Combining a microscope, incubator and high-sensitivity digital camera into one powerful system

Live Cell Imaging Solutions
The BioStation IM-Q incorporates a microscope, an incubator and a high-sensitivity cooled CCD camera in a compact body. This all-in-one package provides a stable environment for live cells and advanced solutions for simple long-term time-lapse data acquisition. Moreover, focus drift caused by thermal change and mechanical instability has been minimized, and fail-proof data acquisition is possible even during lengthy time-lapse imaging. The BioStation IM-Q eliminates the need for a darkroom for fluorescence imaging, meaning it can be installed anywhere.

**Exceptional high-sensitivity fluorescence images**

The high sensitivity of the built-in CCD camera, equivalent to ISO800, reduces exposure time, which minimizes photobleaching and damage to specimens while increasing throughput for multipoint acquisition. The cooling mechanism prevents heat-induced noise and allows even weak fluorescence to be captured. The fluorescence equipment employs a noise terminator mechanism in order to eliminate stray light. This enables high-contrast imaging with high S/N ratios.
**Cell-friendly environmental control**

Cell culture and image capture functions are beautifully integrated. No complex setup or alignment procedures that conventional time-lapse observation systems require are necessary. The vibration-proof and heat-insulated structure enables stable image acquisition even over long periods.

The standard specimen chamber can be sterilized in an autoclave (a high-temperature, high-pressure steam sterilizer).

Red LED illumination is used for phase contrast imaging. The fluorescence illuminator shutter opens only when capturing images, therefore reducing phototoxicity of live cells.

BioStation IM-Q contains four sensors for precise control of an environment of 37 °C. In addition, the humidifier maintains a humidity level of 95 % or higher and the CO2 gas mixer provides a stable supply of CO2 of 5 % concentration.

**Accurate recording of live-cell dynamics over a number of days**

Focus drift during lengthy time-lapse observations has been greatly reduced, enabling reliable time-lapse imaging even for several days. The temperature of the chamber, the chamber exterior and microscope unit is precisely controlled with built-in heaters and fans. The focusing mechanism is made from thermal-stable materials and is therefore resistant to thermal expansion. Moreover, BioStation IM-Q moves the objective lens instead of the stage. This eliminates focus drift caused by vibration of culture dish, minimizing stress on the cells.

**Lengthy time-lapse imaging without focus drift**

Membrane-anchored GFP of rat hippocampal neurons was captured in 120-hour time-lapse imaging.

Photos courtesy of: Dr. Chieko Nakada, Dr. Yuuri Nemoto, Dr. Hiroko Hijikata, Dr. Akihiro Kusumi, Institute for Integrated Cell-Material Sciences, Kyoto University
Simple and easy operation

1 Operation from a PC
BioStation IM-Q provides fully motorized control from a PC, allowing users who are not accustomed to operating a microscope or camera to easily conduct time-lapse imaging. The user only has to set the culture dish in place and program the image recording. Everything from cell management to time-lapse imaging is automatically managed and accomplished.

1 Culture dish setup

2 Setting with intuitive GUI

Live image location indicator: imaging positions can be selected by clicking on the live image

1 Set live image location with XYZ movement control.
2 Configure imaging condition.
3 Select illuminations, filters and magnifications.
4 Input imaging time interval.
5 Start time-lapse imaging.

3 Time-lapse imaging and analysis
Image file output at desired Z-axis planes
Images at different Z-axis planes can be selected from the captured Z-stack images at each time point and assembled into a seamless movie file. This is optimal for imaging a specimen in which the observation point moves along the Z-axis direction, such as with cell division.

Streaming function
Rapid motion changes such as cardiomyocyte beats are captured by high-speed 10 fps imaging at user-defined time intervals.

Ergo controller
An ergo controller allows X, Y and Z directional movement with an operational feel similar to a microscope. It also allows changeover of magnifications, fluorescence filters, imaging/observation methods and fluorescence shutter ON/OFF.

Widefield display
Because a wide 6 mm x 6 mm area can be displayed by image stitching, the point of time-lapse observation can be easily specified from the widefield image.
Cell detection in phase contrast images
CL-Quant automatically detects and measures the cellular area in unstained, label-free phase contrast images. Unique image processing algorithms provide accurate thresholding of phase contrast images, which enables non-invasive quantitative analysis of cells. Cell detection accuracy can be improved through a learning function process.

Imaging software NIS-Elements Ar
Nikon’s proprietary imaging software NIS-Elements Ar allows multi-dimensional image capture, image processing, and data management and analysis of up to 6D. Its intuitive interface simplifies workflow and contributes to archiving and searching of large numbers of Z-stack sequence image files. It also offers diverse optional plug-ins to support sophisticated, cutting-edge research applications.

Deconvolution
Haze and blur of an image that can occur when capturing a thick specimen or a fluorescence image can be eliminated from the captured image.

Cell counting
Images are processed by image analysis routines and the extracted objects can be counted. Their areas and intensities are recorded.

Slice view
Images in three orthogonal planes (sliced images along the XY-, YZ-, and ZX-planes) can be viewed in a single display.

Volume rendering
3D images can be reconstructed from captured Z-stack images.

Dedicated image analysis software for BioStation series—CL-Quant

Cell detection in phase contrast images
CL-Quant automatically detects and measures the cellular area in unstained, label-free phase contrast images. Unique image processing algorithms provide accurate thresholding of phase contrast images, which enables non-invasive quantitative analysis of cells. Cell detection accuracy can be improved through a learning function process.

Analysis option: cell counting, scratch (wound) test, growth curve, tracking, stem cell colony analysis

Scratch (wound) test quantification
CL-Quant automatically segmented the acellular area (blue) in the time-lapse cell migration images that were captured at the beginning (left) and on the second day (right) of a 2-day phase contrast observation. The graph indicates how the acellular area decreased.

Cell detection samples

INS-1
PC12

Original image  Segmented image  Original image  Segmented image
Optional accessories broaden the range of applications

Motorized chamber for four-well culture dish
Automated changeover allows each of the four culture wells to be imaged. Observation of four different conditions is possible in a single time-lapse experiment, facilitating comparative analyses.

Specialized Hi-Q4 culture dish that enables multi-sample observation
This new 35 mm culture dish is divided into four parts and has an incorporated plane parallel top plate. The plate prevents light path distortion by the meniscus, which is the curve at the air-water interface, and enables high-quality phase contrast observation. The observation points in the quadrant of the Hi-Q4 dish can be easily set using BioStation IM-Q software. An adapter is provided to store the Hi-Q4 dish in the right position.
*Use of the Hi-Q4 culture dish is available for the BioStation IM-Q CELL-S2 unit only.
*Patent pending

Perfusion components
The perfusion components allow reagent administration and medium exchange without a change to the culture environment. This apparatus comprehensively supports live-cell research, such as lengthy time-lapse imaging. Researchers can add drugs or medium supplements to their cultures or collect waste products for further analysis.
*Perfusion components cannot be used with a Hi-Q4 culture dish or a motorized chamber for a four-well culture dish.

- The compact unit can be stored inside the temperature controlled section of BioStation IM-Q. A waterbath to pre-equilibrate the medium or medium supplements prior to adding to the culture is not required.
- Two bottles can be stored. Retrieval of the medium after reagent administration enables the clear determination of medicinal effects.
- All perfusion components can be sterilized in an autoclave.

Lab-Tek™ chambered coverglass (Cat. No. 155383, Nunc™)

Operation screen

Observation with four different combinations of medium and reagent can be conducted.

Dish with plate (Hi-Q4)
Dish without plate

The absence of a meniscus allows light to pass through without refraction.
Light refracted by the media’s meniscus causes distortion and poor phase image.

Hi-Q4 dish

Two-bottle installation

Quick and easy reagent administration with a single button

*Syringe pump or peristaltic pump is necessary to pressurize the solution bottles.
Specifications

**CELL-S2**
- (for glass bottom dish)

**CELL-S2-P**
- (for plastic bottom dish)

**Temperature control**
- 37 °C ± 0.1 °C

**Humidity control**
- 95% or higher

**Water supply for humidification**
- Built-in bottle (270 ml)

**CO2 supply**
- Concentration and flow volume set by external mixer

<table>
<thead>
<tr>
<th>Observation vessel</th>
<th>a35 mm glass bottom dish, Hi-Q4 a35 mm culture dish, Nunc™ Lab-Tek™ chambered coverslips (Cat. No. 155383, for the motorized chamber). Glass slide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diaplastic phase contract observation</td>
<td>Phase ring DL Iillumination: red LED</td>
</tr>
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</table>

**Epi-fluorescence observation**
- Illumination: external mercury illuminator Intensilight via fiber cable, filter cube: up to two can be mounted. Field diaphragm: rectangular diaphragm switch interacting with the objective changer, built-in noise terminator

**Objective lens magnification**
- 40x (20x, 40x, 80x by switching tube lens), NA 0.8
- 20x (10x, 20x, 40x by switching tube lens), NA 0.5, with correction ring

**Camera**
- High-sensitivity 1.3-megapixel cooled monochrome camera
- Recording pixels: 1280 x 960, 460 x 480 (binning)

**Data format**
- ICS-IDS, JPEG, BMP, TIFF, PNG (still), AVI (movie)

**Imaging area**
- XY: 6 x 6 mm (by objective lens movement), Z: 1.25 mm

**Time-lapse**
- Up to 99 XYZ-positions can be set. AVI image file output at desired Z-axis and 10-lps imaging at time intervals are possible.

**Image stitching**
- Allows composition of large-area images of 6 mm x 6 mm

**Analysis functions**
- Tone curve adjustment, saturation indicator, light intensity screening, light intensity record display, ratio display, image blur adjustment, etc.

**Temperature record**
- Graph display

**Power consumption**
- 1160 VA (IM-Q: 300 VA, illuminator Intensilight: 130 VA, PC: 475 VA)

**Dimensions**
- 220 (W) x 620 (D) x 400 (H) mm (excluding protrusions)

**Weight**
- Approx. 30 kg (main body only)

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**Research papers stating data obtained with BioStation IM**

- Karine Gouset, Edwin Schiff, Christelle Langevin, Zrinka Marijanovic, Anna Caputo, Duncan T. Browman, Nicolas Chenouard, Fabrice de Chaumont, Angelo Martino, Just Enninga, Jean-Christophe Olivier-Marie, Daniela Männel and Chiara Zunzo.

- Prions hijack tunnelling nanotubes for intercellular spread
- Nature Cell Biology, Volume 11, Number 3, March (2009)


- Analysis of Human Embryonic Stem Cell Behavior in Control and Experimental Conditions Using Time-Lapse Video Microscopy Endpoints
- Biology of Reproduction, July 2009, 8: 667

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**System diagram**

**Introduction case**

**Fraunhofer Institute for Biomedical Engineering**

Department Biophys & Cryotechnology (Prof. Dr. H. Zimmermann and M. Gepp, M.Sc.), Fraunhofer IBMT, which conducts cell management and technological development of long-term storage and thawing, introduced 10 BioStation IM into their laboratory to efficiently conduct the experiments and is researching to improve culture conditions by simultaneously running multiple experiments with BioStation IM.

Contact:
- michael.gepp@ibmt.fraunhofer.de

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