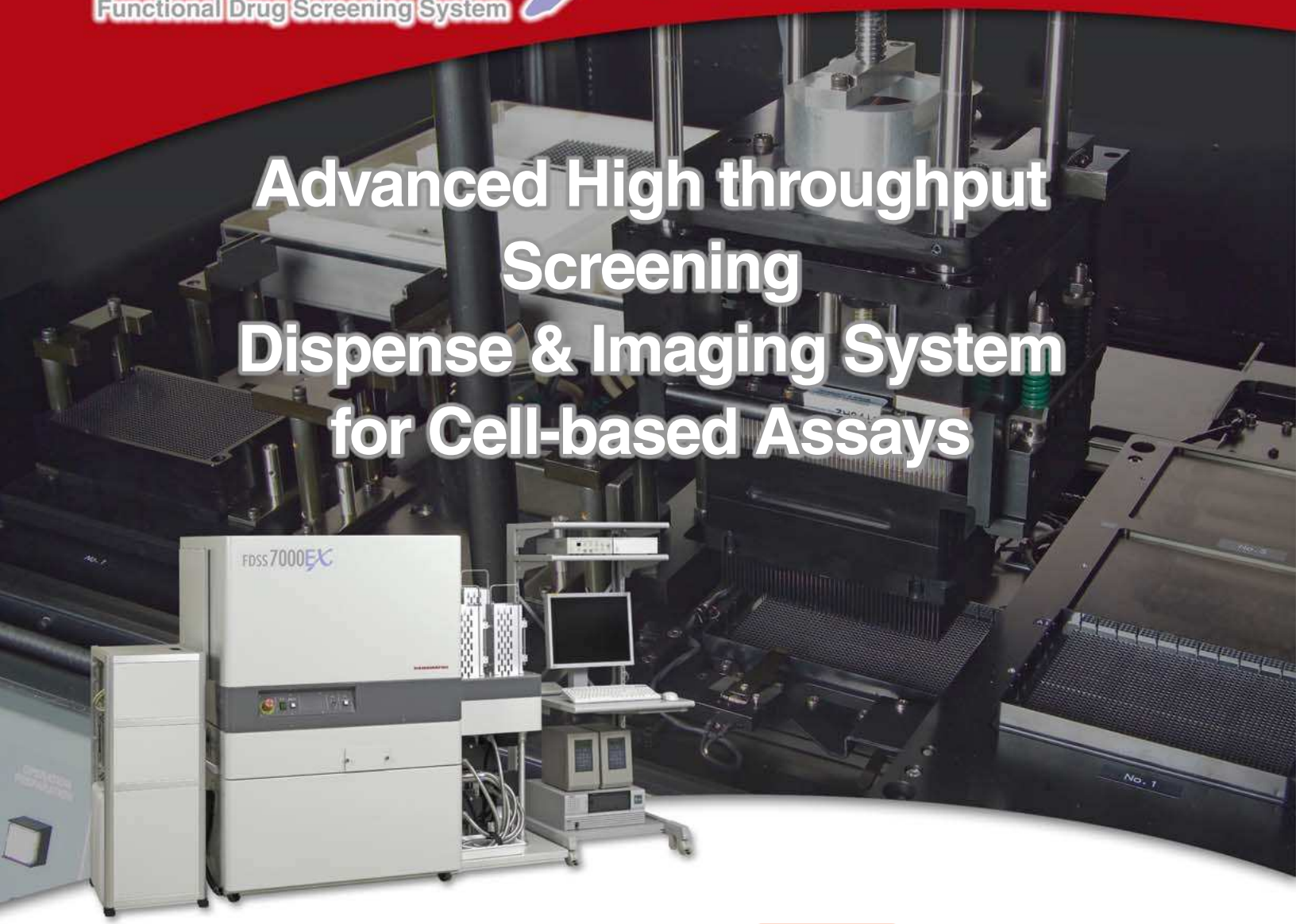
FDSS7000EX

Functional Drug Screening System



Advanced High throughput Screening Dispense & Imaging System for Cell-based Assays

Accepted worldwide for its reliability, the FDSS is capable of 1536-well format and high-sensitivity luminescence measurements.

The FDSS (Functional Drug Screening System) series are designed for cell-based assays in the drug discovery field. These instruments optically detect intracellular reactions and biological signal transmissions, and are used as screening systems to discover new lead compounds which could be candidates for new drugs.

The FDSS7000EX is our high-end model capable of handling 1536-well assays and measuring both fluorescence and luminescence, and is equipped with a variety of functions such as multiple washing. Many kinds of suspended/adherent cells' real-time kinetic reactions can be measured and analyzed. Various optional parts such as FRET, robot connections, etc. are available. In addition, the FDSS7000EX is expandable for future upgrades.

Applications

- Intracellular calcium ion
- Membrane potential
- Ion channel
- Aequorin
- Luciferase
- FRET
- Suspended cell

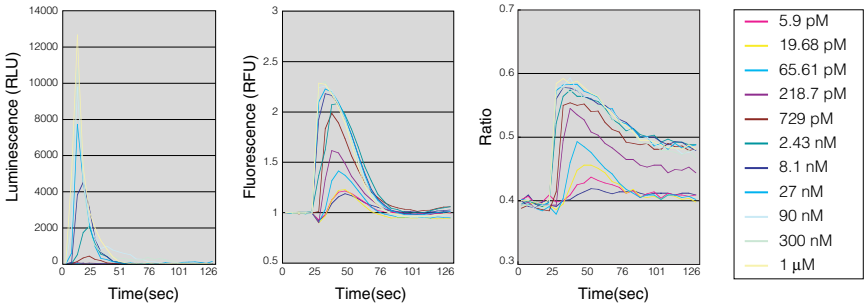
HAMAMATSU

PHOTON IS OUR BUSINESS

Do more with an expandable modular system

Intracellular calcium ion

Comparison of calcium mobilities using Aequorin, Fluo-3, and Fura-2 receptor-expressing cells.



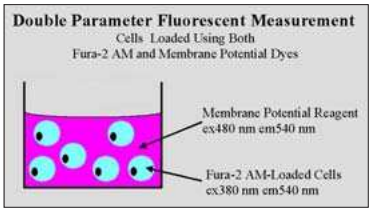
▲ Aequorin ▲ Fluo-3 ▲ Fura-2

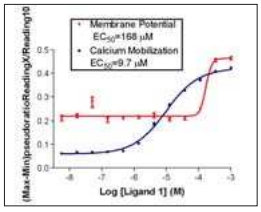
Membrane potential

Multiplex assays using Fura-2AM and a membrane potential fluorogenic reagent

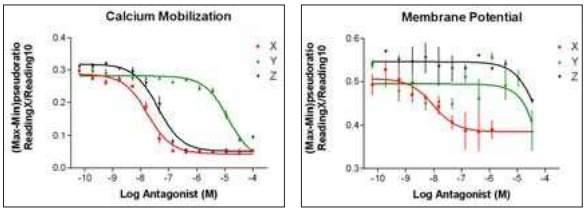
This is an example of an multiplex assay that concurrently measured membrane potential and calcium mobilization. In this example, (1) a FMP measurement with an excitation wavelength of 480 nm and a fluorescence wavelength of 540 nm and (2) a Fura-2 measurement with an excitation wavelength of 380 nm and a fluorescence wavelength of 540 nm are performed alternately, and then the mobilizations of (1) and (2) are measured concurrently.

·Fura-2AM: ex380 / em540
·Membrane potential: ex480 / em540





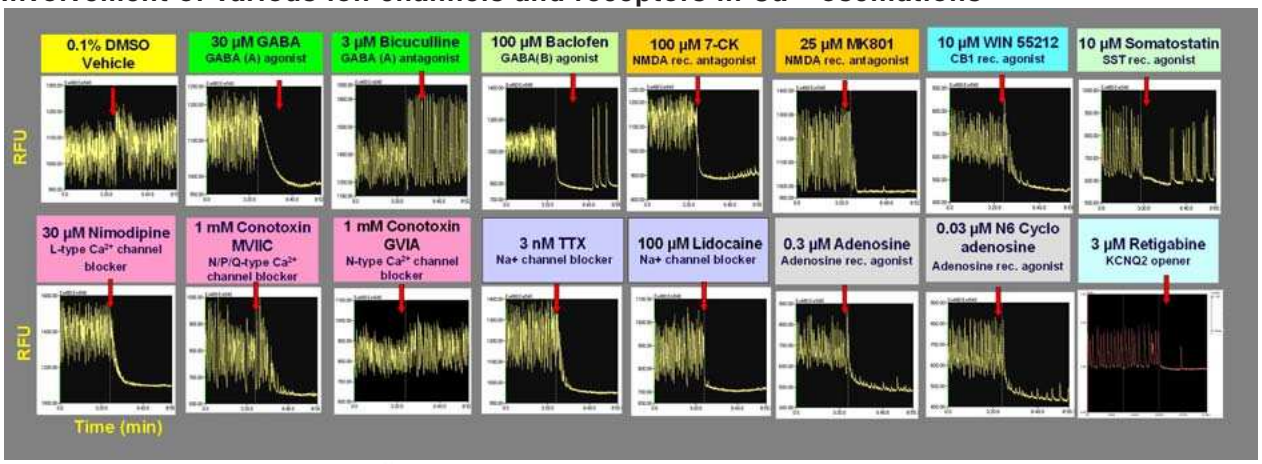
▲ Calcium and membrane potential response curves according to the changes in the ligand concentration



▲ Calcium mobilization according to the changes in the concentration of three types of antagonists with a fixed ligand concentration

Ion channel

Involvement of various ion channels and receptors in Ca^{2+} oscillations



SANOFI EXPLORATORY Unit

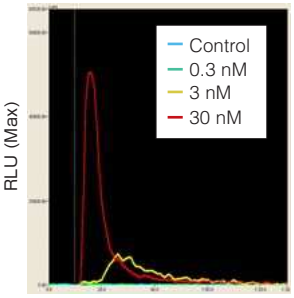
Presented at the 8th FENS Meeting - Amsterdam - July 3-7, 2010
Session 015 Epilepsy 1, n°015.36

Aequorin

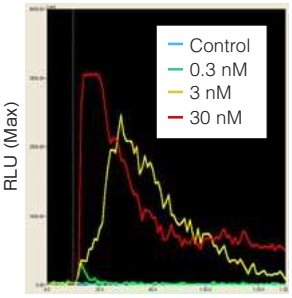
Comparison of dose responses provided by an aequorin assay

Signals in the extremely low concentration range can also be detected by highly sensitive, luminescence sensors.

- Cell: CHO
- Substrate: h-CTZ
- Ligand: ATP
- Measurement time: The ligand is dispensed 10 seconds after measurement starts.
  Measured at 1 second intervals for 1 minute and 30 seconds.



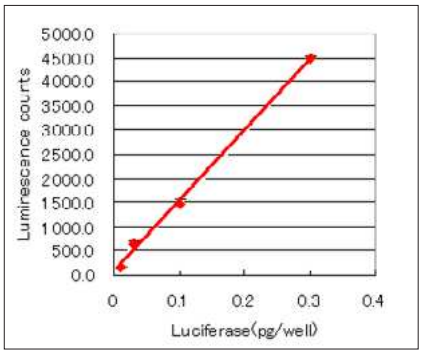
▲ Fluorescence/luminescence sensor unit



▲ Fluorescence sensor unit

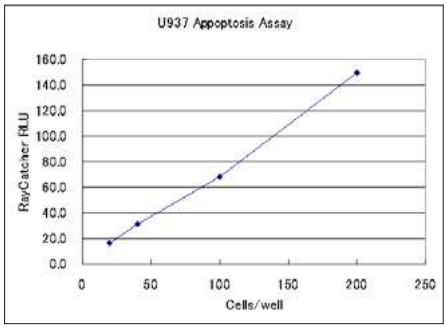
Luciferase

KIT: Bright-Glo™ Luciferase Assay System (Promega E2610)
20 µL per well for 384 black microplate
10 min incubation at RT



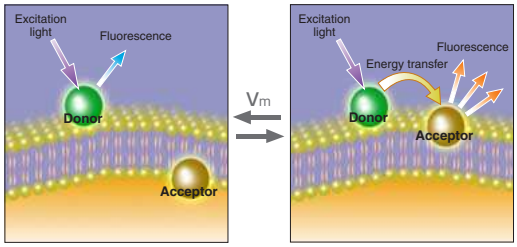
Cell: U937
(10 µg/mL Mitomicin-C induced apoptosis)
5000 cells/well ～ 20 cells/well
(25 µL per well for 384 black microplate)

KIT: Caspase-Glo®Assays (Promega G8090)
Add 25 µL reagent to 25 µL medium containing cells for 384 black microplate
30 min incubation at RT

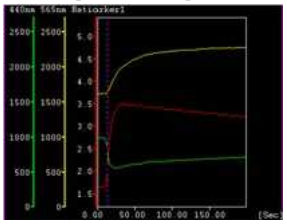


FRET

Fluorescence resonance energy transfer (FRET) through the use of a coumarin dye (CC2-DMPE) and an oxonol dye (DISBAC).



【FRET VSP】



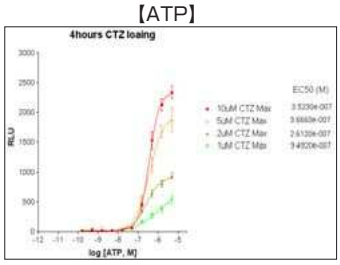
Emission Ratio =

$$\frac{\text{Donor (CC2-DMPE) Emission (460 nm)}}{\text{Acceptor (DISBAC) Emission (580 nm)}}$$

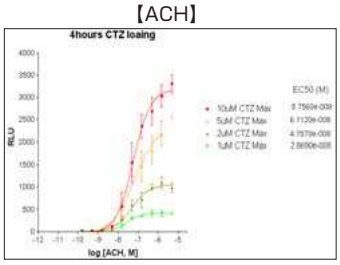
Suspended cell

This is an example in which an aequorin assay was used to measure suspended cells at different CTZ concentrations.
10 000 CHO cells genetically engineered to express GPCR that can be stimulated by a neurotransmitter were dispensed to a single well.
Cells loaded over 4 hours with substrate concentrations of 1 µM, 2 µM, 5 µM, and 10 µM were stimulated by ATP and ACH, which are endogenous ligands.

【ATP】



【ACH】



Sophisticated system structure

■ Dispenser

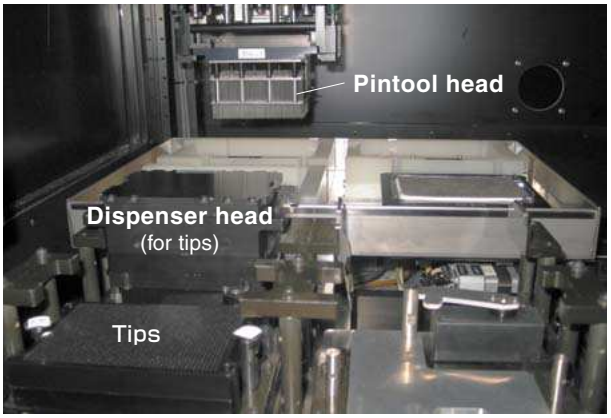
Can be equipped with various dispenser heads

- 96-, 384-, or 1536-tip dispenser heads are selectable. The tips are exchangeable.
- 384- and 1536-pintool heads are also supported.
- The main unit is equipped with an automatic tip loading feature.
- As standard, three types of compounds can be dispensed. If you use the back plate loading line, up to four types of compounds can be dispensed.
- The dispenser heads can be easily changed by the user.

NEW

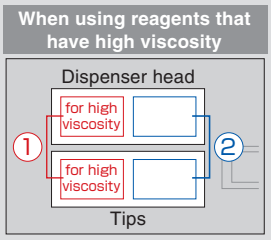
Pintool head (1536 and 384)

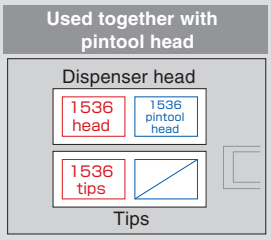
Dispensing involves setting metal pins in the tip positions and then attaching the reagent to the ends of the tips. This enables the dispensing of minute amounts of solution and reuse.



Two dispenser heads capability

Two heads can be installed at the same time, which makes it possible to use separate heads for compounds that have high viscosity or to use separate heads for agonists and antagonists.



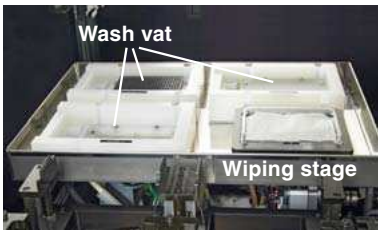


Tips are changed each time for ①.
Normal reagent is dispensed for ②.

■ Washing unit

Equipped with a variety of washing features

- Up to three solvents are supported, which enables washing with no carry over.
- Tips can be washed during measurement.
- An ultrasound washing feature is also available.
- Equipped with a wiping stage to dry tip ends.

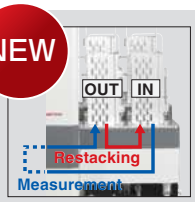


■ Plate stacker unit

Plate stacker feature for 20 or 50 plates

- Using the plate stacker makes it possible to perform automatic measurements even without the use of a robot.
- You can select 20 plates or 50 plates.
- Stacker cassette method makes it easy to set plates.
- Can be equipped with a barcode reader.

NEW



Restacking function

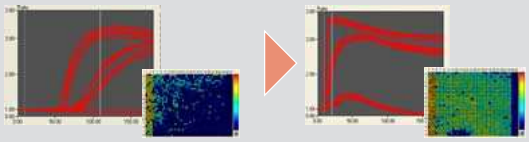
A stacker equipped with a feature that returns all microplates that have reached the OUT side back to the IN side is also available.

■ Plate shaking features

Plate shaking provides stable response detection.

- Measurements can be performed while applying fine vibrations to the whole plate.
- Cells and reagents can be mixed effectively and quickly.
- This is also effective for assays that use suspended cells.

Plate shaking effect for a Fluo-4 assay



▲Mixing OFF ▲Mixing ON

■ Others

Auto compound feeder

A new reagent feeder that drastically reduces dead volume can also be installed.

NEW

Temperature control function

The FDSS7000EX can also be equipped with a heater unit. The internal temperature sensor is used to maintain a stable temperature.

■ Fluorescence/luminescence sensor, Fluorescence optics

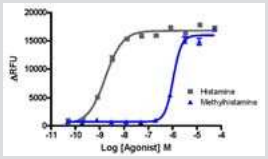
Supports fluorescence assays and luminescence assays with a single sensor

Can also be combined with a highly sensitive luminescence sensor

- This sensor has a fluorescence detection sensitivity that far exceeds that of conventional fluorescence sensors.
- Because the excitation light can be lowered, the cost of purchasing excitation light sources can be reduced.
- In addition to high sensitivity, the FDSS7000EX also has a high dynamic range.
- The fluorescence changer makes FRET measurements possible.

* Conventional fluorescence sensors can also be selected.

H1 NFAT HEK293 cells:
Calcium measurement by Fluo-4

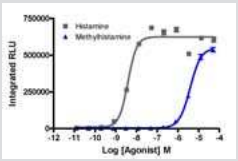


	Histamine	Na-Methylhistamine
EC_{50}	1.7305e-009	1.0661e-006

Compound	Histamine	Na-Methylhistamine
EC_{50}	1.73 nM	1.0 μM
S/B ratio	19	25
Z'	0.66	0.67

* Reagents and data provided by Life Technologies, USA

H1 NFAT HEK293 cells:
Calcium measurement by BacMam Aequorin



	Histamine	Na-Methylhistamine
EC_{50}	3.8659e-009	3.8809e-006

Compound	Histamine	Na-Methylhistamine
EC_{50}	3.87 nM	3.9 μM
S/B ratio	142	182
Z'	0.84	0.68

* Reagents and data provided by Life Technologies, USA

Various assays with xenon lamp & filter combination (multiple excitation and emission)

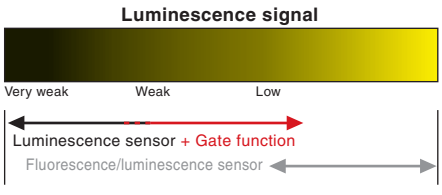
- Good wavelength separation by epi-illumination optics
- Fura-2 assay with dual excitation (340 nm & 380 nm)
- FRET (C/Y, Membrane potential) with emission filter changer
- 2 dichroic mirror and 4 emission filter slots for various assays
- White light xenon lamp with wattage options (150 W, 300 W, 600 W)
- 6 filter slots for excitation
- Uniform plate illumination

UV	Blue	Green
Fura-2(Ca^{2+})	Fluo-3	YFP
SBFI(Na^{+})	Calcium Green	JC-1
PBFI(K^{+})	Sodium Green	CoroNa Red
MQAE, DiH-MZA(Cl^{-})	CoroNa Green	Rhod-2
DAPI(DNA)	BCECF	Rhodamine
VSP-1(FRET)	GFP	FMP
	FITC	
	Di-8-ANNEPS	

■ Luminescence sensor

Equipped with a gate function, which improves the dynamic range during luminescence measurements

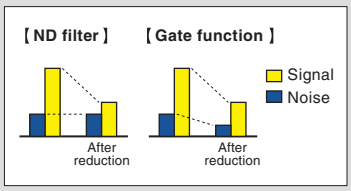
A highly sensitive luminescence sensor that can acquire the weak signals that cannot be acquired by the fluorescence/luminescence sensor is also available. The new gate function enables measurements of samples with a large amount of light. By combining this feature with the fluorescence/luminescence sensor, the FDSS7000EX can support an even wider range of luminescence signals.

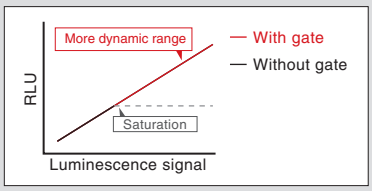


NEW

Gate function

For samples that have a large amount of light, a neutral-density filter (an ND filter) is normally used. However, in this situation, only the signal is attenuated, so the signal-to-noise ratio (S/N) worsens.
On the other hand, the gate function gates both the signal and the noise, so this method has a better S/N.





All kinds of assays can be executed with simple operations

■ Basic operation

① Select mode

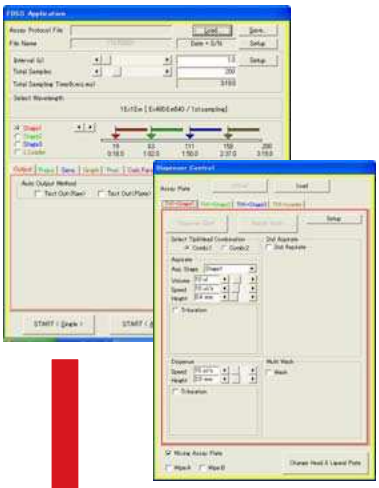
[Protocol mode]
Set up protocol and start the assay automation.

[Check mode]
Check the status of the system and image.

▲Camera/Filter control ▲Live image

[Viewing mode]
Open the measured data for analysis.

② Set up protocol



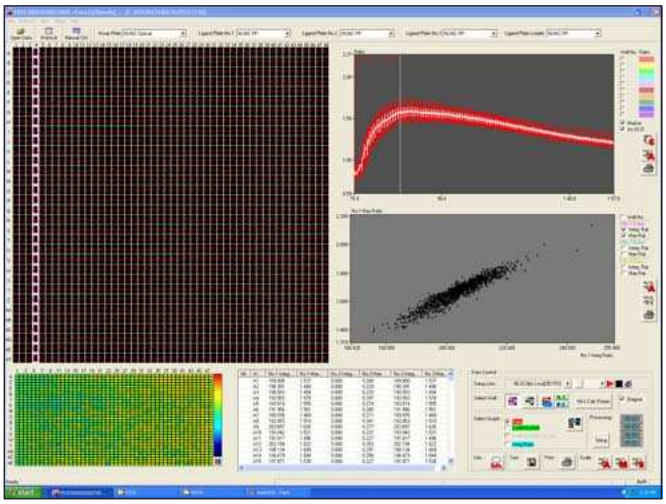
Assay protocol configuration

- Configure addition, wash frequency and sequence in measurement
- Automation from measurement to data output

Dispensing protocol

- Configure height, dispense speed, and tip mixing
- Plate shaking On/Off

③ Get results



▲Measured data

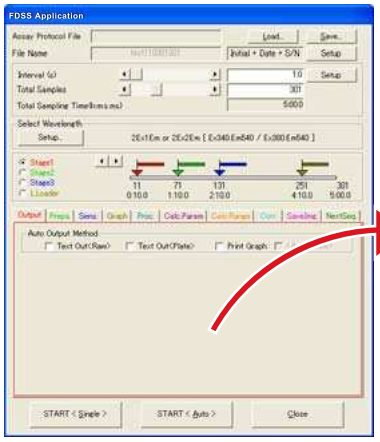
Measurement / Analysis

- Displays the kinetic data, auto-scale graph, correlation diagram, and analysis results for all wells
- Equipped with a variety of analysis features and output features

【Data analysis】
- Negative control
- Positive control
- Subtract bias
- Spatial uniformity
- Peak calculation
- Hit identification

【Data output】
- Raw data
- Text
- Bitmap (graph)

■ Detailed settings

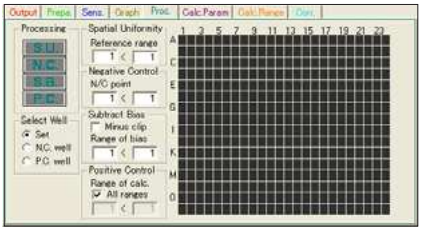


Assay protocol configuration

- Up to 4000 samples can be taken for one protocol.
- Alternatively switch between two sampling intervals (up to three times).

Graph

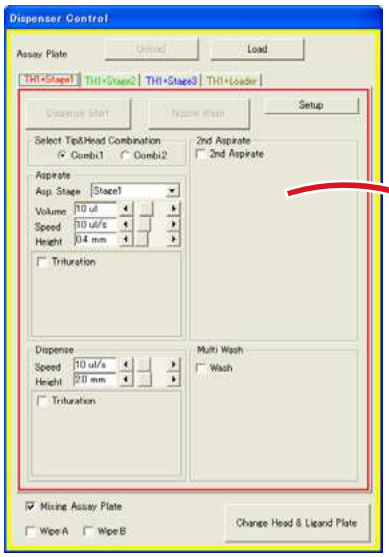
Correction



Analysis

Range

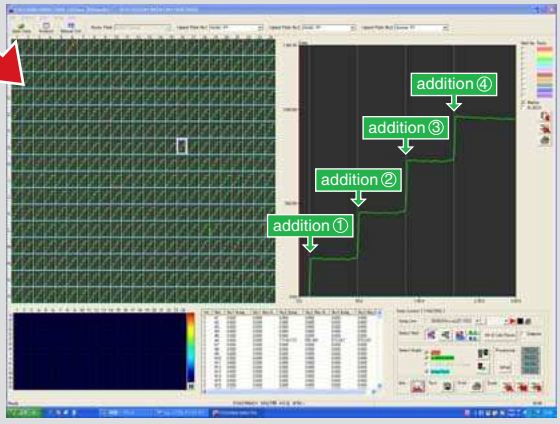
Use the tabs to configure a variety of settings.



Dispensing protocol

- Settings such as the dispensing amount and speed can be configured.
- Settings can also be configured for operations such as washing and tip trituration.

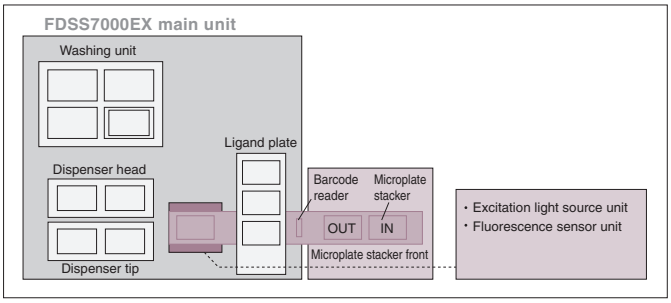
Up to four additions can be performed in a single protocol!



Flexible system for diverse needs

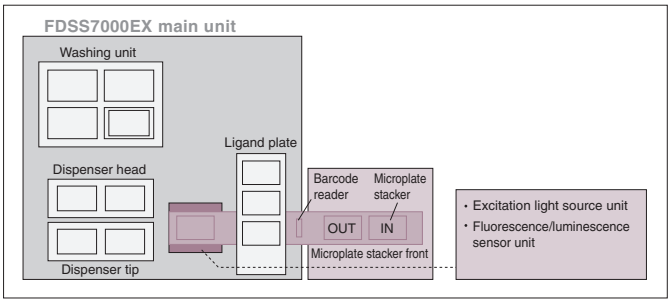
Fluorescence measurements

Calcium ion assays are in ever increasing demand in areas such as lead discovery, pharmacological study, and food product function research. The FDSS7000EX supports various types of ion channel assays such as Na^+, K^+, Cl^-, and pH as well as calcium ion assays using fluorescent dyes such as Fura-2, Fluo-3, and Fluo-4.



Fluorescence/Luminescence

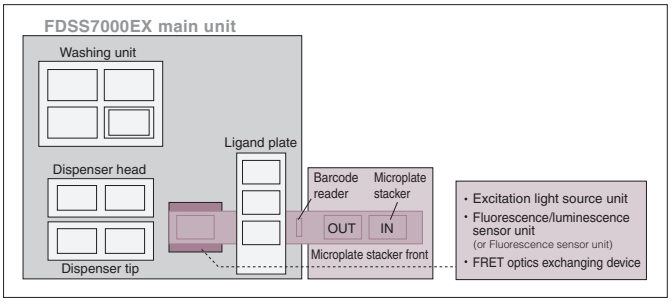
The fluorescence/luminescence sensor is capable of detecting both types of emission. Adding a filter changer enables FRET measurements.



* For weak-luminescence detection, use an ultrasensitive luminescence sensor with even higher sensitivity.

FRET measurement

The FDSS7000EX is utilized in assays where two different fluorescence wavelengths are measured, for example FRET probes (VSP-1, Premo™), cAMP dyes (FICRhR), simultaneous calcium and membrane potential dyes (multiplexing), and dual reporter gene assays (GFP and DsRed).

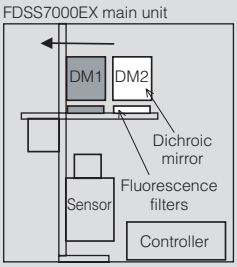


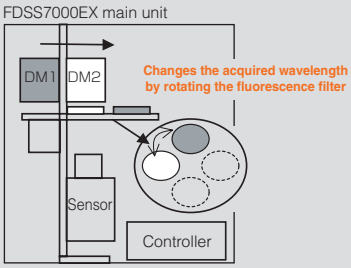
【FRET optics exchanging device A8472-04】

The A8472-04 automatically switches between the fluorescence filters and the dichroic mirrors.
This device is used for assays that handle dual-wavelength fluorescence such as FRET or VSP.

Filter switching interval *	0.3 s
Number of installed dichroic mirrors	Max. 2
Number of installed fluorescence filters	Max. 4

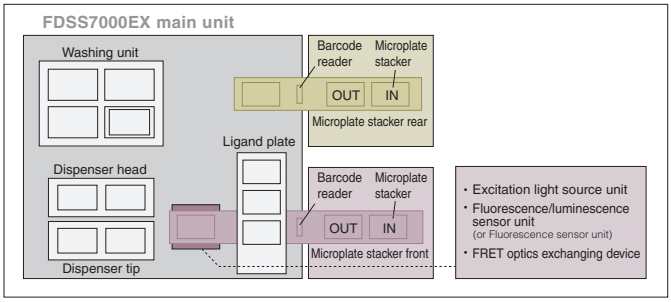
* Switching interval between adjacent filter positions





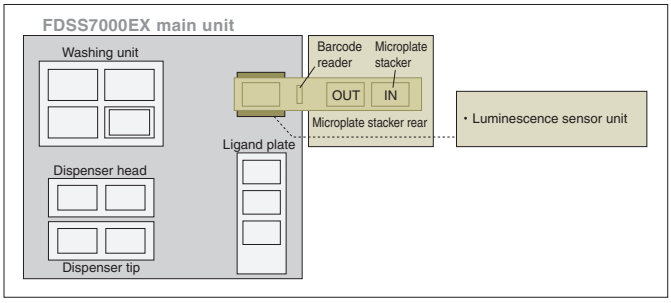
Fluorescence and luminescence measurement (4-reagent dispensing structure)

The standard configuration has three compound/ligand plate positions. By adding the rear loader, you can have the fourth compound/ligand plate for dispensing. The rear loader plate can be kept inside the FDSS7000EX and can be used for the next protocol if required.



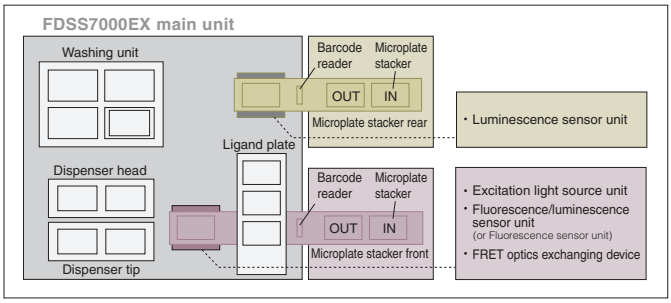
Luminescence measurement

The FDSS7000EX is ideal for calcium ion assays using a calcium-sensitive photoprotein "aequorin" along with reporter gene assays that make use of luciferin-luciferase reactions, high-sensitivity protein interaction analysis (two-hybrid assays), and luminescence experiments where the amount of light emissions cannot be predicted.



Fluorescence and luminescence measurements

The FDSS7000EX is a stand-alone system integrated with powerful functions for cell-based kinetic assays, and capable of detecting a wide variety of fluorescent and luminescent phenomena utilizing 96, 384, and 1536 well plates.

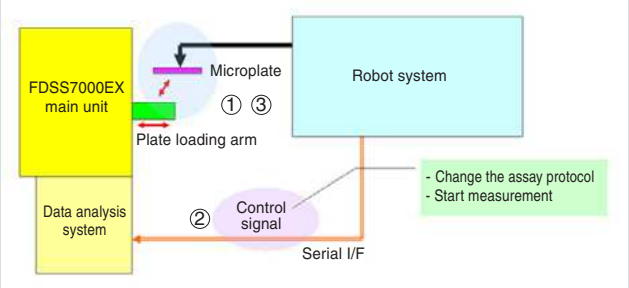


Robot connection

Interface for connecting a robot is available.

① Plate from the robot system to FDSS plate loading arm
② FDSS measurement by robot control
③ After the measurement, robot takes out plate from the FDSS plate unloading arm

【 Manufacturers of compatible products 】
Thermo Scientific, Beckman Coulter,
HighResBiosolution, Hamilton, Agilent



A rich variety of optional parts makes it possible to design a system that meets your specific needs

Component

Dispensing unit One-unit and two-unit versions are available Equipped with an automatic tip loading feature	96 tip type dispensing unit (10-200 µL)	A10118-24
	384 tip type dispensing unit (1-30 µL)	A10118-26
	1536 tip type dispensing unit (0.5-5 µL)	A10118-28
Pintool head	384 pintool head for short pins	A10118-30
	384 pintool head for long pins	A10118-31
	1536 pintool head for short pins	A10118-27
	1536 pintool head for long pins	A10118-29
Washing unit A one-solvent washing version (equipped with an ultrasound washing feature) to a three-solvent washing version are available Equipped with an automatic wiping stage	Washing unit	A10118-47
	Additional washing unit	A10118-48
	96 chimney plate	A10118-44
	384 chimney plate	A10118-43
	1536 chimney plate	A10118-46
Microplate stacker	Microplate stacker front (without lid opener)	A10118-04
	Microplate stacker rear (without lid opener)	A10118-05
	Microplate stacker front (lid opener)	A10118-94
	Microplate stacker rear (lid opener)	A10118-95
	Microplate restacker front (without lid opener)	A10118-07
	Microplate restacker rear (without lid opener)	A10118-08
	Single plate holder	A10118-96
	Microplate stacker cassettes	A10118-92
	Microplate stacker cassettes	A10118-93
Fluorescence sensor unit	Fluorescence sensor unit (1 lamp)	C10512-11
	Fluorescence sensor unit (2 lamps)	C10512-12
	Fluorescence sensor unit (4 lamps)	C10512-13
Fluorescence/luminescence sensor unit *1	Fluorescence/luminescence sensor unit (1 lamp)	C11653-01
	Fluorescence/luminescence sensor unit (2 lamps)	C11653-02
	Fluorescence/luminescence sensor unit (4 lamps)	C11653-03
Luminescence sensor unit for 1536 wells		C10520-11
FRET optics exchanging device		A8472-04
Barcode reader		A10118-50
Auto cell feeder		A10118-55
Heater unit *1 *2		A10118-09

*1 To use the fluorescence/luminescence sensor and the heater unit at the same time, the FDSS7000EX requires a water cooling device. For details, contact your Hamamatsu sales representative.

*2 You can only select the heater unit at the time of purchase.

Consumable

Tips

Tips for 96 wells (10 racks)	A8687-32
Tips for 384 wells (10 racks)	A8687-62
Tips for 1536 wells (10 racks)	A8687-52

Optical filter

* See the back page for details.

Maintenance

To maintain long-term stability of this device, we recommend that you purchase the maintenance contract. For details, contact your Hamamatsu sales representative.

Dispensing unit

■ 1536 format

Dispensing unit A10118-28

Tips A8687-52

Chimney plate A10118-46

■ 384 format

Dispensing unit A10118-26

Tips A8687-62

Chimney plate A10118-43

■ 96 format

Dispensing unit A10118-24

Tips A8687-32

Chimney plate A10118-44

■ Pintool head (for 384/1536)

* In this photograph, pins are already attached.
Note that the pins are not included.

Excitation light source unit

Excitation light source unit (150 W)

Excitation light source unit (300 W)

Excitation light source unit (600 W)

Pump unit

Pump unit

Microplate stacker

Microplate stacker

Microplate stacker cassettes

Filter changer

Filter changer

System configuration

A rich variety of optional parts makes it possible to design a system that meets your specific needs

Consumable

Optical filter

Application	Excitation filter 1	Excitation filter 2	Dichroic mirror	Emission filter 1	Emission filter 2
Fura-2 (Ca^{2+})	340 nm	380 nm	UV	520 nm to 560 nm	-
SBFI (Na^{+})	340 nm	380 nm	UV	520 nm to 560 nm	-
PBFI (K^{+})	340 nm	380 nm	UV	520 nm to 560 nm	-
MQAE, diH-MQA (Cl^{-})	360 nm	-	UV	440 nm to 470 nm	-
DAPI (DNA)	360 nm	-	UV	440 nm to 470 nm	-
VSP-1	387 nm	-	for VSP-1	465 nm	565 nm
CFP/YFP	440 nm	-	for C/Y	475 nm	535 nm
Fluo-3, Fluo-4, Fluo-8 (Ca^{2+})	480 nm	-	B	520 nm to 560 nm	-
Calcium Green (Ca^{2+})	480 nm	-	B	520 nm to 560 nm	-
Sodium Green, CoroNa Green (Na^{+})	480 nm	-	B	520 nm to 560 nm	-
BCECF (pH)	480 nm	450 nm	B	520 nm to 560 nm	-
GFP	480 nm	-	B	520 nm to 560 nm	-
FITC	480 nm	-	B	520 nm to 560 nm	-
YFP	500 nm	-	for Y	542 nm	-
Di-8-ANNEPS	480 nm	-	B	645 nm long pass	-
JC-1	540 nm	-	for JC-1	570 nm to 600 nm	-
CoroNa Red (Na^{+})	531 nm	-	for FMP	560 nm to 640 nm	-
Rhod-2, Rhod-3, Rhod-4 (Ca^{2+})	560 nm	-	for FMP	590 nm to 650 nm	-
Rhodamine	560 nm	-	for FMP	590 nm to 650 nm	-
FMP	531 nm	-	for FMP	593 nm	-

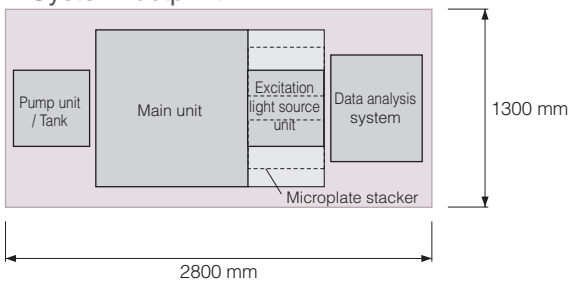
Standard

Option

Dimensions/Weight

Main unit	Approx. 1500 mm (W) × 1030 mm (D) × 1450 mm (H)
	Up to approx. 300 kg
Data analysis system	600 mm (W) × 700 mm (D) × 1500 mm (H)
	Approx. 50 kg
Pump unit / Tank	500 mm (W) × 500 mm (D) × 1200 mm (H)
	Approx. 50 kg

System footprint



HAMAMATSU PHOTONICS K.K. **www.hamamatsu.com**

HAMAMATSU PHOTONICS K.K., Systems Division
812 Joko-cho, Higashi-ku, Hamamatsu City, 431-3196, Japan, Telephone: (81)53-431-0124, Fax: (81)53-435-1574, E-mail: export@sys.hpk.co.jp
U.S.A.: Hamamatsu Corporation: 360 Foothill Road, P. O. Box 6910, Bridgewater. N.J. 08807-0910, U.S.A., Telephone: (1)908-231-0960, Fax: (1)908-231-1218 E-mail: usa@hamamatsu.com
Germany: Hamamatsu Photonics Deutschland GmbH: Arzbergerstr. 10, D-82211 Herrsching am Ammersee, Germany, Telephone: (49)8152-375-0, Fax: (49)8152-2658 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, United Kingdom, Telephone: 44-(0)1707-294888, Fax: 44(0)1707-325777 E-mail: info@hamamatsu.co.uk
North Europe: Hamamatsu Photonics Norden AB: Thorshamnsgatan 35 SE-164 40 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/E, 20020 Arese, (Milano), Italy, Telephone: (39)02-935 81 733, Fax: (39)02-935 81 741 E-mail: info@hamamatsu.it
China: Hamamatsu Photonics (China) Co., Ltd.: 1201 Tower B, Jiaming Center, 27 Dongsanhuan Road North, Chaoyang District, Beijing 100020, China, Telephone: (86)10-6586-6006, Fax: (86)10-6586-2866 E-mail: hpc@hamamatsu.com.cn

Cat. No. SBIS0050E04
JAN/2013 HPK
Created in Japan