. The image shows that the anticancer drugs (foreign matter) are taken into cells and exist locally in the cell nucleus and around the outside of the nucleus. It is shown that intra cellular pathways for drug uptake can be readily discerned.

Distribution of materials in a superconductor
The figure shows an image of a superconductor.
R: Gd123/a/b oriented
G: CeO$_2$
B: Gd123
C: Gd123/underdoped
Y: NiFe$_2$O$_4$
RAMAN-11 enables to observe the distribution of various compounds used for advanced materials.

Observation of a wide-field of view
Raman imaging of large areas is possible by combining the motorization stage with the standard laser beam scanning function. The image shows the distribution of high quality diamonds (shown in green) and low quality diamonds (shown in yellow).
**Software**

RAMAN-11 supports various user applications with significant software operability.

**Quick data acquisition**

RAMAN-11 software consists of two different software programs. One is for measurement, and the other is for spectral analysis. With the measurement software you can quickly and easily select a measurement area by directing a laser spot on a microscope image of the sample. In addition, the measurement procedure can be immediately started by setting the laser wavelength, strength, exposure time, range of spectrum measurement and so on.

**Intuitive visualization**

The distribution of Raman intensity, peak area, peak shift, intensity difference and intensity ratio can be intuitively visualized by simply color assignments to Raman peaks.

**Superimpose**

Analysis and verification are easy by superimposing the Raman image on the microscope image from transmitted or reflected light.
High-speed and high-definition Raman imaging
The greatest characteristic of RAMAN-11 is that the Raman image can be easily and quickly acquired. Conventional measurement time needs several hours, but with RAMAN-11 measurement is completed in several minutes. The operation is simple that the operator only has to choose the measuring area with a mouse and then click the measurement button. The cross-sectional Raman image is also obtained by the confocal optics, as well as the conventional Raman surface image.

The “ezPointing” spectrum measurement
The Raman spectrum of any point on the sample can be measured by simply clicking the mouse while the pointer indicates the measuring point. As we use laser scanning technology, no stage movement is necessary.

Peak-shift imaging
Even very small peak shifts can be clearly visualized by Gauss or Lorenz function fitting.

Abundant data-handling functions
The following data-handling functions are necessary to analyze the sample.

- Fluorescence and background rejection
- Peak dimension analysis
- Smoothing (x-y-z-λ)
- Intelligent peak detection
- Median filter (x-y-z-λ)
- Binning (x-y-λ)
- Cosmic ray rejection filter
- Image processing with principal component analysis and least-square approach
- Component spectrum estimation by non-negative constraint

*Please consult with us about the customization of an analytical software.
Innovation

Nanophoton continues developing innovative technology to consistently lead the world as a specialized maker of laser microscopes. RAMAN-11 embodies those results.

Four Technologies to ensure high-speed and high-definition imaging

**Laser beam scanning**
- High-speed scanning is possible.
- The image is clear by vibration- and drift-free scanning.

**Line illumination**
- RAMAN-11 features line illumination to generate a line-shaped Raman-scattering light.
- Nanophoton developed original optics that ensures uniform intensity distribution.
Multi-spectrum simultaneous measurement

- High-speed and high-definition imaging is achieved by acquisition of line-shaped Raman scattered light. Each line scan is composed of 400 individual spectra.

Slit confocal

- Confocal optics for high-resolution imaging
- Original confocal optics were developed to enable high-speed imaging.
RAMAN-11, Specifications

### Main components

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optical Microscope</td>
<td>Upright or Inverted type, should be selected at time of order.</td>
</tr>
<tr>
<td>Scanner</td>
<td>Galvanometer mirrors for fast X-Y imaging. A motorized stage for Z direction scanning with 50nm step width. Illumination mode is selectable from three modes. Point focus illumination, Line-shaped illumination and flying-spot line illumination.</td>
</tr>
</tbody>
</table>
| Laser             | Standard wavelength: 532nm and/or 785nm  
- 532nm laser TEM00  
  High brightness (500mW)  
  High intensity stability (<2% rms)  
- 785nm laser TEM00  
  High brightness (500mW)  
  High intensity stability (<1.5% rms)  
* Other laser wavelengths are available upon request. |
| Spectrograph      | Three gratings with motorized turret  
- Imaging spectrograph eliminated astigmatism  
- High efficiency coating  
- Adjustable slit width in 1µm steps (10–1000µm)  
- Focal length: 500mm  
- Accuracy: 0.2nm  
- Repeatability: 0.05nm |
| Electrically cooled CCD Detector | 1340×400 Pixels  
- Vacuum sealed (metal seal)  
- Cooling temp.: -70°C  
- Read out noise: 5e rms  
- Pixel rate: 100kHz and 2MHz  
- Dynamic range: 16bit |

### Imaging performance (with an objective lens (x100, NA=0.9))

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatial resolution (X direction)</td>
<td>350nm</td>
</tr>
<tr>
<td>Spatial resolution (Z direction)</td>
<td>800nm</td>
</tr>
<tr>
<td>Field of view</td>
<td>90×120µm</td>
</tr>
</tbody>
</table>

### Spectroscopy performance (with a 1200/mm-groove grating)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectral resolution</td>
<td>1.6cm⁻¹</td>
</tr>
<tr>
<td>Raman shift detection range</td>
<td>80–4000cm⁻¹</td>
</tr>
</tbody>
</table>

### Physical Dimensions

<table>
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<tr>
<th>Parameter</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatial Dimensions</td>
<td>Width: 800mm, Height: 650mm, Depth: 670mm</td>
</tr>
<tr>
<td>Weight</td>
<td>120kg</td>
</tr>
</tbody>
</table>

### Examples of specifications by models

<table>
<thead>
<tr>
<th>Model</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAMAN-11-VIS</td>
<td>Laser 532nm 0.5W</td>
</tr>
<tr>
<td></td>
<td>CCD Peak QE 50% at wavelength range of 450–975nm</td>
</tr>
<tr>
<td>RAMAN-11-NIR</td>
<td>Laser 785nm 0.5W</td>
</tr>
<tr>
<td></td>
<td>CCD Peak QE 55% at wavelength range of 450–1050nm</td>
</tr>
<tr>
<td>RAMAN-11-VIS-NIR-HQ</td>
<td>Laser 532nm 0.5W / 785nm 0.5W</td>
</tr>
<tr>
<td></td>
<td>CCD Peak QE 90% at wavelength range of 200–1075nm</td>
</tr>
</tbody>
</table>

### Options

- Database (KnowItAll by Bio-Rad)
- Polarized Raman measurement
- Motorized stage for wide field of view observation
- Cooling/heating stage

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