

LiCellMoTM

LIVE CELL METABOLIC ANALYZER

Continuous, sampling-free measurement of glucose and lactate in culture medium. Visualize real-time changes in cell metabolism. The PHCbi Live Cell Metabolic Analyzer will open the door to new discoveries.

Model Ranges:

Detector MLC-AD240A-PW

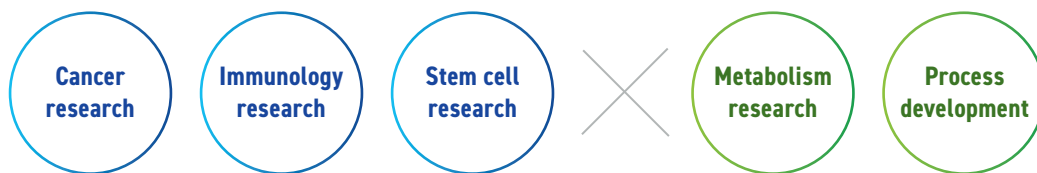
Controller MLC-AC0-PE

This product is for research use only. Do not use for medical purposes.

Cell metabolic analyzer for glycolysis.
 Continuously measure glucose and lactate in the culture medium
 without sampling.
 Visualize cell metabolism by real-time monitoring.

Elucidating the metabolic activity of cells deepens our basic understanding of cell biology and is important in a wide range of research from cancer immunotherapy such as CAR-T cell therapy to regenerative medicine using stem cells. In the manufacture of cell therapy products, high-quality data on glucose uptake and lactate production are useful for optimizing metabolic activity, leading to more efficient manufacture of products with higher yields and improved properties.

At the same time, there are a number of problems with conventional research methods on the glycolytic pathway. The culture medium requires regular sampling to obtain data on how metabolism changes over time. The LiCellMo™ Live Cell Metabolic Analyzer from PHCbi visualizes the state of cells by continuously analyzing cell metabolism. This provides opportunities to overcome existing challenges in metabolic research and achieve new discoveries.

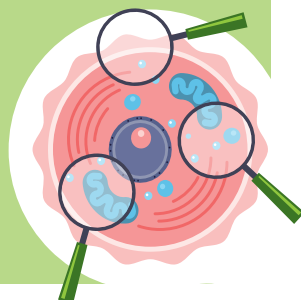


Conventional research methods

- ⊖ Short-term changes and changes over time in cell metabolism cannot be grasped.
- ⊖ The effects of stress cannot be evaluated because lactate cannot be monitored.
- ⊖ The timing of cell passaging and media exchange is not clear from pH and DO.
- ⊖ High sensitivity and large variations arise when the effects on specific culture environments such as specialized plates are unknown.

LiCellMo™ Live Cell Metabolic Analyzer

- + Metabolism can be continuously measured sample-free while culturing cells.
- + By evaluating changes over short and long periods, it is possible to precisely determine the timing of metabolic shifts and to analyze the state of cells with greater accuracy.
- + Measurements can be carried out in the usual culture environment.
- + Glycolysis can be measured directly from changes in glucose and lactate concentrations.



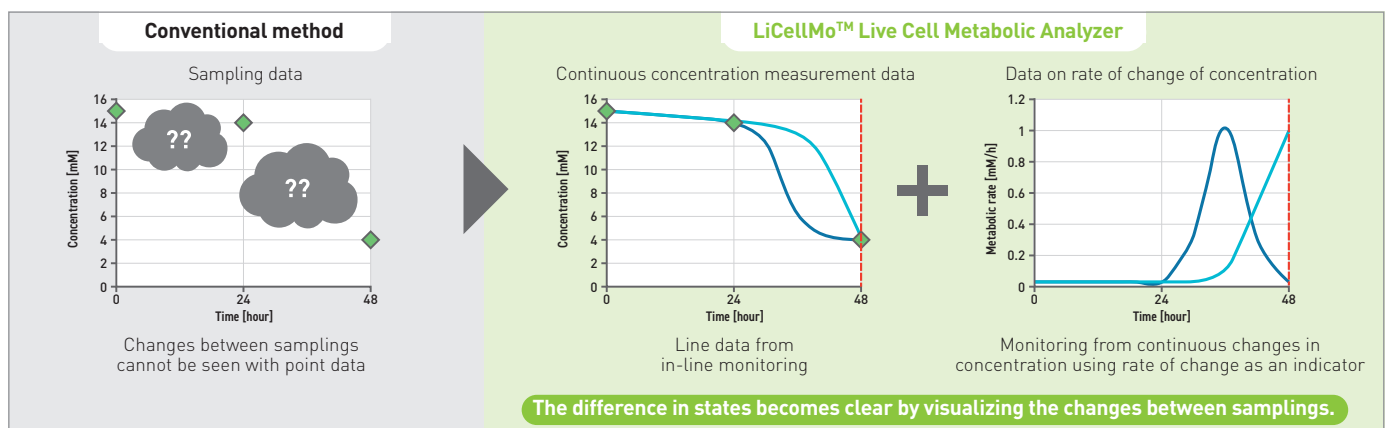
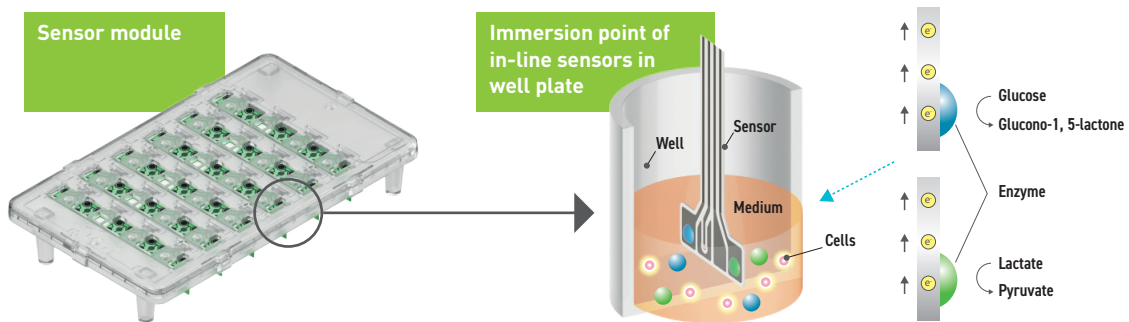
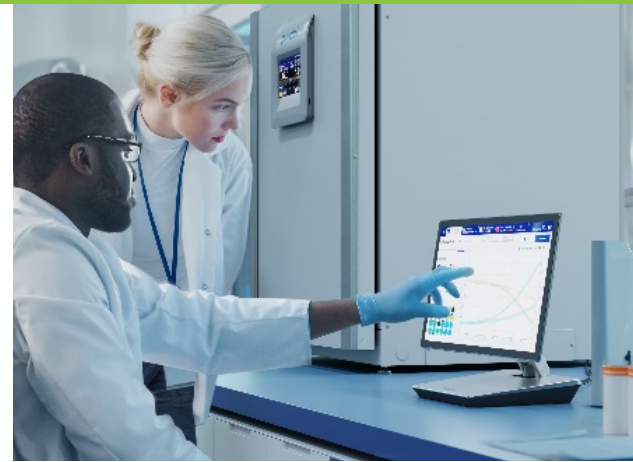
PHC's in-line monitoring technology

PHC's diabetes management business provides high-quality blood glucose monitoring (BGM) systems globally to meet the diverse needs of people living with diabetes mellitus. These BGM systems collect a small amount of blood from the fingertip and measure the blood glucose level to provide people with diabetes the information they need to make decisions about treatment and lifestyle. Since launching the industry's first personalized BGM in 1981, PHC has continued to make improvements through excellence in manufacturing, and currently offers the industry's highest level of accuracy*. PHC's BGM products are among the most accurate and help to precisely monitor blood glucose fluctuations and reliably manage treatment and lifestyle. These products are sold in more than 100 countries and territories and are used by nearly 10 million patients. The LiCellMo™ Live Cell Metabolic Analyzer applies BGM sensor technology together with in-line monitoring technology to measure glycolysis as one of the cellular metabolic pathways.

* Klaff LJ, Brazg R, Hughes K, Tideman AM, Schachner HC, Stenger P, Pardo S, Dunne N, Parkes JL. Accuracy evaluation of contour next compared with five blood glucose monitoring systems across a wide range of blood glucose concentrations occurring in a clinical research setting. *Diabetes Technol Ther.* 2015 Jan;17(1):8-15. doi: 10.1089/dia.2014.0069. PMID: 25260047.

Visualization of continuous changes in cell metabolism. Continuous measurement of glucose and lactate using in-line sensors.

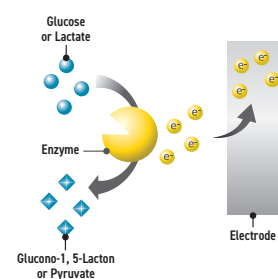
Glycolysis is one of the main pathways of cellular energy metabolism and involves cellular uptake of glucose and production of lactate. In conventional analysis of cellular metabolism, changes in the metabolic state of cells were determined from point data for glucose and lactate concentrations based on a few samplings per day. Using unique high-precision in-line sensors, the LiCellMo™ Live Cell Metabolic Analyzer from PHCbi can perform real-time, continuous measurement of glucose taken into cells for growth and differentiation in culture medium and lactate produced during this process. And because cell activity can be measured without sampling the medium, the cells can also be used for separate evaluation after assay.



What are LiCellMo™ in-line electrochemical sensors?

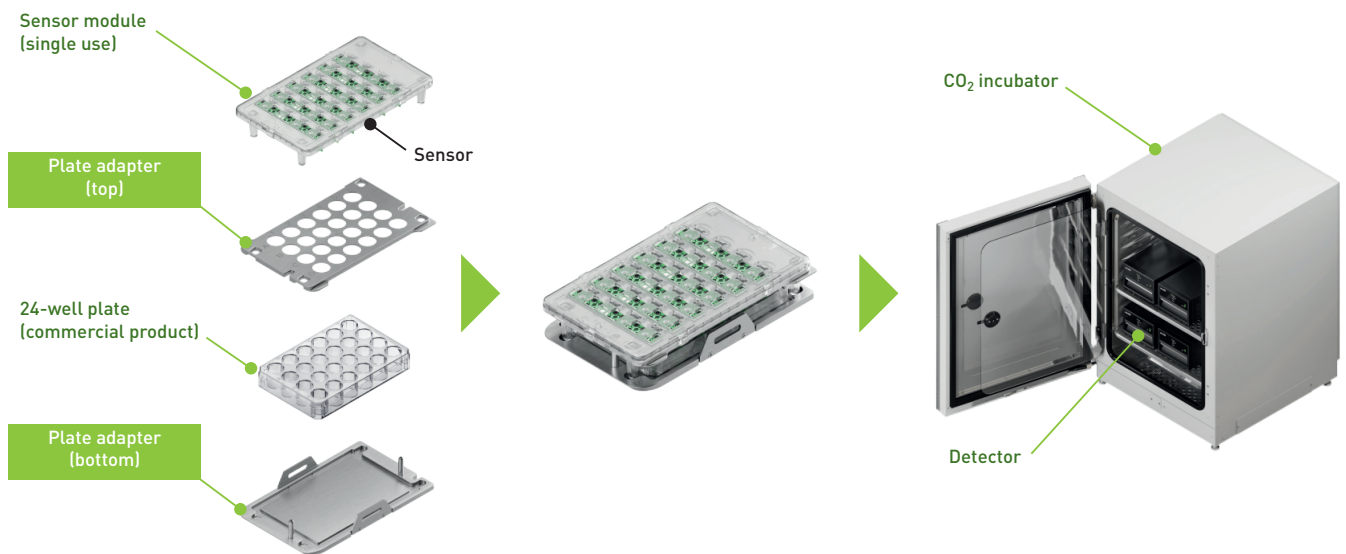
These sensors use electrical changes arising from chemical reactions. The concentration of the analyte is converted into an electrical signal through enzymatic reactions and redox reactions and then quantified.

The electrochemical in-line sensors used in the LiCellMo™ Live Cell Metabolic Analyzer carry enzymes that react specifically with glucose and lactate. By determining the amount of electrons generated through these reactions in the medium, the sensors can measure the concentrations of glucose and lactate continuously and with high accuracy. Glucose dehydrogenase (GDH) at the glucose working electrode oxidizes glucose in the medium to produce glucono-1,5-lactone, and lactate dehydrogenase (LDH) at the lactate working electrode oxidizes lactate in the medium to produce pyruvate. These oxidation reactions generate electrons in proportion to the amount of glucose and lactate present. Glucose and lactate in the medium can be assayed by determining the amount of electrons generated by the enzymatic reaction as the current value in an electrochemical measuring system.



Measurements can be carried out in the usual culture environment. Consumables used for routine culture can be used without modification.

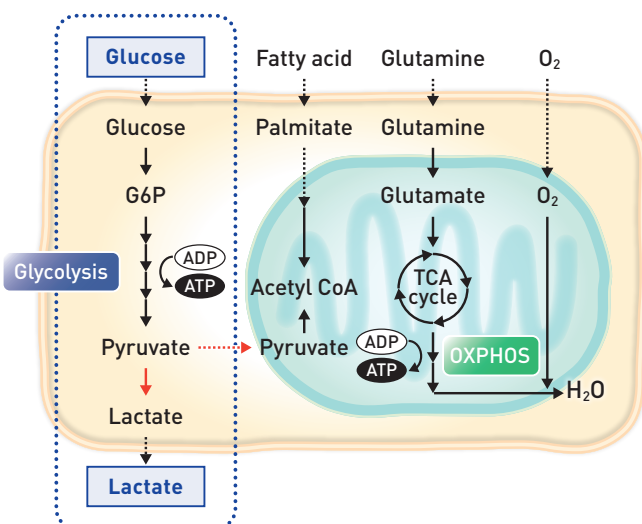
The detector is inserted in the CO₂ incubator before use. The sensor module and plate adapter can be attached to a standard 24-well plate. Then, once the plate is placed in the detector, real-time measurements can be checked easily using the touch-panel controller. This simple configuration is suitable for any laboratory space. Commercially available consumables can be used for cell culture, and plate adapters compatible with five different commercial 24-well plates are available separately. (Please purchase the plate adapter compatible with your well plate separately.)



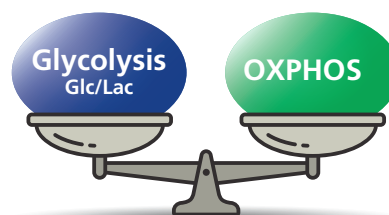
MECHANISM OF ACTION

MEASURE GLYCOLYSIS DIRECTLY FROM CHANGES IN GLUCOSE AND LACTATE CONCENTRATIONS. EVALUATE GLYCOLYTIC CHANGES DIRECTLY.

Changes in the glycolytic pathway can be evaluated directly by measuring the culture medium concentrations of glucose



taken up by cells and the lactate produced. The state of cellular metabolism can be visualized as the rate of metabolic change using the consumption rate and production rate based on concentration values. Monitoring the efficiency of conversion from glucose to lactate makes it possible to evaluate not only glycolysis, but also changes in the balance with other cellular metabolic processes, such as oxidative phosphorylation.



Glycolysis and oxidative phosphorylation are two of the main metabolic pathways in cells, and dependence on these pathways varies according to cell type and environment. By measuring changes in glycolysis, the cellular metabolic balance can be evaluated.

METHOD OF USE

1 Preparation of sample and equipment

- 1.1) Sterilize the plate adapter in an autoclave and return the refrigerated sensor module to room temperature in advance.
- 1.2) Using a standard 24-well plate, seed the samples according to the cell culture protocols of your laboratory.



Sensor module

Plate adapter (top)

Plate adapter (bottom)

*The sensor module and 24-well plate are both single use. Do not use them more than once.

Supported 24-well plates

- Corning Costar
- Corning Falcon
- Greiner CELLSTAR
- Thermo Nunc
- Sumitomo Bakelite SUMILON

2 Installation of sensor module



Install the sensor module in the samples for assay in the biological safety cabinet.

- 2.1) After seeding the samples, set the 24-well plate in the plate adapter (bottom) and cover with the plate adapter (top).
- 2.2) Place the sensor module over the 24-well plate and close. It is now ready to be placed in the detector. The electrode at the tip of each sensor is immersed in the medium in each well so that cells can be continuously monitored during culture without the need to sample the medium.

3 Insertion in the detector



- 3.1) Insert the sensor module in the detector within the CO₂ incubator. A maximum of 4 detectors can be connected to one controller.

Insertion in a PHC CO₂ incubator

- Left) MCO-50 series (1 detector)
 Right) MCO-170 series/MCO-171AICD series/
 MCO-230 series (max. 4 detectors)

* If inserting 2 detectors on a shelf, use a dedicated reinforced tray [MCO-170RT-PW / MCO-230RT-PW].



4 Assay and analysis using the controller

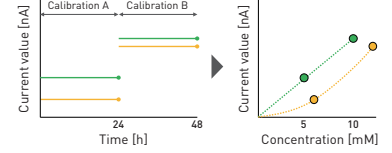
Assay, analysis, and data extraction are carried out from the controller as described below.

ASSAY WORKFLOW [COMPLETE]

Calibration
[24 h × 2 times]

Check sensor response values according to concentration

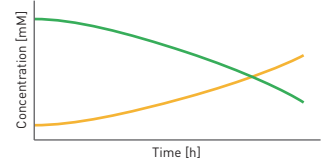
- Prepare two types of calibration solution based on the medium being assayed
- Assay the two calibration solutions for 24 h each (Calibration A/B)
- Create a calibration curve from the current values and concentrations



Assay
[Max. 10 days]

Assay continuously during cell culture [data at 1-minute intervals]

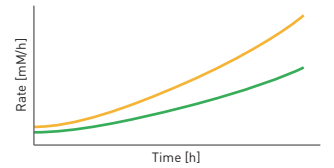
- Seed cells in 24-well plates and install sensor module
- Continuously assay glucose and lactate during culture
- Replace medium and add reagents such as metabolism inhibitors as required
- Assay for up to 10 days with one sensor module



Data analysis

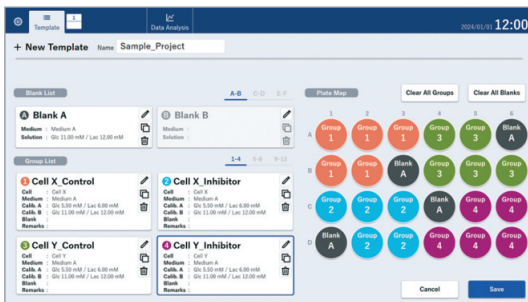
Calculate metabolic rate [data at 15-minute intervals]

- Carry out smoothing processing to remove noise in the assay data
- Calculate the glucose consumption rate and lactate production rate from continuous concentration changes
- Correct for sensor changes over time using a blank



CREATION OF ASSAY TEMPLATE

The assay template is created based on the experimental conditions. Information on the cells, medium, and well layout is entered in the assay template. The glucose and lactate concentrations of the calibration solutions prepared based on the assay medium are needed to create the assay template.



Grouping of culture cells in the well plate

Click the Edit button for any group and enter the group information.

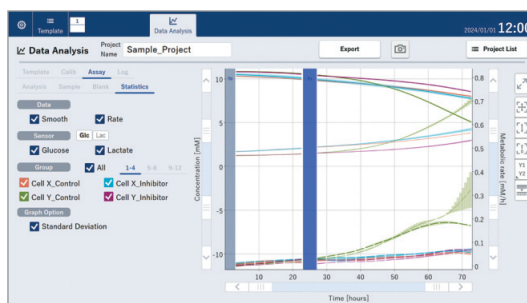
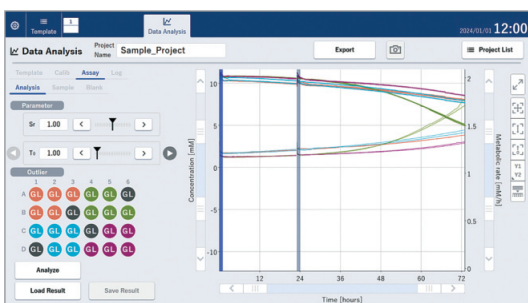
- Name** Enter the name of the group (optional)
- Cell** Enter the name of the assay cell (optional)
- Medium** Enter the name of the assay medium (optional)
- Calib. A Glc/Lac** Enter the glucose and lactate concentrations of calibration solutions A and B (required).
- Calib. B Glc/Lac**

DATA ANALYSIS

Calculation of metabolic rate

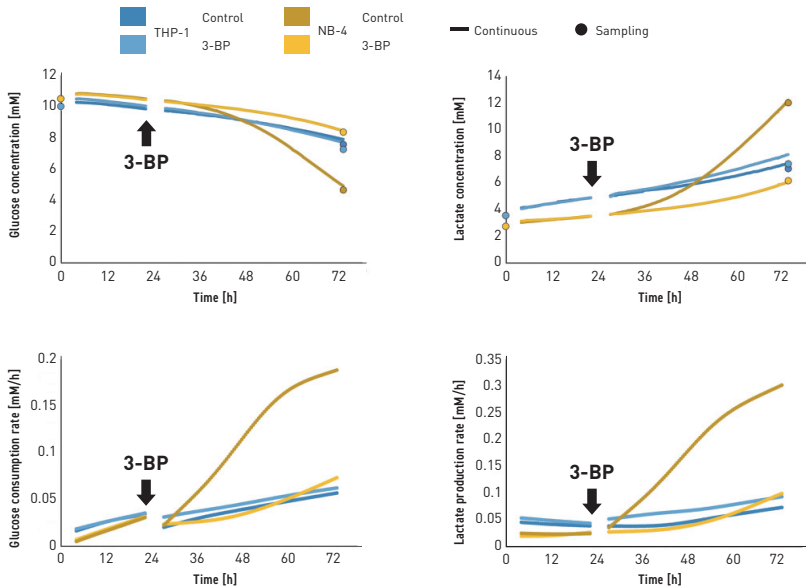
The data are analyzed after the assay is completed. The rates of glucose consumption and lactate production can be calculated by eliminating the noise in the measured values and performing differentiation on the data. Data analyzed with the controller can be output to a USB memory stick. Analysis parameters can be set, including the 'smoothing parameter', which defines the degree of smoothing of the analysis data, and the 'duration of instability after assay start/resumption', which excludes from data analysis the period of unstable sensor sensitivity after start/resumption of the assay.

The mean and standard deviation of the analysis results can also be displayed.

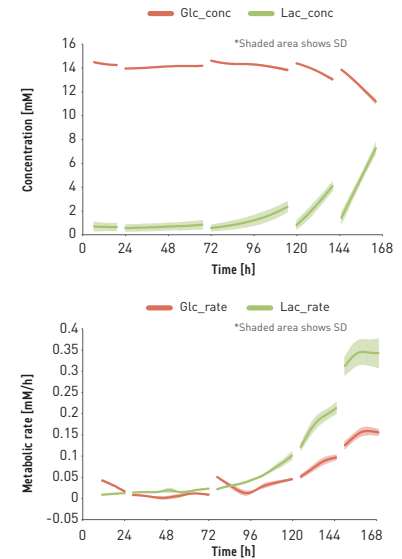


APPLICATIONS

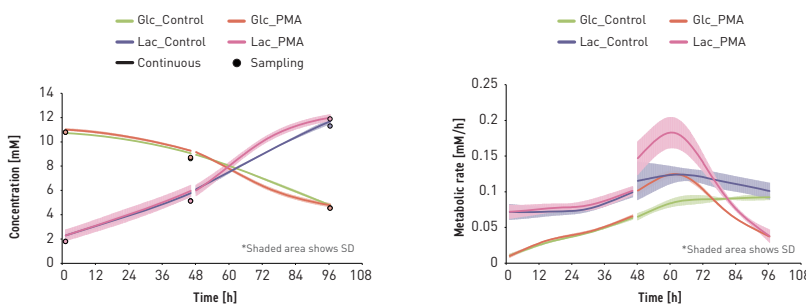
Visualization of the metabolic profile of immune cells using metabolism inhibitors



Metabolic rate monitoring of undifferentiated iPS cells and expression analysis of differentiation markers



Monitoring of metabolic shifts in immune cell differentiation



Application Notes can be downloaded [here](#)



FREQUENTLY ASKED QUESTIONS

What are the unique features of this device compared with other devices for measuring culture media?

Regular culture medium analyzers require sampling of the medium, whereas the LiCellMo™ Live Cell Metabolic Analyzer is capable of continuous measurement without sampling. Also, while there are methods using sensors or near-infrared for continuous measurement, the LiCellMo™ Live Cell Metabolic Analyzer allows simultaneous measurements to be carried out easily using 24-well plates. This makes it very convenient for situations such as comparing cell cultures under different experimental conditions.

How is the device configured?

The LiCellMo™ Live Cell Metabolic Analyzer consists of a detector that measures metabolism in a CO₂ incubator and a controller for operating the detector and checking the measurement data. The sensor module incorporates 24 sensors so that glucose and lactate concentrations can be measured simultaneously in each well of a 24-well plate.

Which types of cells can be used?

Measurements have been confirmed with various cell lines, T cells and iPS cells. The effect of the sensor on cells has been confirmed by

cytotoxicity tests with reference to ISO 10993-5:2009. Measurement results will depend on the experimental conditions, so trial runs are recommended to confirm performance.

What media and reagents are supported?

The measurement range is 1–27 mM for glucose and 1.5–15 mM for lactate. Measurements have been confirmed with RPMI 1640 medium, DMEM medium, and other specialized media. Measurements have also been confirmed with the reagents 3-bromopyruvate and oligomycin. Measurement results will depend on the experimental conditions, so trial runs are recommended to confirm performance.

How should the device be sterilized and cleaned?

The sensor module provided has undergone gamma irradiation. It is for single use only and should not be used more than once. The plate adapter can be sterilized in an autoclave and used repeatedly. The exterior and part of the interior of the detector for use in CO₂ incubators can be cleaned with ethanol. Hydrogen peroxide should not be used for decontamination. A pick-up cleaning service is available from the manufacturer for any customers concerned about contamination inside the detector due to use in the humid environment of the CO₂ incubator.

PRODUCT LIST & SPECIFICATIONS

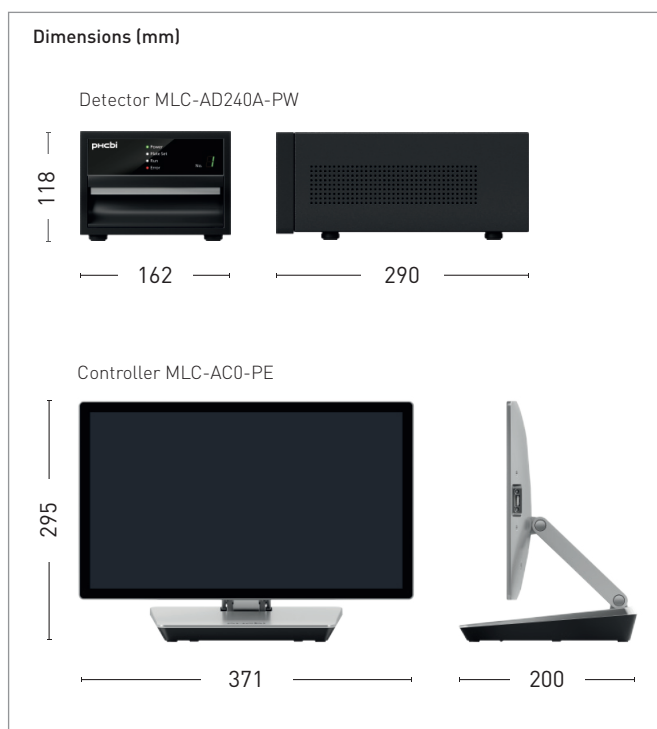


Product name	Product number	Comments
Device		
Controller	MLC-AC0-PE	
Detector	MLC-AD240A-PW	1 plate adapter (bottom) included
Sensor, Plate adapter		
Sensor module	MLC-AS240A-PW	3 included (consumables)
Plate adapter (top)	MLC-ATAD2410-PW	For Corning Costar
Select according to the plate used	MLC-ATAD2420-PW	For Corning Falcon
	MLC-ATAD2430-PW	For Greiner CELLSTAR
	MLC-ATAD2440-PW	For Thermo Nunc
	MLC-ATAD2450-PW	For Sumitomo Bakelite SUMILON
Options		
Plate adapter (bottom)	MLC-ABAD2410-PW	
Access port heater	MLC-APH0-PW	

*Please contact our office for information on prices. *There is a separate fee for installation.

Detector	MLC-AD240A-PW	
External dimensions (WxDxH)	162 mm x 280 mm x 118 mm	
Weight	4.7 kg	
Installation	Inside CO ₂ incubator	
Number of units installable in PHC incubators*	MCO-50 series	Max. 1 unit
	MCO-170 series, MCO-171AICD series, MCO-230 series	Max. 4 units (2 units x 2 shelves)
Controller	MLC-AC0-PE	
External dimensions (WxDxH)	371 mm x 200 mm x 295mm	
Weight	2.5 kg (excluding accessories)	
Screen	15.6-inch-wide touch panel display	
Extendability	Wired connectivity for up to 4 detectors	
Product Summary		
Items monitored	Glucose, lactate (simultaneous continuous measurement of both items)	
Main device components	Controller, Detector, Plate adapter (optional product)	
Main consumables	Sensor module (single use)	
Compatible plates	24-well plate *Compatible with 5 commercial products	
Monitoring duration	Maximum 10 days	
Measurement range	Glucose: 1–27 mM (0.18–4.86 g/L) Lactate: 1.5–15 mM (0.14–1.35 g/L)	

* If installing two detectors on one shelf, use a dedicated reinforced tray (MCO-170RT-PW / MCO-230RT-PW).



- This product is for research use only. Do not use for medical purposes.
- Product ratings and design may be subject to change without notice for improvements, etc.
- The actual colors of the product may differ slightly from the printed colors.
- Precautions for use are displayed on the actual product.

PHC Europe

A Member of PHC Group

Eikdonk 1 | 4825 AZ Breda | Netherlands
T: +31 (0) 76 543 3833

www.phcd.com/eu/biomedical

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