Raman Update

HORIBA JOBIN YVON

Spring 2005

LabRAM *ARAMIS*

Advanced Raman Instrumentation with Intelligent Automation

The intelligent automation of the LabRAM *ARAMIS* represents a major advance in Raman instrumentation. It provides easy computer controlled operation for quality control, analytical and research applications alike.

The system maintains the market leading flexibility and performance of the award winning LabRAM series to provide the most comprehensive analytical tool available.

Ease of use

Confocality

Automation

Raman mapping and imaging

For further information on the intelligent automation of the LabRAM *ARAMIS* go to www.jobinyvon.com/Raman and click on LabRAM *ARAMIS*, or contact your closest HORIBA Jobin Yvon office.

SEE US NEXT AT:

12-14th April 2005
Semicon Europa
Munich, Germany

22-26th May 2005
IUMAS
Florence, Italy

29th May - 1st June 2005
ESOPS
Kerkrade, The Netherlands

31st May - 3rd June 2005
MRS Spring
Strasbourg, France

11-15th July 2005
Semicon West 2005
San Francisco, USA

31st July - 4th August 2005
Microscopy & Microanalysis 2005
Honolulu, Hawaii

See our new application notes:
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and click on 'Application Notes'

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Welcome to the Raman Update, produced by HORIBA Jobin Yvon's Raman Team, to provide our customers, colleagues & friends with up-to-date information in the field of Raman Instrumentation and Application.

See us next at:

IUMAS
22-26th May 2005
Florence, Italy

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A Comparison of Raman and EDXRF Chemical Imaging for Use in Formulation Process Development and Quality Control

By Fiona Clarke, Andrew Whitley**, Sergey Mamedov**, Fran Adar**, Neil Lewis***, and Eunah Lee****

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Dispersion of the API (active pharmaceutical ingredient) and excipients in pharmaceutical formulations e.g. tablets is of vital importance to the performance of the final product. Among other things the components' particle size, morphology and distribution can determine correct dosage as well as correct chemical behavior between the components during dissolution following ingestion and also in determining shelf life. It is typically not possible to determine particle size, morphology and distribution in a formulation via a simple visual inspection. By utilizing the hyper-spectral imaging capabilities of Raman and EDXRF (Energy Dispersive X-Ray Fluorescence) microscopy the chemical distribution of the components in pharmaceutical formulations can be directly observed.

In a recent study, in collaboration with the Pfizer Process Analytical Support Group at the Sandwich Laboratories in Kent, we have compared the information provided by Raman and EDXRF microscopy; these two techniques provide molecular and elemental images respectively. Both analytical techniques are being used in pharmaceutical process development and quality control. Raman microscopy permits very high spatially resolved molecular maps (1 µm), which show very accurately particle size and distribution in a formulation.

The EDXRF microscope provides a rapid method to obtain hyper-spectral elemental images with a 10 µm spatial resolution.

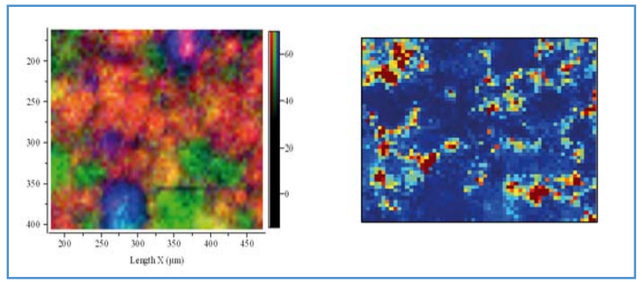


Figure 1a: Raman maps showing the distribution of the different components in the pharmaceutical formulation. First map shows microcrystalline cellulose, dicalcium phosphate and sodium starch glycolate distributions. Second map shows magnesium stearate distribution.

For both techniques little or no sample preparation is required.

Magnesium and calcium are common components of pharmaceutical formulations. Previously the distribution of one of the excipients, magnesium stearate, which is often added because of its lubricating properties, has been proven particularly difficult to study because it is present in low concentration, spreads very finely and has weak spectral bands in Raman, FT-IR, NIR and EDXRF spectroscopy.

The simplest method of preparing chemical maps is to bracket peaks of the species of interest and then color-map the intensity at each pixel of the various species. This works well as long as each species has a spectral band that does not overlap with bands of other species. The reality is that for complex organic species this requirement is often not met in multifiles of Raman as well as other spectra. In such cases treatment of the spectra with multivariate techniques enables one to separate the variances of the individual species. In addition, this multivariate approach can also be helpful in EDXRF, even though the spectra are much simpler, there is a possibility of overlapping between elemental lines.

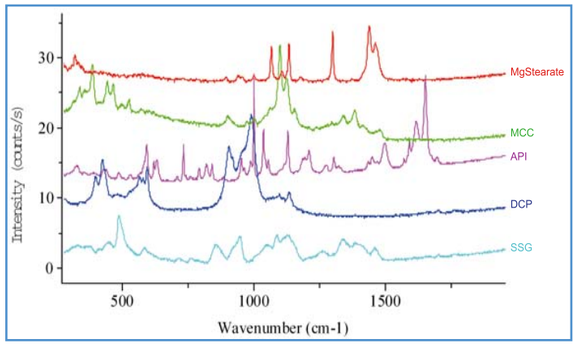


Figure 1b: Raman spectra of 4 excipients plus API

Figure 1a shows first a Raman image (RGB micrograph) of microcrystalline cellulose (MCC), dicalcium phosphate (DCP), and sodium starch glycolate (SSG). This has been produced by bracketing the bands of the Raman spectra of each component, shown on figure 1b. The second map shown in figure 1a corresponds to the distribution of magnesium stearate, this map has been produced using multivariate algorithms of ISys™ *(Spectral Dimensions)*.
Figure 2 presents the EDXRF maps of magnesium, calcium and phosphore elements. The results show a particular similarity between the distribution and the morphology of magnesium sterate using both techniques.

In addition to producing such intensity maps, the ISys™ software enables statistics to be performed on the multifile, to set thresholds in the maps, and to calculate the percentage of area that is occupied by the species of interest. This capability then allows particle size, morphology and concentrations to be estimated.

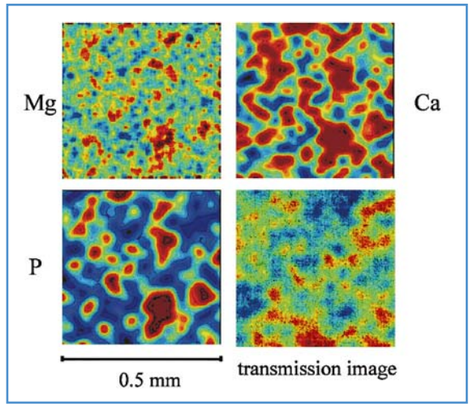


Figure 2. EDXRF map of Mg, Ca and P and the X-ray transmission image acquired with the 10 µm capillary.

Conclusions: This study shows that chemical and elemental imaging can be complementary, helping to provide an informative picture of the distribution of components in a pharmaceutical product.

The XGT-5000

The 10µm Innovation

Unique spatial resolution
- Micron scale resolution
- Speed

Analysis at atmospheric pressure
- Water containing samples
- Fine powders

Dual XRF/X-ray transmission detection
- Additional contrast
- Location of region of interest

Raman Spectroscopy for Semiconductor Applications

Combination of UV and VIS Raman for the Investigation of SiGe layers and strained Si top layer in SiGe based devices.

By Myriam Moreau and Gwénaëlle Le Bourdon, HORIBA Jobin Yvon S.A.S.

Epitaxial Silicon Germanium (SiGe) layers on Silicon (Si) is a material of high importance in microelectronic with a large number of applications depending on their properties.

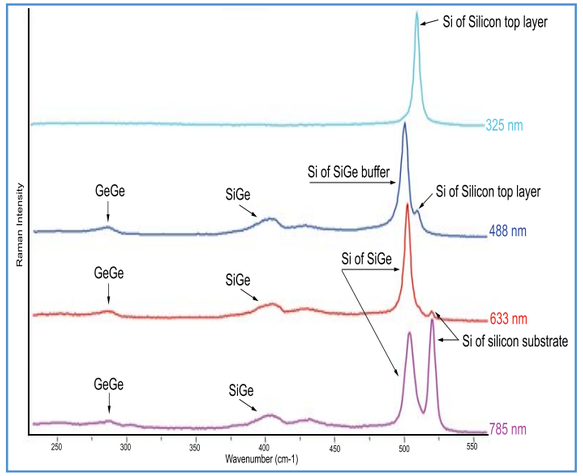
Raman spectroscopy is one of the most important tools for the investigation of these properties as it enables the determination of the composition (Ge content) and degree of relaxation of the SiGe layer, but also the characterisation of the stress induced in the top silicon layer. Indeed, Raman spectroscopy has been demonstrated to be very sensitive for stress measurements, especially in silicon layers, as the frequencies of the Raman modes are directly correlated to the stress applied to the crystal. By measuring the Raman modes of the Si-Si, Si-Ge and Ge-Ge bonds, it is possible to determine the stress in the strained Si layer and to calculate the composition and the strain in the SiGe film.

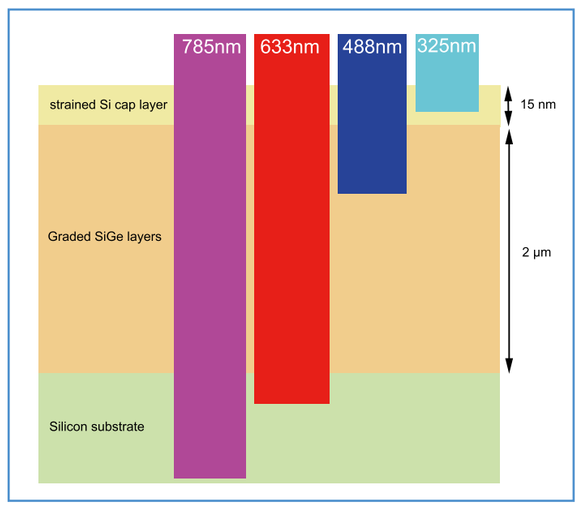
The choice of the laser excitation is of critical importance for these investigations, as the penetration depth and probed volume are strongly correlated to the laser wavelength. The use of UV lasers greatly improves the spatial resolution by taking advantage of the shorter wavelength and much smaller optical penetration depth, allowing very thin silicon top layers to be probed.

Combining both visible and UV Raman measurements enables a complete characterisation of the SiGe based devices. Indeed, the UV Raman spectrum will characterise only the top layer whereas the spectrum measured in the visible will show the Raman modes characteristic of SiGe, allowing the calculation of Ge content and the determination of strain in the SiGe layer.

Laser wavelenth (nm)	Penetration depth of Si (nm)	Penetration depth of Ge (nm)
633	3000	90
514	762	19.2
488	569	19
457	313	18.7
325	~10	15
244	~1	

Raman spectroscopy is a technique of choice for the characterisation of SiGe based wafers. This versatile technique which is also fast and clean room compatible can therefore also be a suitable method for process control in fabrication.





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Stress metrology : the Challenge for the next generation of engineered wafers, Tiberj et al., MRS Symp-Proc- Vol 809, 2004