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PHOTON IS OUR BUSINESS

Pharmaceutical Analysis

by MOEMS-based Near Infrared spectrometers

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Sep. 2021

Hamamatsu MOEMS-based NIR Spectrometers

Molecules each have unique vibrations, thereby absorbing infrared light of a specific wavelength. Infrared spectroscopic analysis, which utilizes this characteristic to analyze the components contained in substances, is used in a variety of fields from scientific research to industry. NIR spectrometers is normally the stationary type, which requires analysis to be done by bringing samples to a laboratory or specialized institution. For this reason, Hamamatsu Photonics has developed a palm-sized NIR spectrometers. Its compact size means it can be incorporated into portable analytical instruments, so it is expected to realize real-time infrared spectroscopic analysis at the location of the measurement subject.

FTIR engine

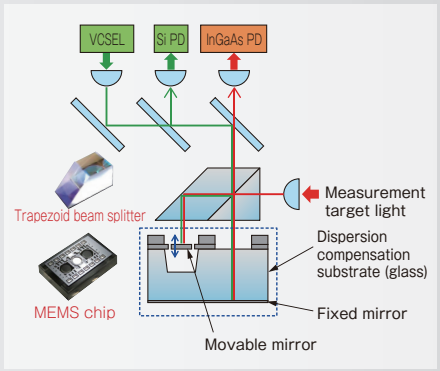
The Fourier transform infrared spectrometer (FTIR) engine is compact enough to carry in just one hand. A Michelson optical interferometer and control circuit are built into a palm-sized enclosure. Spectrum and absorbance can be measured by connecting a PC via USB.

Mini-spectrometer TF series

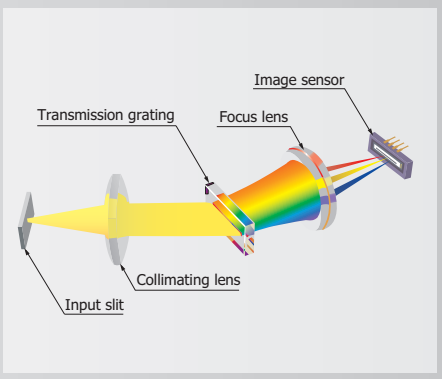
Grating type mini-spectrometer TF series is a polychromator provided in a compact, thin case that houses optical elements, image sensor, and driver circuit. Spectrum data can be acquired by guiding measurement light into a mini-spectrometer through an optical fiber and transferring the measured results to a PC via the USB connection.

MEMS-FPI spectroscopic module

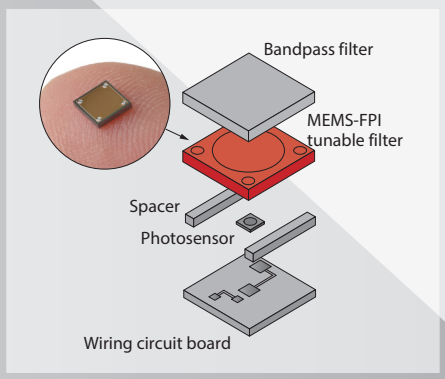
Spectroscopic module is a compact module integrating with MEMS-FPI (Fabry-Perot Interferometer) spectrum sensor, light source and control circuit. Spectrum and absorbance can be measured by connecting a PC via USB.



[Optical system of FTIR engine]

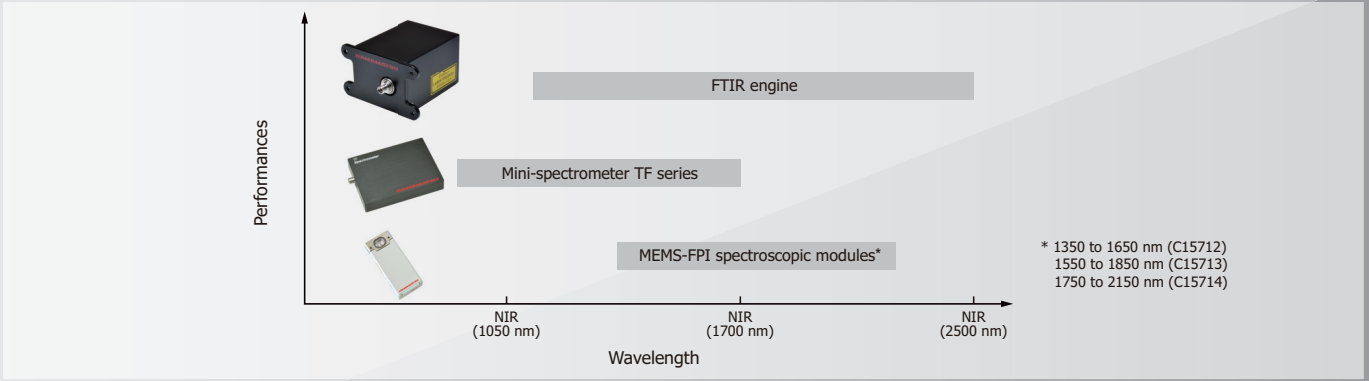


[Optical system of mini-spectrometer TF series]



[Internal structure of MEMS-FPI spectrum sensor]

■ Selection from size and wavelength



LINEUP

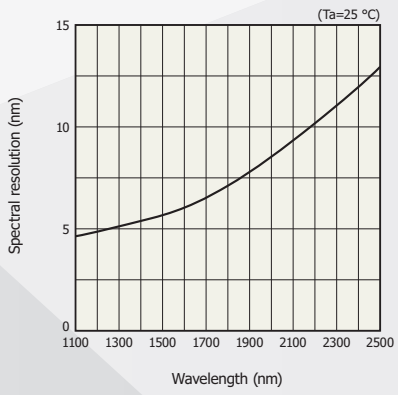
Hamamatsu prepares three types of spectrometers that supports near infrared light with a wavelength from 0.95 μm to 2.5 μm. Please select suitable spectrometers with your needs.

Product	FTIR engine	Mini-spectrometer	MEMS-FPI spectroscopic module
Appearance			
Type No.	C15511-01	C14486GA	C15712, C15713, C15714
Features	・Wide wavelength range ・Suitable for detailed analysis*1 ・High wavelength accuracy (calibration using built-in LD)	・High-speed ・Integration time adjustable (Dispersive optical system and arrayed sensors enable simultaneous measurement at multiple wavelengths)	・Small size, low cost ・Light source integrated (sensor only type is also available) ・Second derivative improves measurement performance*2
Structure	Michaelson interferometer + 1 ch PD + MEMS actuacter	Grating (MEMS process) + image sensor	Fabry-Perot tunable filter + 1ch PD
Dimensions (W × D × H)	57 × 76 × 49 mm	80 × 60 × 12 mm	32 × 74 × 16 mm
Spectral response range	1100 to 2500 nm	950 to 1700 nm	1350 to 1650 nm (C15712) 1550 to 1850 nm (C15713) 1750 to 2150 nm (C15714)
Spectral resolution (FWHM)	5.7 nm typ. (λ =1533 nm)	5.0 nm typ.	22 nm max. (λ =2150 nm)

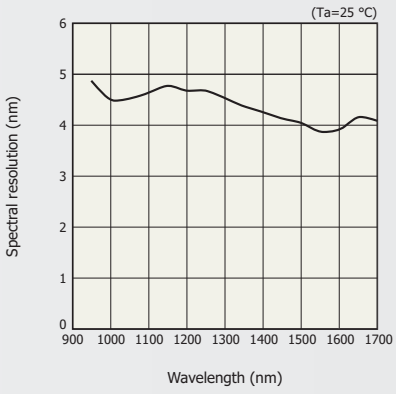
*1: Many data points, processing of interferograms, etc.
*2: Realizes performance closer to the FTIR engine and mini-spectrometer.

■ Spectral resolution vs. wavelength (typical example)

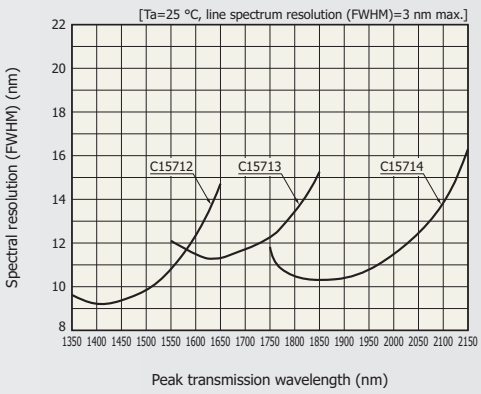
C15511-01



C14486GA



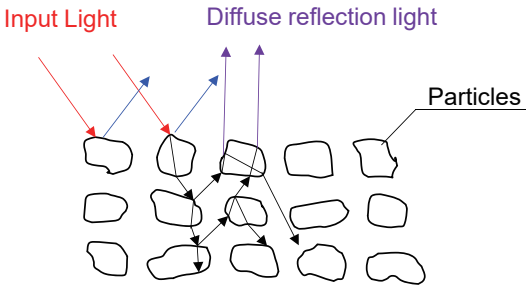
C15712, C15713, C15714



Examples of Pharmaceutical Analysis

Principle of Diffuse Reflection Method

In diffuse reflection, a portion of light irradiated onto a sample is reflected by the particles covering the sample surface while the rest of the light penetrates the sample. The light is repeatedly diffused through refractive transmission, light scattering, and surface reflection inside the sample. Some light is emitted from the sample surface.
Because the light is repeatedly transmitted through the interior of the sample during the diffusion process, the diffuse reflection spectrum can be considered similar to the absorption spectrum. In diffuse reflection measurement, common logarithms of a ratio between transmitted light level I_0 (reference measurement) and transmitted light level I_1 (sample measurement) can be taken for analysis.



■ Equation of Diffuse Reflection

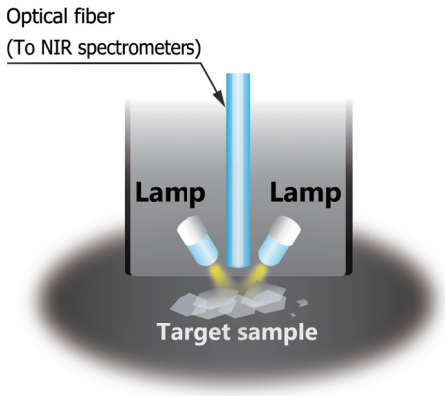
$$\frac{K}{S} = \frac{(1-R)^2}{2R} = \cosh\left[\log_{10}(1/R)\right] - 1 \cong \log_{10}\left(\frac{I_1}{I_0}\right)$$

K/S: Kubelka-Munk
S: scattering coefficient
K: absorption coefficient

R: Reflectance = I_1 / I_0
I_1: transmitted light level
I_0: incident light level

Recommended structure of diffuse reflection light source

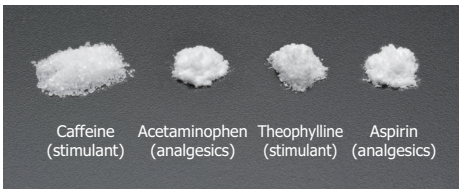
Diffuse reflection signals are generally very weak. Multiple lamps are placed in close proximity to the sample, and diffuse reflected light is taken into the NIR spectrometer via an optical fiber to improve the light detection efficiency.
The structure below is recommended for a diffuse reflection light source.

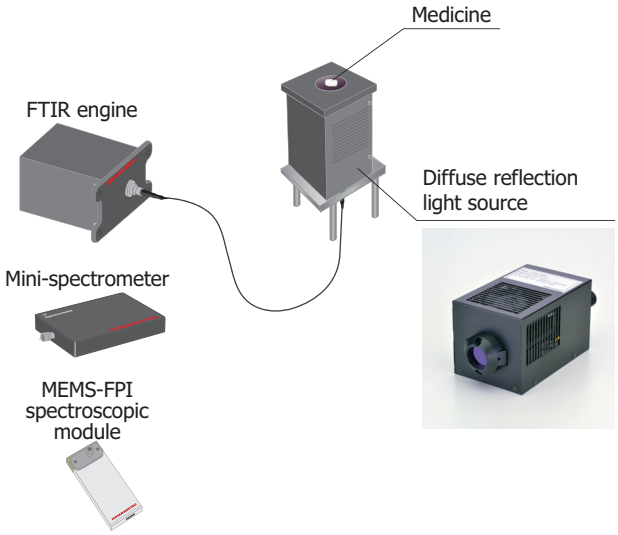


Benchtop FT-NIR instrument vs. Hamamatsu NIR spectrometers

Reflection measurement of several substances

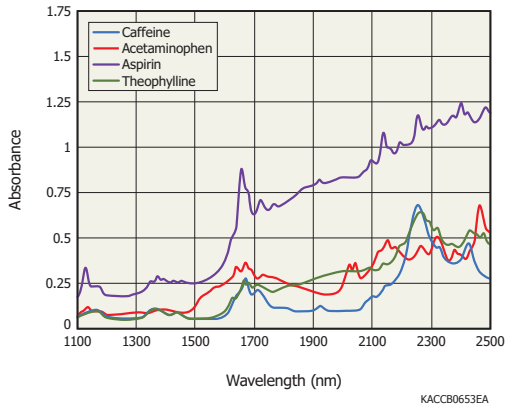
Followings are measurement results of following 4 substances using NIR spectrometers.





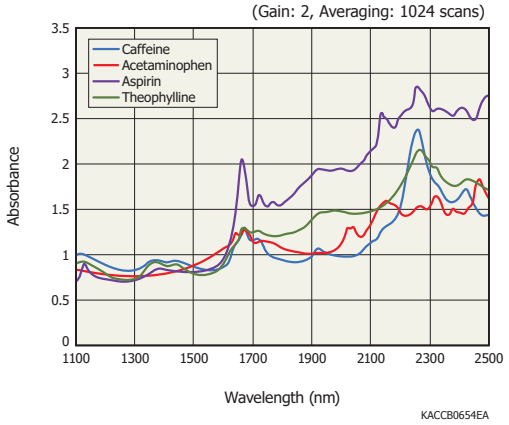
FTIR engine C15511-01 produces spectra equivalent to that produced by benchtop FT-NIR instrument, and at a fraction of the cost (the unit price is less than 1/10 of the benchtop type).
The grating type mini-spectrometer C14486GA is achieved same level as C15511-01 in the wavelength range up to 1700 nm.
The MEMS-FPI spectroscopic module C15713 allows detailed analysis by processing the data, although the absorbance peaks obtained appear rather small (see P.12).

Benchtop FT-NIR instrument



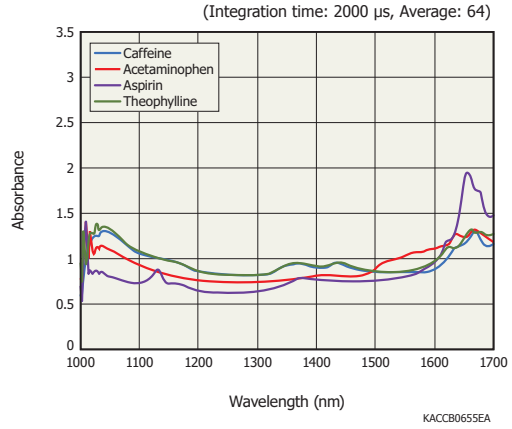
FTIR engine C15511-01

(Gain: 2, Averaging: 1024 scans)



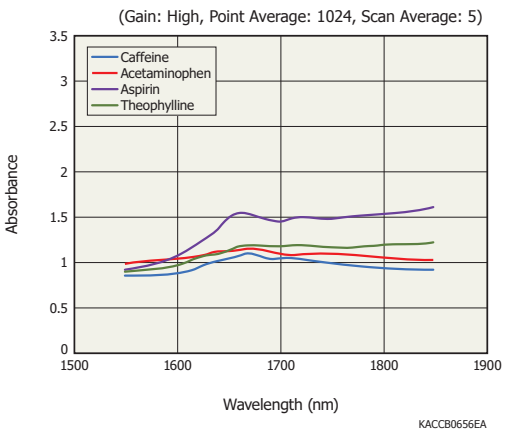
Mini-spectrometer C14486GA

(Integration time: 2000 µs, Average: 64)



MEMS-FPI spectroscopic module C15713

(Gain: High, Point Average: 1024, Scan Average: 5)

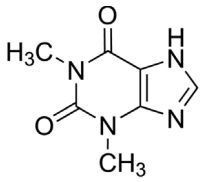


Measurement cooperated by: Hamamatsu Central ResearchLaboratory

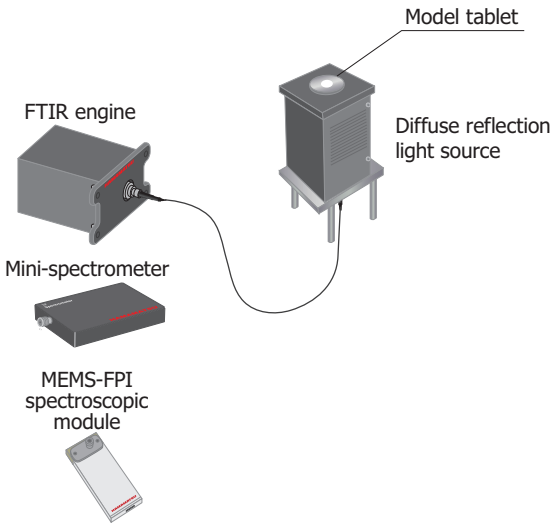
Spectral assignment of Theophylline Anhydrate

Measurement of Theophylline component

Theophylline anhydrate is a phosphodiesterase inhibiting medicine used in therapy for respiratory diseases.

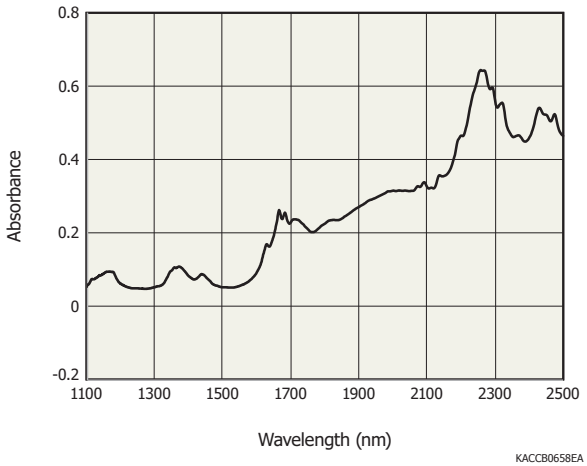


Theophylline component is measured using Hamamatsu NIR spectrometers (FTIR engine: C15511-01, Mini-spectrometer: C14486GA, MEMS-FPI spectroscopic module: C15713) and peaks in the specific spectrum is assigned and consistent with a published paper 1).

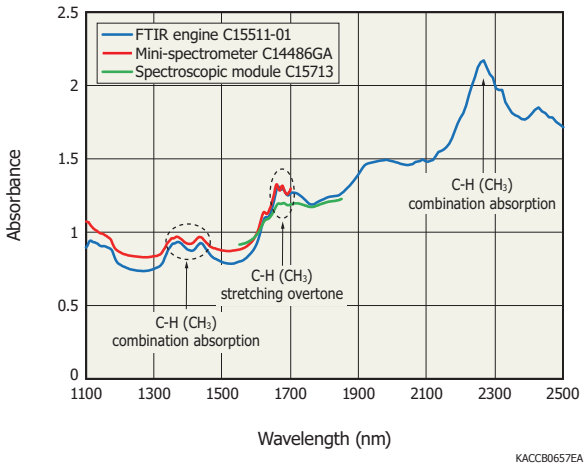


1) K Ikegaya, et al., Nippon Shokuhin Kogyo Gakkaishi, 34(4), p255(1987)

Benchtop FT-NIR instrument



Hamamatsu NIR spectrometers



Measurement cooperated by: Hamamatsu Central Research Laboratory

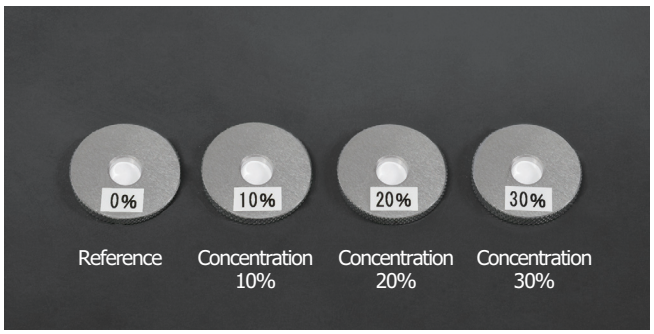
Quantitative Analysis of Theophylline in Tablets

Measurement of Theophylline content ratio

NIR spectrometer can be applied for process monitoring by quantative analysis.
Followings are measurement example using tablets which have a different Theophylliine contents (10 %, 20 %, 30 %) using Hamamatsu three types of NIR spectrometers.

■ Samples

- Theophylline concentration 10% (2pcs)
- Theophylline concentration 20% (3pcs)
- Theophylline concentration 30% (3pcs)
- Reference sample: 0% Theophylline concentration (lactose and starch)



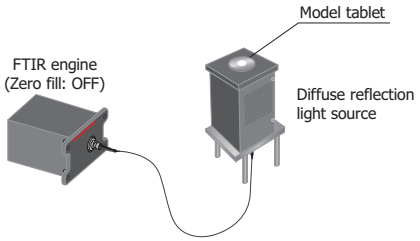
■ Spectrometers [conditions]

Measurement are done using following NIR spectrometers and conditions
① FTIR engine: C15511-01[Zero fill: OFF] (1100 to 2500 nm)
② FTIR engine: C15511-01[Zero fill: ON (Level2)] (1100 to 2500 nm)
③ Mini-spectrometer: C14486GA (950 to 1700 nm)
④ MEMS-FPI spectroscopic module: C15713 (1550 to 1850 nm)

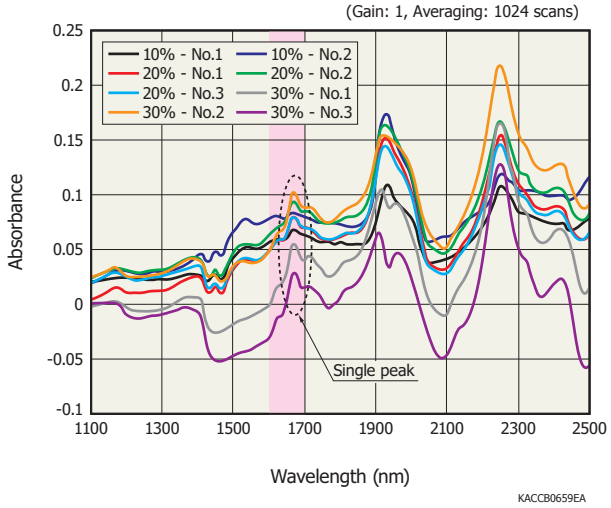
① FTIR engine C15511-01 (Zero fill: OFF)

Normally, theophylline has double peaks in a region from 1600 to 1700 nm. However, when an absorbance measurement is performed without zero-fill processing* by the FTIR engine, the peaks are combined into a single peak, and the double peaks can not be detected even with the second derivative processing.

* See P.13 for details.

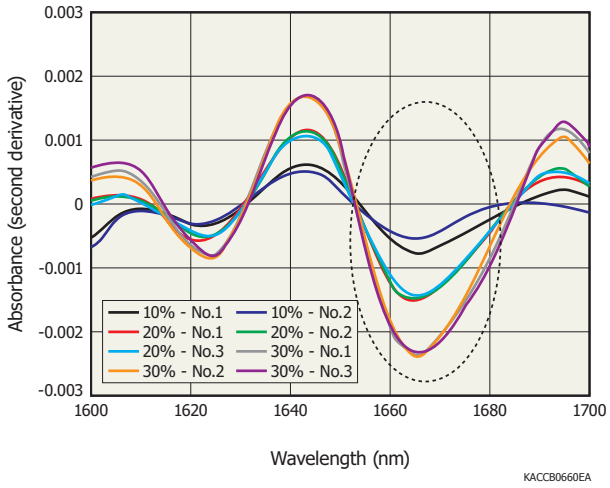


■ NIR diffuse reflection spectra of the tablets (concentration level)

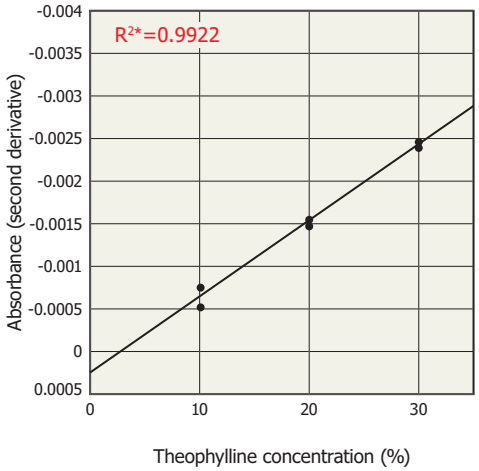


Second deriative

■ Data analysis by second derivative of absorbance



■ Calibration curve of Theophylline at 1666 nm



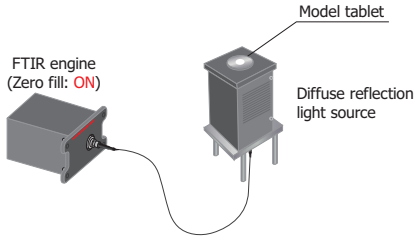
* R^2= Coefficient decision

KACCB0661EA

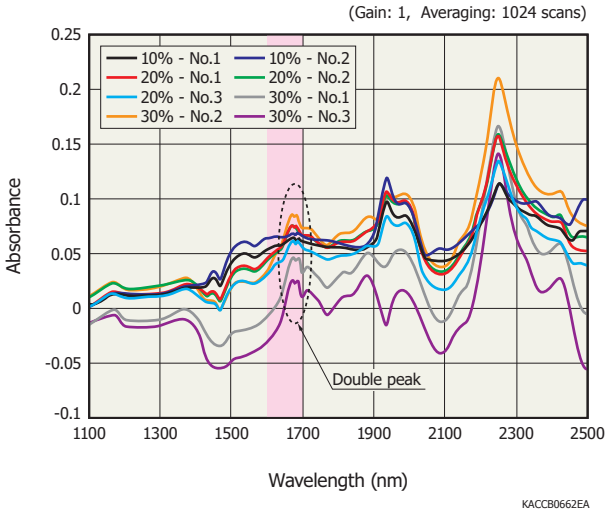
Measurement cooperated by: Hamamatsu Central Research Laboratory

② FTIR engine C15511-01 [Zero fill: ON (level 2)]

The increase in the number of data points due to zero fill processing makes it easier to detect double peaks sharply.
And second deriative processing of absorbance, double peaks are distinguished clearly.
The coefficient of determination R^2 is 0.9924 at a calibration curve of 1664 nm, indicating that highly accurate measurement can be realized.

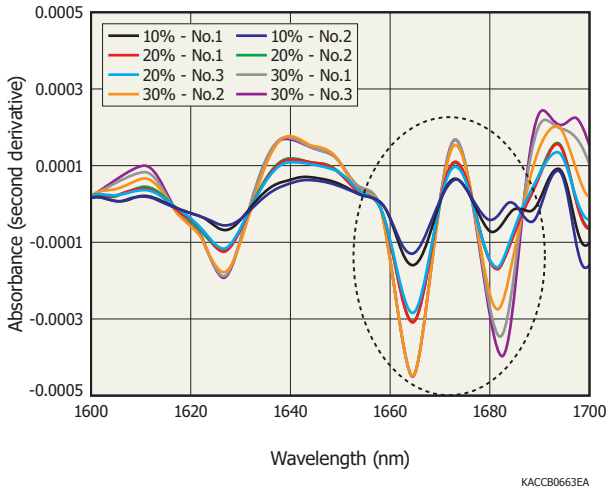


■ NIR diffuse reflection spectra of the tablets (concentration level)

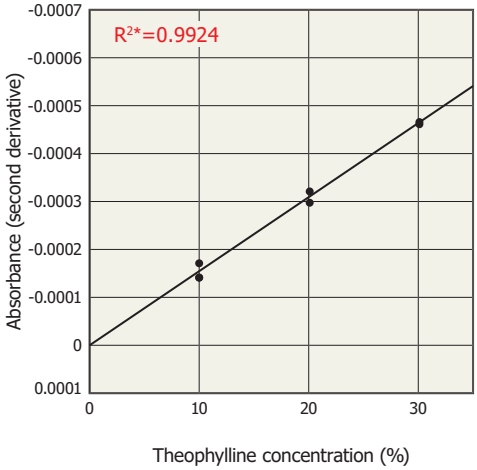


Second deriative

■ Data analysis by second derivative of absorbance



■ Calibration curve of Theophylline at 1664 nm



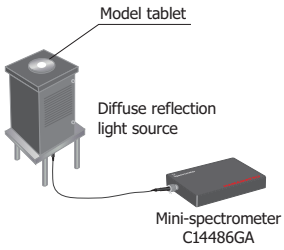
* R^2= Coefficient decision

KACCB0664EA

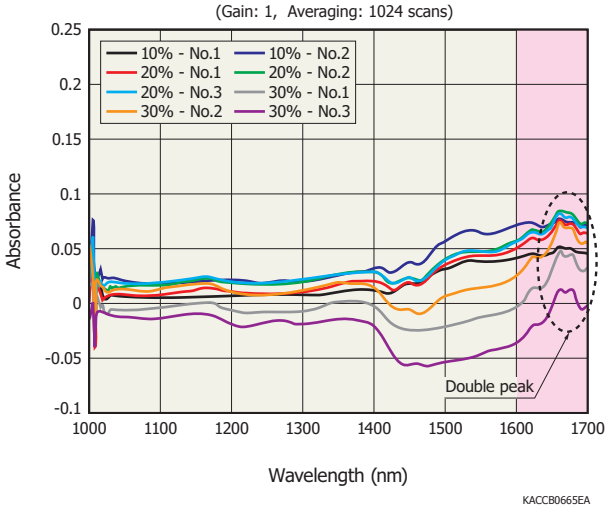
Measurement cooperated by: Hamamatsu Central Research Laboratory

③ Mini-spectrometer C14486GA

C14486GA only supports up to 1700nm, but it shows high resolution within the spectral response range.
It has comparable performance, although it has a narrower wavelength range than the FTIR engine.

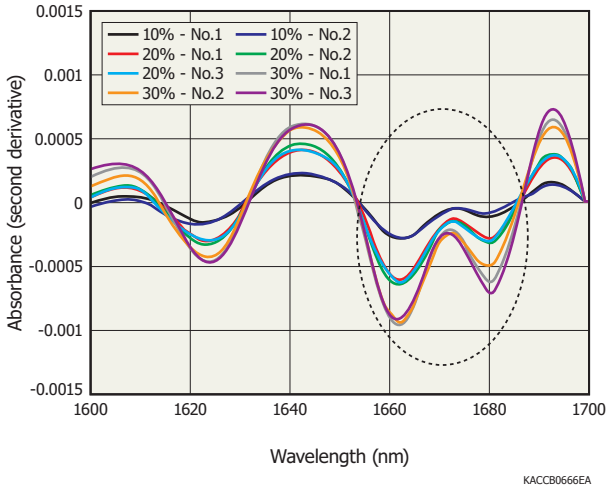


■ NIR diffuse reflection spectra of the tablets (concentration level)

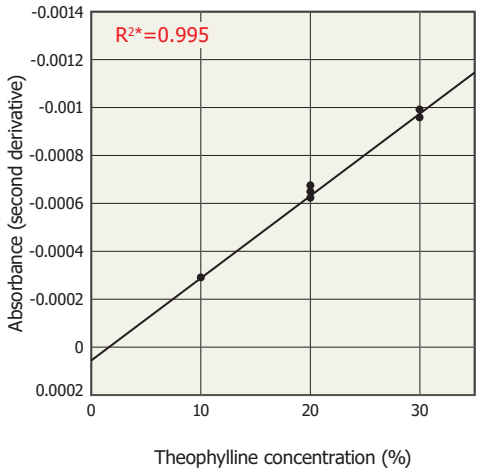


Second deriative

■ Data analysis by second derivative of absorbance



■ Calibration curve of Theophylline at 1662 nm



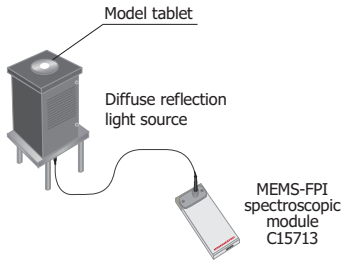
* R^2= Coefficient decision

KACCB0667EA

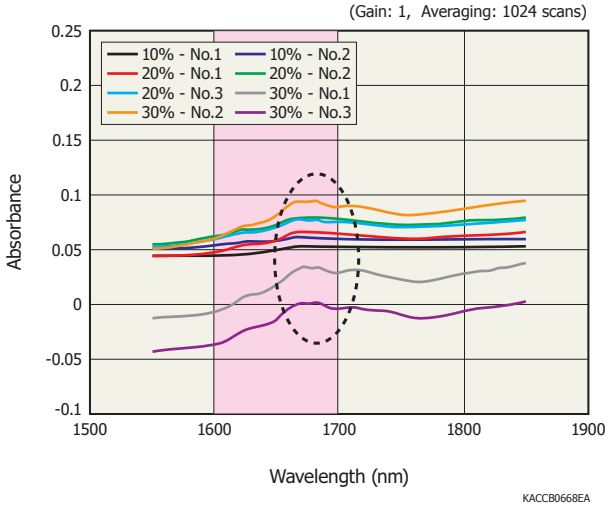
Measurement cooperated by: Hamamatsu Central Research Laboratory

④ MEMS-FPI spectroscopic module C15713

C15713 is difficult to see the difference only by the absorbance, but the double peaks can be confirmed by performing the second derivative processing.
The MEMS-FPI spectroscopic module, which features advantages in cost and size, has characteristics close to the FTIR engines and the mini-spectrometers in the coefficient of determination R^2.

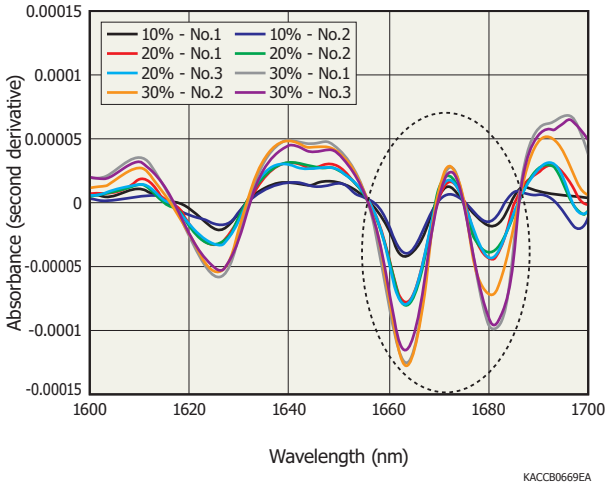


■ NIR diffuse reflection spectra of the tablets (concentration level)

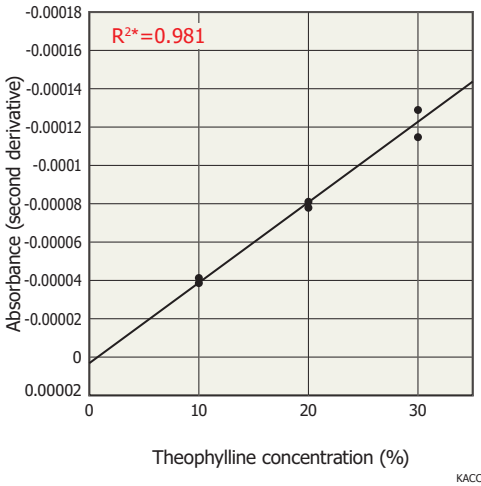


Second deriative

■ Data analysis by second derivative of absorbance



■ Calibration curve of Theophylline at 1664 nm



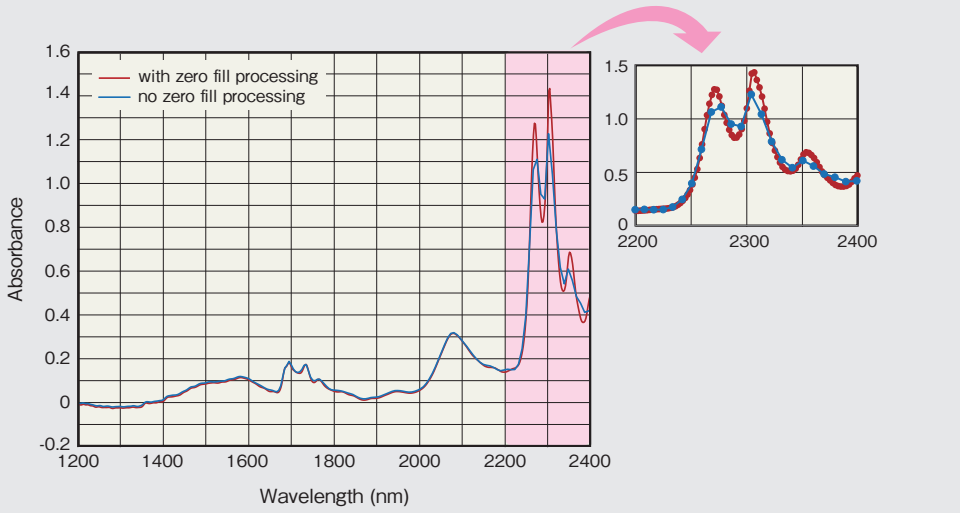
Measurement cooperated by: Hamamatsu Central Research Laboratory

[FTIR engine C15511-01]

“Zero Fill Processing” Enables Spectrum Detailed Analysis

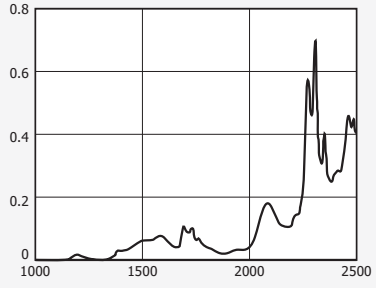
Zero fill processing is a technique of processing the spectrum data to obtain finer detail. It is a process of adding zeros to each end of an optical interference signal before a Fourier transform is applied. This allows for interpolation between points that are plotted after the Fourier transform.
The red graph using the zero fill processing achieves similar data compared with the above reference data.

■ Ethanol absorption spectrum



KACCB0674EA

□ Reference: literature data



Reference:
Yukihiro Ozaki, Near-Infrared Spectroscopy, 2015

■ Technical notes

FTIR engine
https://www.hamamatsu.com/resources/pdf/ssd/ftir_engine_kacc9012e.pdf

Mini-spectrometers
https://www.hamamatsu.com/resources/pdf/ssd/mini-spectrometer_kacc9003e.pdf

MEMS-FPI spectrum sensors, spectroscopic modules
https://www.hamamatsu.com/resources/pdf/ssd/mems-fpi_kacc9008e.pdf

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