HAMAMATSU

PHOTON IS OUR BUSINESS

Pharmaceutical Analysis

using Diffuse Reflection Light Source and Near Infrared Spectrometers

CONTENTS

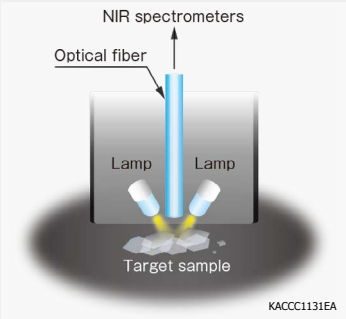
Sep. 2024

Near-Infrared Spectroscopy Solutions Using Hamamatsu Photonics Spectroscopic Technology

Molecules each have unique vibrations, thereby absorbing near-infrared light of a specific wavelength. NIR 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. For real-time composition analysis using near-infrared light, Hamamatsu Photonics has developed a diffuse reflection light source and near-infrared spectrometers. Compact analyzers combining these parts are expected to automate the quality control process in manufacturing lines such as for pharmaceuticals, and improve production efficiency and quality control reliability.

Diffuse reflection light source

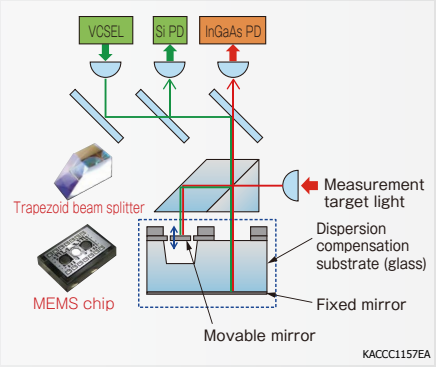
Diffuse reflection light source integrates lamps and bundled optical fibers. Light from lamps is irradiated to a sample, and is diffused and reflected. The light which is guided into the optical fibers can be used for spectroscopic analysis by connecting with a near-infrared spectrometer. By arranging multiple lamps and optical fibers close to each other, it can effectively detects the weak diffused light emitted from the sample.



[Structure of diffuse reflection light source]

FTIR engine (FT-NIR spectrometer)

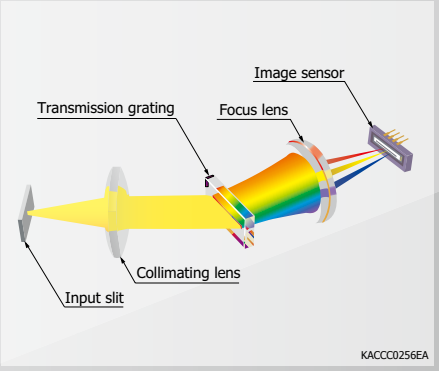
The Fourier transform infrared spectrometer (FTIR) engine is compact enough to carry in just one hand. A Michelson optical interferometer and control circuit are built into a palm-sized enclosure. Spectrum and absorbance can be measured by connecting a PC via USB.



[Optical system of FTIR engine]

Mini-spectrometer TF series

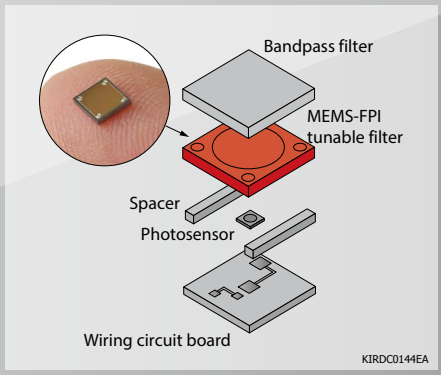
Mini-spectrometer TF series is a polychromator provided in a compact, thin case that houses optical elements, image sensor, and driver circuit. Spectrum data can be acquired by guiding measurement light into a mini-spectrometer through an optical fiber and transferring the measured results to a PC via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



[Optical system of mini-spectrometer TF series]

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.



[Internal structure of MEMS-FPI spectrum sensor]

LINEUP

Hamamatsu Photonics offers light emitters and photosensors for real-time composition analysis in the spectral range from 950 to 2500 nm.

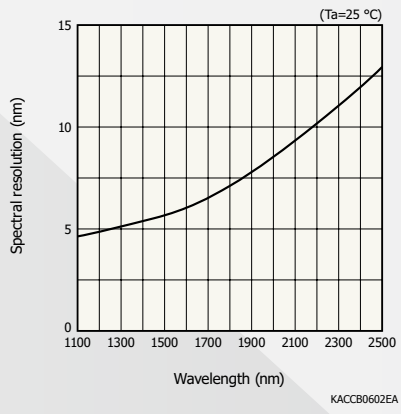
Parameter	Light source	Detectors (NIR spectrometers)		
	Diffuse reflection light source	FTIR engine (FT-NIR spectrometer)	Mini-spectrometer	MEMS-FPI spectroscopic module
Appearance				
Type No.	**L16462-01**	**C15511-01**	**C14486GA**	**C15712, C15713, C15714**
Features	· Compact · Long life · High detection efficiency	· 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*2 · Light source integrated (Sensor only type is also available)
Structure	Tungsten lamp (×4)	Michelson interferometer + 1 ch photodiode + MEMS actuacter	Grating (MEMS process) + image sensor	Fabry-Perot tunable filter + 1 ch photodiode
Dimensions (W × D × H)	φ28 × 35.5 mm	57 × 76 × 49 mm	80 × 60 × 12 mm	32 × 74 × 16 mm
Spectral response range [Wavelength range]	[400 to 2500 nm]	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.

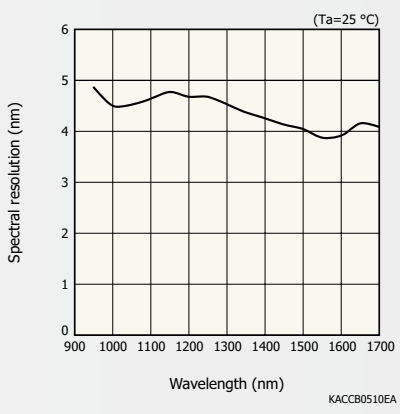
*2: Calibration curve accuracy with PLS regression analysis by second derivative processing achieves performance close to FTIR engine and mini-spectrometers.

■ Spectral resolution vs. wavelength (Detectors)

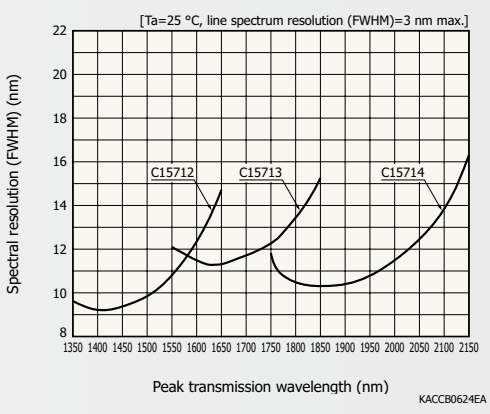
FTIR engine C15511-01



Mini-specctrometer C14486GA



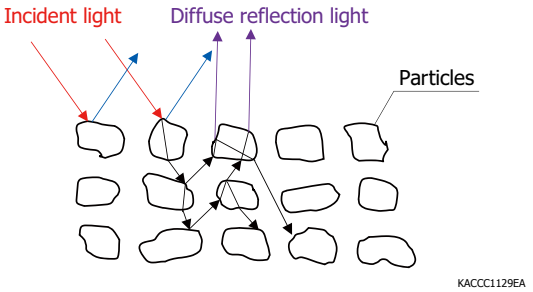
MEMS-FPI spectroscoic module C15712, C15713, C15714



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 incident light level I_0 (reference measurement) and transmitted light level I_1 (sample measurement) can be taken for analysis.



■ Equation of absorbance

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

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

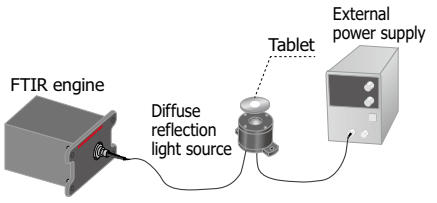
R: Reflectance = I_1/I_0
I_1: transmitted light level
I_0: incident light level

Quantitative Analysis of Theophylline Anhydrate
(Diffuse Reflection Light Source, FTIR Engine)

Measurement using a diffuse reflection light source and an FTIR engine

Tablets containing theophylline, caffeine, and additives were analyzed using Hamamatsu's diffuse reflection light source L16462-01 and FTIR engine C15511-01. Using the same measurement samples (6 tablets with different theophylline concentrations), only theophylline was quantitatively measured. Theophylline content is predicted by making a calibration curve from previously acquired training data*1 and doing PLS*2 regression analysis. The coefficient of determination on the calibration curve is R^2=0.997, showing high accuracy measurements are possible. Even in conditions in which the tablets contain caffeine and theophylline, which have similar spectra in the near-infrared region, it is possible to quantitatively analyze only theophylline.

*1: When quantifying a substance, this is data that expresses the change with respect to concentration by measuring absorbance of the standard substance in advance.
*2: Partially Square Regression



KACCC1135EC

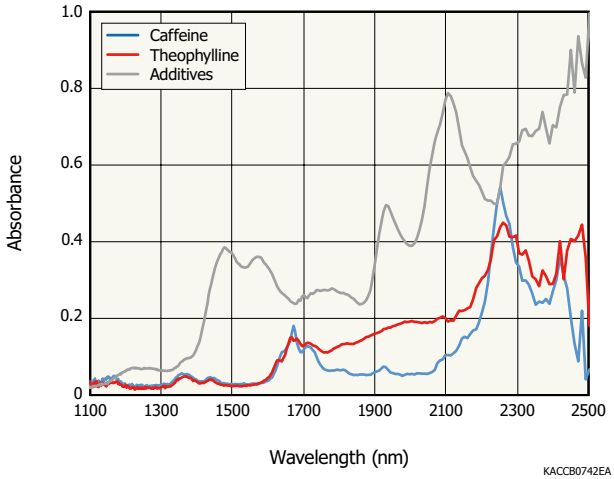
■ Measurement samples

Sample No.	t0	t10	t20	t30	t40	t50
Theophylline	0%	10%	20%	30%	40%	50%
Caffeine	20%	20%	20%	20%	20%	20%
Additives (Starch, Lactose)	80%	70%	60%	50%	40%	30%

■ Measurement conditions

- Program: Uses Python's scikit-learn module
- Samples with 0% content (t0) were excluded from the analysis to determine the MAPE (mean absolute percentage error)
- Number of PLS principal ingredients : 3

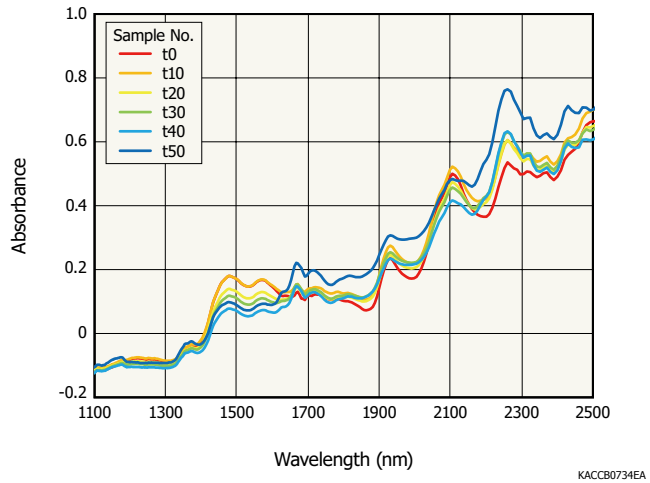
■ Absorption spectra of the components included in the tablet



KACCB0742EA

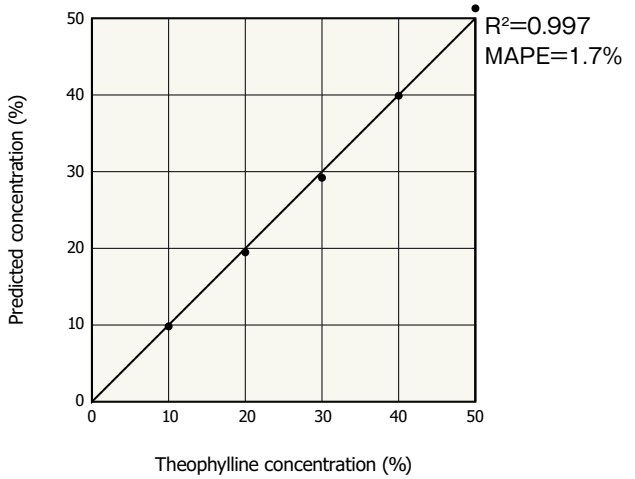
* Caffeine and theophylline are close in spectrum in the near-infrared region 1100 nm to 1700 nm.

■ Absorbance spectra of the tablets



KACCB0734EA

■ Calibration curve of Theophylline



KACCB0741EA

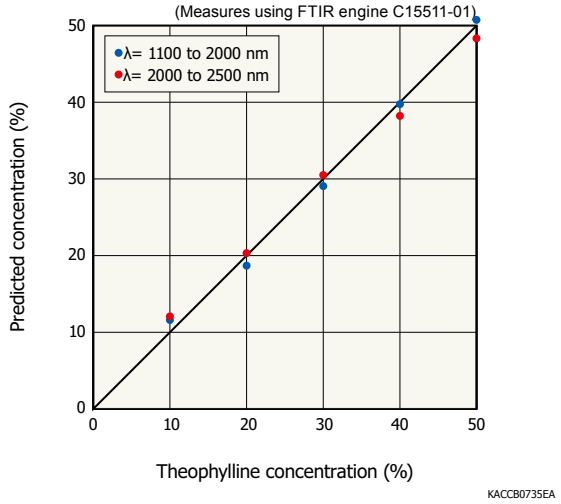
Measurement cooperated by: Hamamatsu Central Research Laboratory

Comparison of commercial light source and diffuse reflection light source

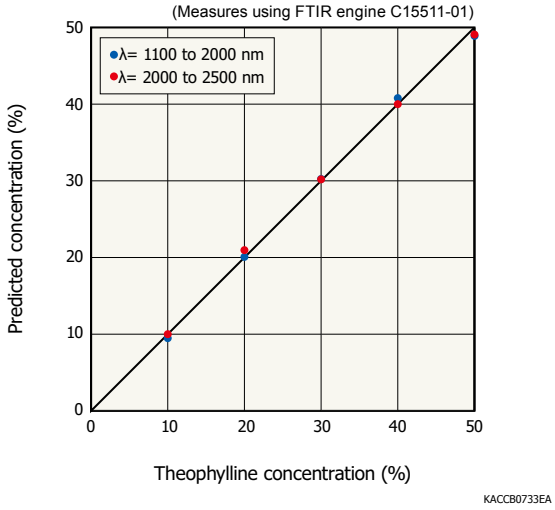
In two wavelength ranges, 1100 nm to 2000 nm and 2000 nm to 2500 nm, using a commercial light source and Hamamatsu's diffuse reflection light source L16462-01, each theophylline concentration was measured.
Typical commercial light sources have low quantification accuracy in the long wavelength range of 2000 nm and above. In contrast, Hamamatsu's diffuse reflection light source has high photon detection efficiency in the near-infrared region up to 2500 nm, so compared to commercial light sources, it achieves high quantification accuracy even when measuring wavelengths of 2000 nm or above.

■ Calibration curve of Theophylline

Commercial light source



Diffuse reflection light source L16462-01



■ PLS regression analysis by wavelengths

PLS regression analysis	Commercial light source		**Diffuse reflection light source L16462-01**	
	● 1100 to 2000 nm	● 2000 to 2500 nm	● 1100 to 2000 nm	● 2000 to 2500 nm
Constant of determination R^2	0.993	0.968	0.998	**0.998**
Root mean square deviation RMSE	0.0115	0.0144	0.0064	**0.006**
Mean absolute percentage error MAPE	5.6%	6.6%	2.1%	**1.5%**

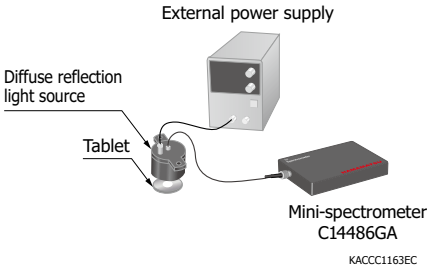
Measurement cooperated by: Hamamatsu Central Research Laboratory

Quantitative Analysis of Theophylline Anhydrate
(Diffuse Reflection Light Source, Other NIR Spectrometers)

Measurement using mini-spectrometer

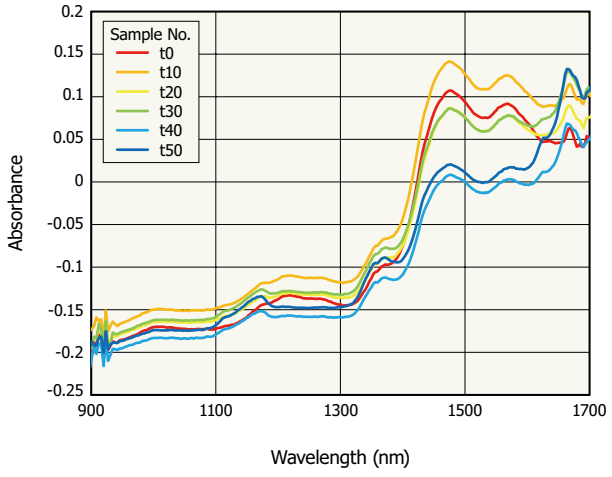
Theophylline anhydride was measured by mini-spectrometer C14486GA. C14486GA only supports up to 1700 nm, but it shows high resolution within the spectral response range. It has comparable performance, although it has a narrower wavelength range than the FTIR engine.

Note: Measurement samples and measurement conditions are the same as on page 6.



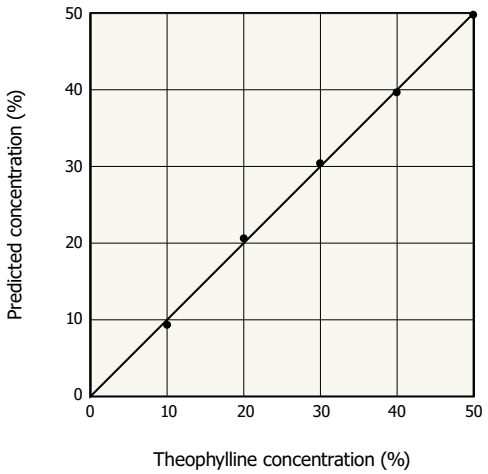
KACCC1163EC

■ Absorbance spectra of the tablets



KACCB0736EA

■ Calibration curve of Theophylline



R^2=0.998
MAPE=2.5%

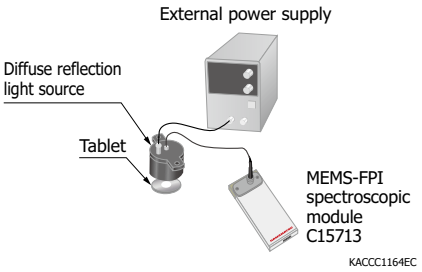
KACCB0737EA

Measurement cooperated by: Hamamatsu Central ResearchLaboratory

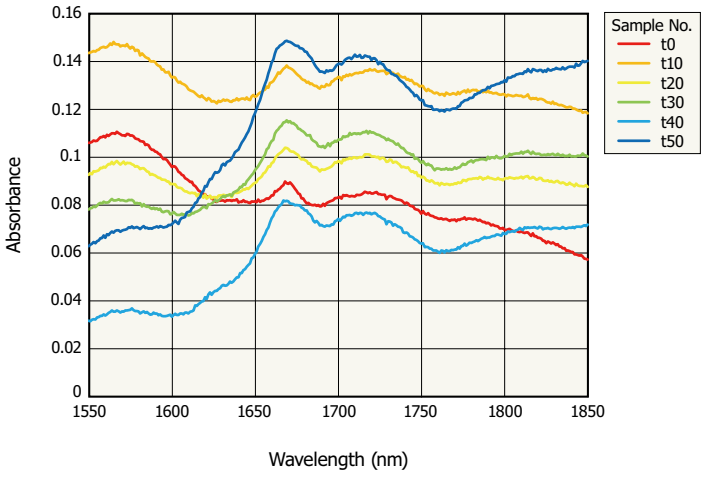
Measurement using MEMS-FPI spectroscopic module

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.
Compared to the built-in light source, when using the diffuse reflection light source L16462-01, high accuracy concentration prediction is possible in wavelength-specific PLS regression analysis.

Note: Measurement samples and measurement conditions are the same as on page 6.

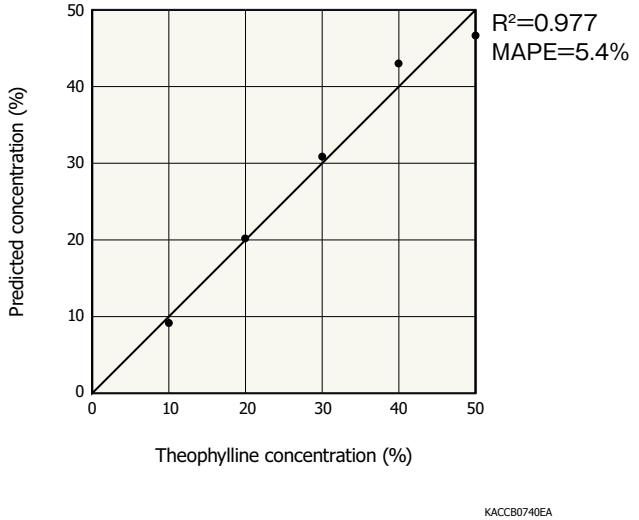


■ Absorbance spectra of the tablets

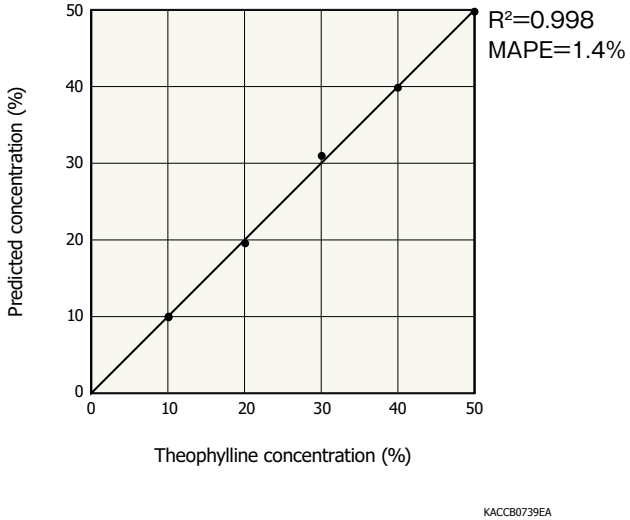


■ Calibration curve of Theophylline

Built-in light source



Diffuse reflection light source L16462-01



Measurement cooperated by: Hamamatsu Central Research Laboratory

■ Technical notes

FTIR engine (FT-NIR spectrometer)
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

HAMAMATSU

www.hamamatsu.com

HAMAMATSU PHOTONICS K.K., Solid State Division
1126-1 Ichino-cho, Chuo-ku, Hamamatsu City, 435-8558 Japan, Telephone: (81)53-434-3311, Fax: (81)53-434-5184
U.S.A.: HAMAMATSU CORPORATION: 360 Foothill Road, Bridgewater, NJ 08807, U.S.A., Telephone: (1)908-231-0960, Fax: (1)908-231-1218
Germany: HAMAMATSU PHOTONICS DEUTSCHLAND GMBH: Arzbergerstr. 10, 82211 Herrsching am Ammersee, Germany, Telephone: (49)8152-375-0, Fax: (49)8152-265-8 E-mail: info@hamamatsu.de
France: HAMAMATSU PHOTONICS FRANCE S.A.R.L.: 19 Rue du Saule Trapu, Parc du Moulin de Massy, 91882 Massy Cedex, France, Telephone: (33)1 69 53 71 00, Fax: (33)1 69 53 71 10 E-mail: infos@hamamatsu.fr
United Kingdom: HAMAMATSU PHOTONICS UK LIMITED: 2 Howard Court,10 Tewin Road, Welwyn Garden City, Hertfordshire, AL7 1BW, UK, Telephone: (44)1707-294888, Fax: (44)1707-325777 E-mail: info@hamamatsu.co.uk
North Europe: HAMAMATSU PHOTONICS NORDEN AB: Torshamnsgatan 35, 16440 Kista, Sweden, Telephone: (46)8-509-031-00, Fax: (46)8-509-031-01 E-mail: info@hamamatsu.se
Italy: HAMAMATSU PHOTONICS ITALIA S.R.L.: Strada della Moia, 1 int. 6 20044 Arese (Milano), Italy, Telephone: (39)02-93 58 17 33, Fax: (39)02-93 58 17 41 E-mail: info@hamamatsu.it
China: HAMAMATSU PHOTONICS (CHINA) CO., LTD.: 1201, Tower B, Jiaming Center, 27 Dongsanhuan Beilu, Chaoyang District, 100020 Beijing, P.R. China, Telephone: (86)10-6586-6006, Fax: (86)10-6586-2866 E-mail: hpc@hamamatsu.com.cn
Taiwan: HAMAMATSU PHOTONICS TAIWAN CO., LTD.: 13F-1, No.101, Section 2, Gongdao 5th Road, East Dist., Hsinchu City, 300046, Taiwan(R.O.C) Telephone: (886)3-659-0080, Fax: (886)3-659-0081 E-mail: info@hamamatsu.com.tw

Cat. No. KACC0015E04 Sep. 2024