Nikon

BioPipeline LIVE

Microscope Automated Incubation
and Imaging System

Experiment Pipeline

Incubation

Cultured cells must be maintained until time to perform imaging on the microscope. After imaging, cells must return to the incubator.

Free Instrument Time

Sharing time on a microscope can be challenging, especially if there is not a clear schedule. With experiments requiring multiple rounds of imaging, usage of instrumentation can be very inefficient.

Getting Samples to and from the Instrument

Sometimes when the instrument is free and idle, the time of day is not convenient. Or, it may be that sensitive samples need to spend as little time outside the incubator as possible.

Imaging

Experiments are run and images acquired in an automated fashion.

Processing and Analysis

During and post-acquisition, processing and analysis functions are performed to generate statistics for further interpretation.

Data Archival

Storage of experimental data, especially large data, can be difficult if it has to be transferred off of the acquisition workstation.

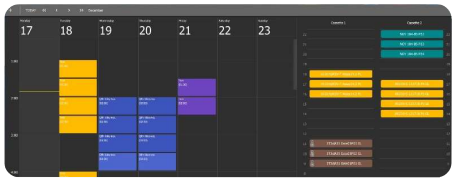
Potential Bottleneck

BioPipeline LIVE

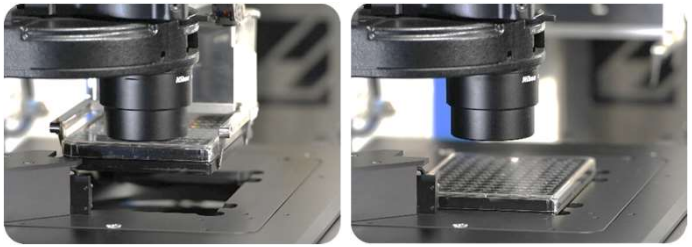
streamlines experiment protocols by introducing organized automation and data storage capabilities.

✓ A scheduler keeps track of plates, owners, and experiment times.

NIS Scheduler

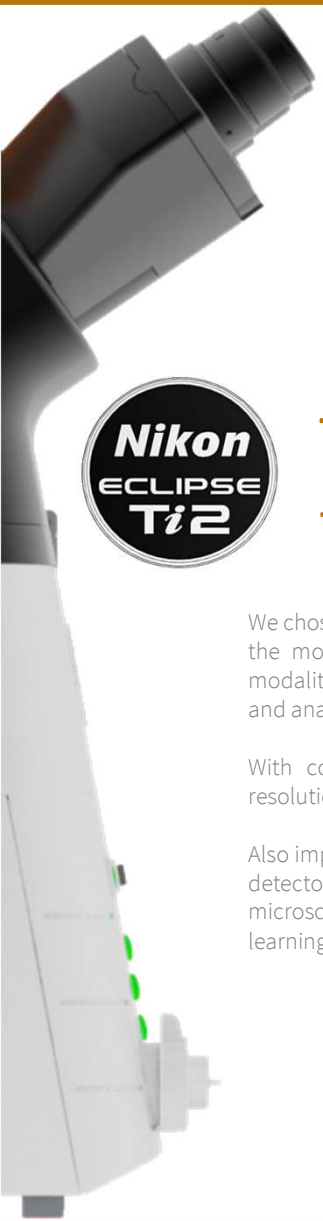


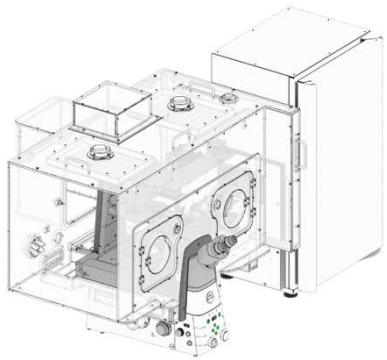
✓ Robotics transfer plates to and from the incubator.



✓ A dedicated server can manage offline processing, analysis, and storage.

Key Features





The Perfect Platform for High Content

We chose our inverted microscope platform for high content because it was the most flexible: the largest selection of objective lenses, detectors, modalities and applications available to apply to high content acquisition and analysis.

With confocal modalities, 3-dimensional high content at the highest resolution can be acquired.

Also important is the ease of modification or upgrade of the system for new detectors and modalities. With a unified software package across all microscope platforms, data can be easily shared and visualized as well as learning time reduced.

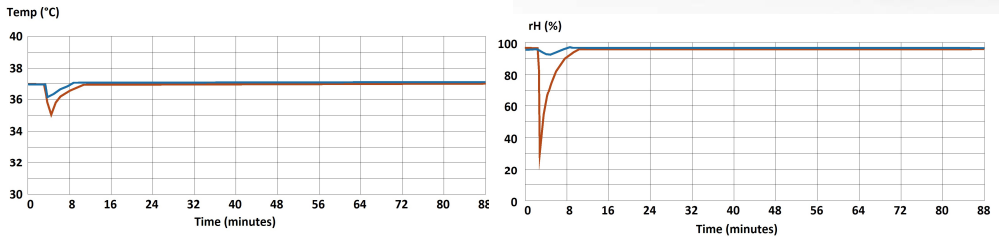
Incubation

Environmental stability is maintained by a 44-plate capacity incubator (two stackers each housing up to 22 plates).

With a main door for plate loading, and a side door for direct robotic transfer to the microscope stage, temperature and humidity can be quickly recovered and constantly maintained.

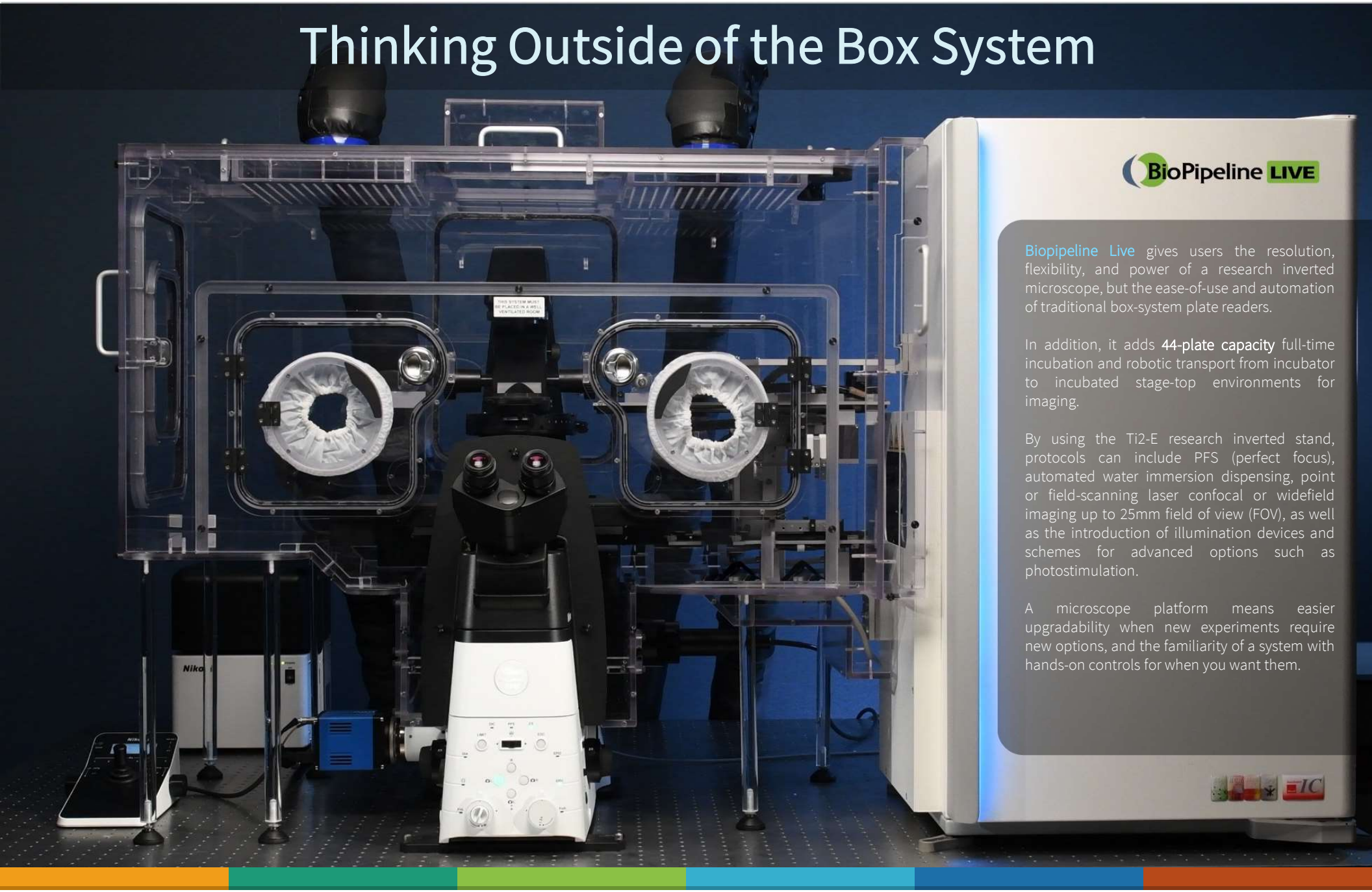
Environmental information is logged during acquisition sessions, and the incubator illuminates a color-coded light on the outer door so status can easily be seen even from across the room.

An internal robot picks plates and loads them through a side door to a second robot which transfers plates directly to the microscope stage, all inside an incubated environmental chamber.



*(Above) Temperature and humidity plots over time after front door (**red**) or side door (**blue**) were opened. In these examples, the side door was not enclosed in a microscope enclosure / incubator. With our included microscope enclosure, even more temperature and humidity stability is maintained between the microscope stage and the incubator.*

Thinking Outside of the Box System



Biopipeline Live gives users the resolution, flexibility, and power of a research inverted microscope, but the ease-of-use and automation of traditional box-system plate readers.

In addition, it adds **44-plate capacity** full-time incubation and robotic transport from incubator to incubated stage-top environments for imaging.

By using the Ti2-E research inverted stand, protocols can include PFS (perfect focus), automated water immersion dispensing, point or field-scanning laser confocal or widefield imaging up to 25mm field of view (FOV), as well as the introduction of illumination devices and schemes for advanced options such as photostimulation.

A microscope platform means easier upgradability when new experiments require new options, and the familiarity of a system with hands-on controls for when you want them.

Software

NIS-Elements Scheduler keeps track of plates in the incubator and their owners.
Owners can schedule time blocks directly within the scheduler to execute JOBS experiment runs.

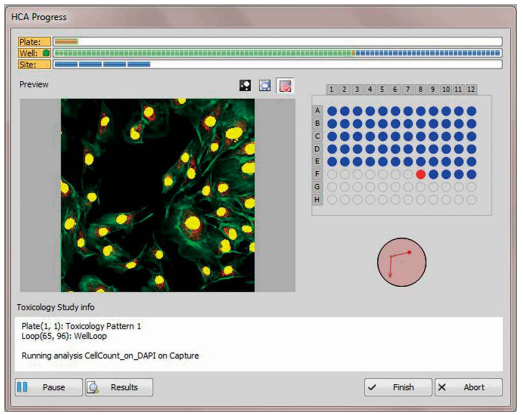
The NIS-Scheduler then initiates NIS-Elements HC, loads plates, executes experimental runs, returns plates to the incubator, and closes NIS-Elements automatically.

Optionally, the scheduler can email an owner when plates are finished run, or in case of any issues. NIS-Elements can additionally email or SMS text message a user during a plate run with updates defined by the user (e.g., cell counts).

NIS-Elements HC (High Content) allows users to create custom experimental protocols or use turn-key templates to run on multiple plates.

Plate assays and image storage can be shared or specified user by user, and accessed by NIS-Elements Scheduler.

In addition to automated microscopy, NIS-Elements can perform processing and analysis functions including analysis assays either during experiment runs, or later offline on the BioPipeline dedicated server.



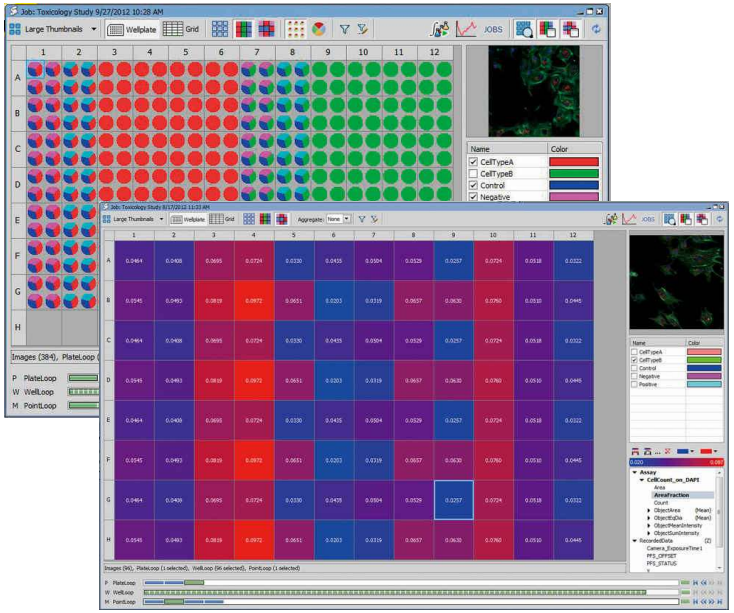


Plate runs can be visualized in a number of methods, including images, labels, and heat maps: giving users an overview of results.

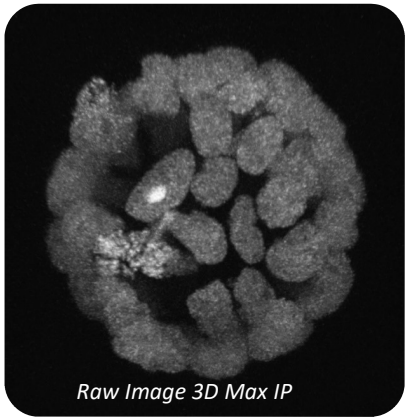
Since analysis can be performed during acquisition, analysis results can be summarized during the experiment or be ready as soon as the experiment completes for viewing.

Image Processing

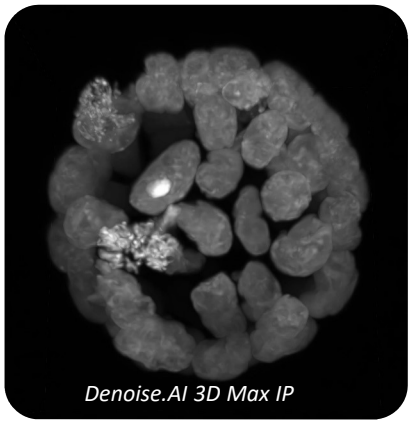
Artificial Intelligence Denoising extends acquisition times

An artificial intelligence neural network trained to recognize and removed Poisson (shot) noise can be applied to confocal images to enhance image details.

Such improvements allow users to collect data at shorter exposures and lower illumination power than ever before, allowing more time points to be collected.

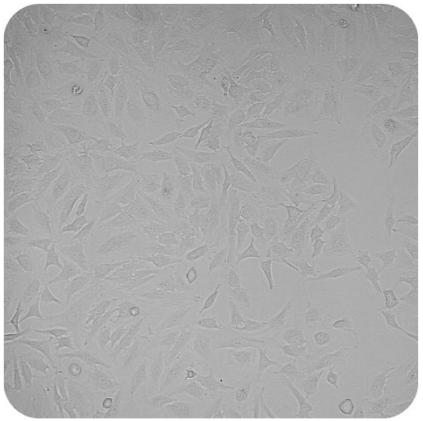


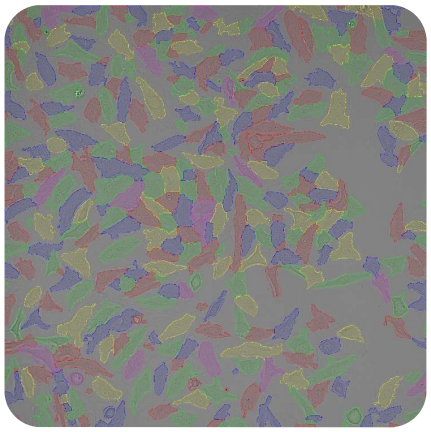
Raw Image 3D Max IP



Denoise.AI 3D Max IP

Label-Free Imaging with Volume Contrast



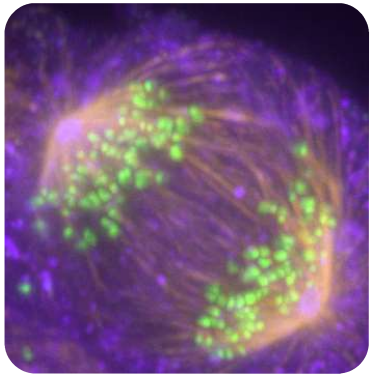


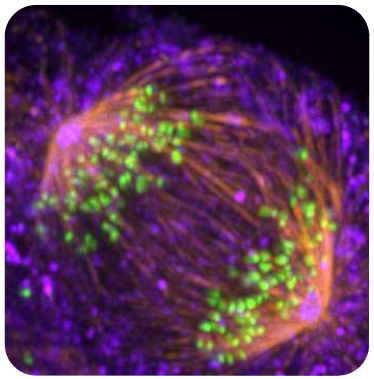
Acquisition of a transmitted light image without contrast (no phase contrast or DIC) can now be used to compute a Volume Contrast enhanced result image in which the volumetric shape of objects produces contrast. The contrast image can be used for segmentation.

Deconvolution enhances 3D structures

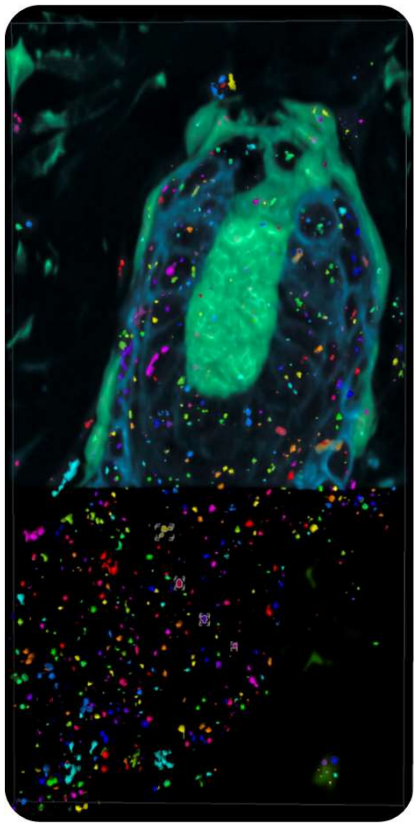
Advantageous to 3-Dimensional high content imaging is the ability to perform 3D Deconvolution on data sets to improve contrast and sharpness of images. BioPipeline can run deconvolution during acquisition, or automatically on images in target folders on its server post-acquisition.

Deconvolution is supported by GPU-acceleration for maximum speed.





3D Processing and Segmentation



Z stacks can be processed as voxels to incorporate objects in 3 dimensions for preprocessing and enhancement, as well as 3 dimensional thresholding and binary processing. Volumetric measurement information for field and objects can be queried.

Image Analysis

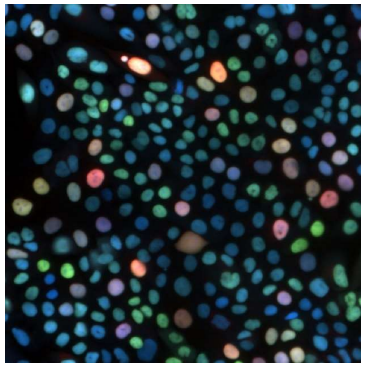
NIS-Elements' General Analysis engine employs a powerful processing and analysis toolbox for users.

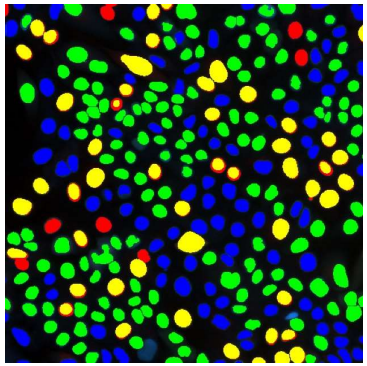
Dedicated turnkey assays can be applied to image data as well as user-customized assays for specific applications.

All routines can be executed during acquisition, for example: to modify the course of an experiment, or post-acquisition on the dedicated server.

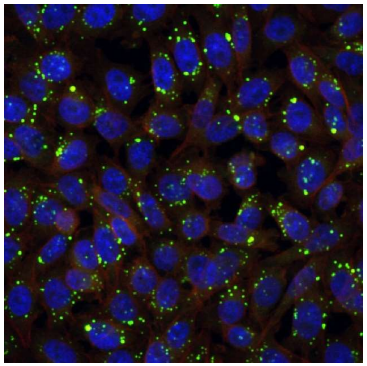
Assay results can be collated and statistical information displayed, or be exported.

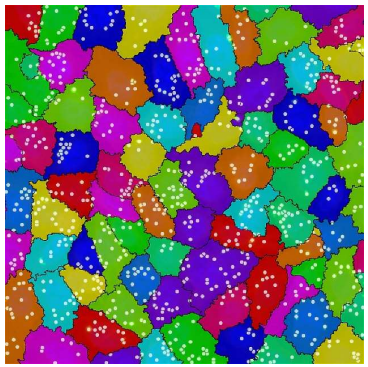
Some example tools are shown here.



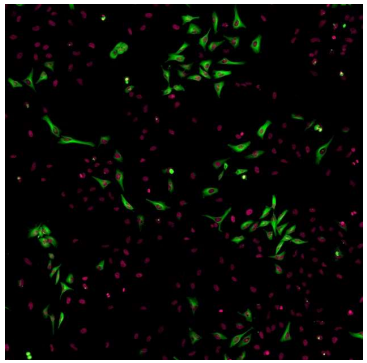


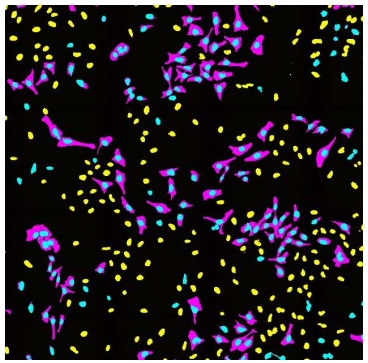
The cell labeling tool detects and counts number of cells labeled with colors, or combination of colors. It also provides the intensities ios of the multiple labels per cell.





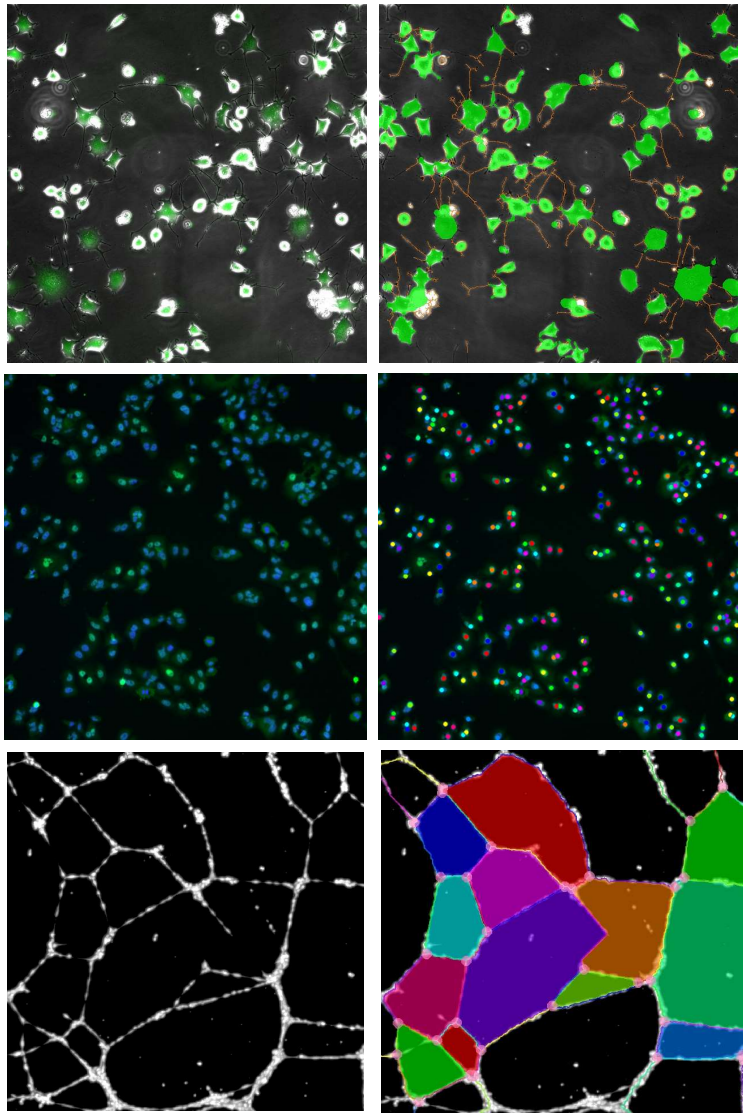
The spot counting tool detects and counts granularity in cells, creating boundaries between cells and reporting number of granules per cell.





The cell classification tool segments and classifies samples into categories for counting and measurement

Image Analysis



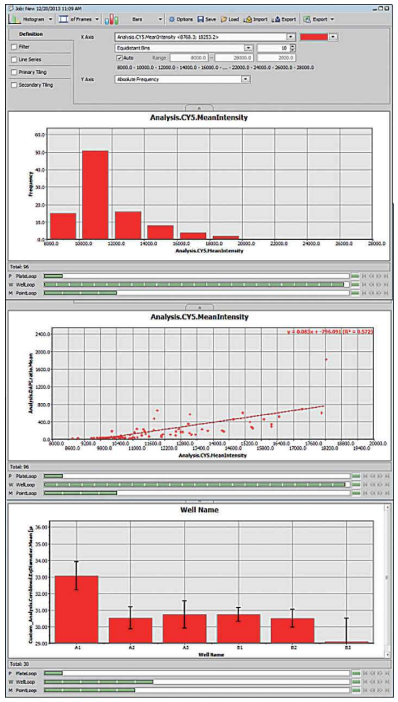
The neurite detection tool highlights neurites and cell bodies, and measures neurite segment length, number of neurites per cell, and branch points per cell.

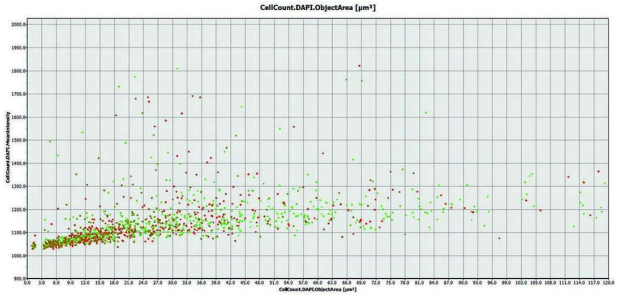
The cell counting tool utilizes low magnification and large FOV to count objects.

This provides accurate and repeatable count information that can be applied across multiple plates.

The angiogenesis tool detects tube formation and measures tube number, area, nodes, segment number, and segment lengths.

Analytics can be performed within wells, across wells, or across multiple samples. Statistics and graphs can be generated all within NIS-Elements, or data can be exported in common file formats.



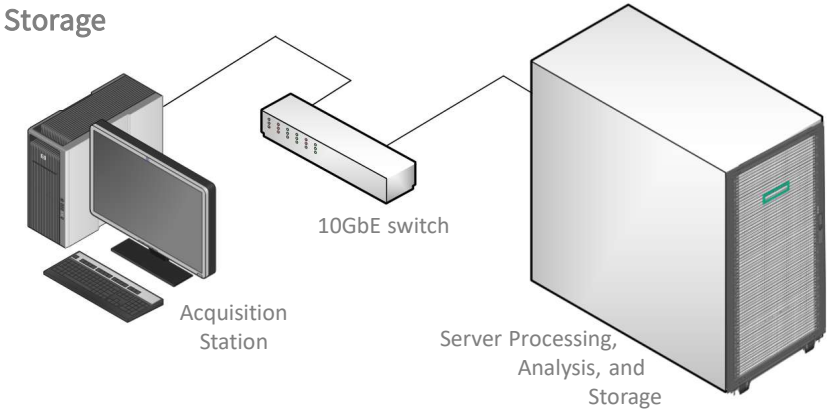


Dedicated Server

Server-side Processing, Analysis, and Storage

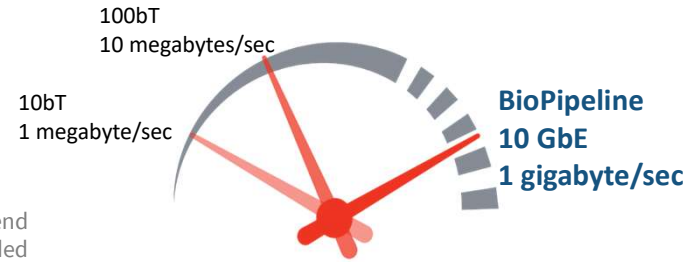
Because data can be saved directly to the server, it means multiple users can view their data while the system is busy acquiring new images. Likewise, the server can perform processing and analysis tasks automatically on designated locations when data is placed there.

Because the server is connected to the imaging workstation by a dedicated switch, slow traffic on the existing network will not affect the transfer speed between acquisition and storage devices.



Data Transfer

BioPipeline's data transfer rates from the imaging workstation to the dedicated server exceed most traditional networks by 10-100x by using dedicated 10 GbE connections.



Storage Capacity

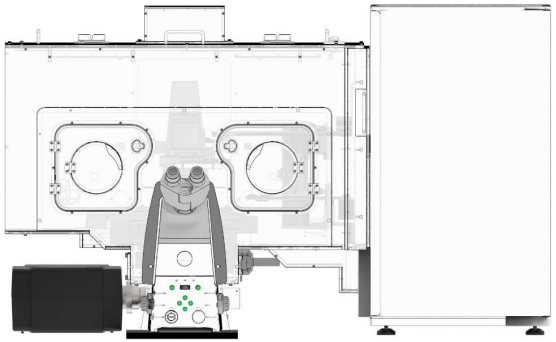
Having **over 30x** the storage capacity of a typical high-end imaging workstation, with expandability for more, the included **BioPipeline Server** with direct dedicated 10GbE network connection allows for more uninterrupted imaging and offline processing and analysis.

Typical Imaging workstation: 6TB

BioPipeline Server: 200TB*

**expandable*

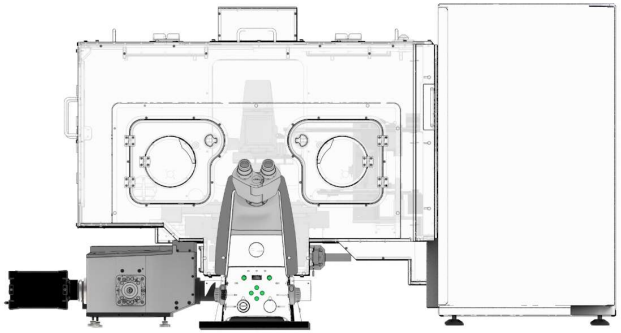
Configurations



A1 R HD25

A confocal point scanner with high speed, gentle resonant scanner and a 25mm FOV allows high content point scanning confocal to become a reality. Extremely short dwell times coupled with large FOV means more data over a longer time lapses.

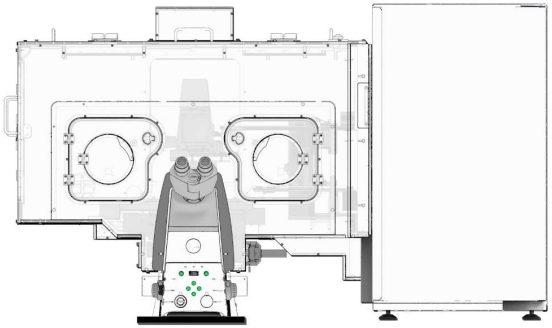
Or utilize confocal scan zoom to achieve the optical resolution limits of the microscope at any objective lens, and not be limited by the camera pixel size.



LFOV Spinning Disk

A spinning disk with a large 25mm FOV and a selection of sCMOS detectors allows for fast multidimensional imaging in multiple wavelengths. An enhanced pinhole design maximizes optical sectioning and minimizes spinning disk pinhole crosstalk for thicker specimens.

Different pinhole disks allow users to customize the spinning disk pattern to the magnification and specimen being used.



Open Detector

Connect any detector to the left microscope port including widefield options, spinning disks, point scanning confocal, or optical pixel reassignment super resolution systems with the open detector configuration.

Choose to maintain the 25mm large FOV, or stage-up the microscope to introduce additional epifluorescence modules (if >3 required).

PACKAGES

- Microscope
- Robotics
- Software and modules
- Workstation
- EPI and DIA light sources
- Server storage
- Barcoding
- Anti-vibration table

All base packages of BioPipeline Live include the anti-vibration table, Ti2-E PFS microscope stand, 44-plate incubation and robotics, microscope incubation, Online acquisition workstation and offline server storage and processing, LED Episcopic and diascopic light sources, NIS-Elements software control, and barcode label printing and reading capabilities.

Three different base packages configurations (shown at left) are available. Optional components can be added freely to these base packages.

Selectable Components

Select the detector(s) and objective lenses best suited for your experimental pipeline to add to the base packages.

Likewise, if further automated hardware is required, it can be added as well.

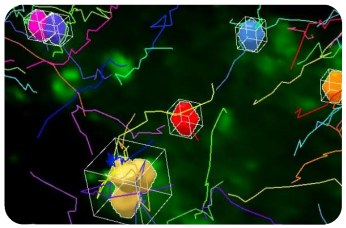
And additional software modules can be added as needed.

- Detectors
- Objectives
- Additional software modules
- Automatic water immersion
- LAPP branches / modules
- Workstation desk

Select from a variety of objective lenses specially designed for
spherical and chromatic correction, long working distance, or large FOV.

Long-term automated timelapse and multiple plate loading and incubation can be achieved with both air objectives and water immersion objectives.

Select a detector if using the Open Detector Package, or add a second detector to the microscope right-side port. NIS-Elements supports all major manufacturers for sCMOS, CCD, and EMCCD detectors and can connect these for hardware triggering of microscope peripheral devices.

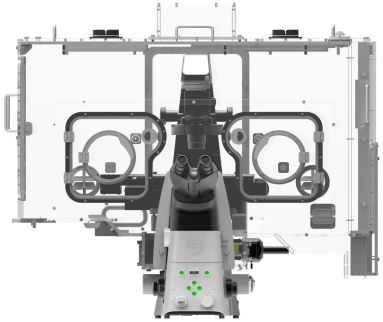


Additional NIS-Elements modules for specific applications such as multidimensional object tracking, co-localization, and FRET are also available.

Utilize the automated water immersion dispenser for maintaining water immersion for long-term timelapses or imaging large specimens. The dispenser can be used for multiple water immersion objectives on the same nosepiece.

Modify BioPipeline Live with additional LAPP modules to meet experiment requirements, including raster scanning or DMD photostimulation devices and additional epifluorescence illuminators (up to 3 on a 25mm FOV configuration; maximum of 5).

Specifications



Microscope Specifications

Imaging Modalities	Transmitted Light Brightfield and phase contrast^ Monochromatic Brightfield (R,G,B) Widefield Epifluorescence Point Scanning confocal (option) Field scanning confocal and Optical Pixel Reassignment (options)
Illumination	8 channel Epifluorescence LED LED transmitted Light Laser illumination for confocal sources (option)
Objectives	All air or water-immersion objectives lenses can be used for high content Oil and Silicone immersion objectives can be used for single specimen observation
Imaging Methods	Multidimensional XY, Z, wavelength, time-lapse, multi-stage position, large image tiling
Autofocus	Perfect Focus 4 for focus stability; software-controlled autofocus
Hardware Triggering	Supports direct hardware triggering of light sources and shutters
Antivibration Table	3' x 6' x 8"

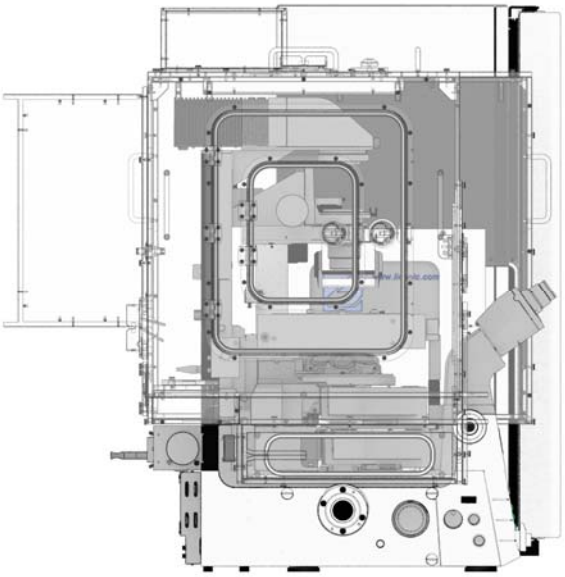
^with optional phase contrast components
**see detector brochures for detector specification details*

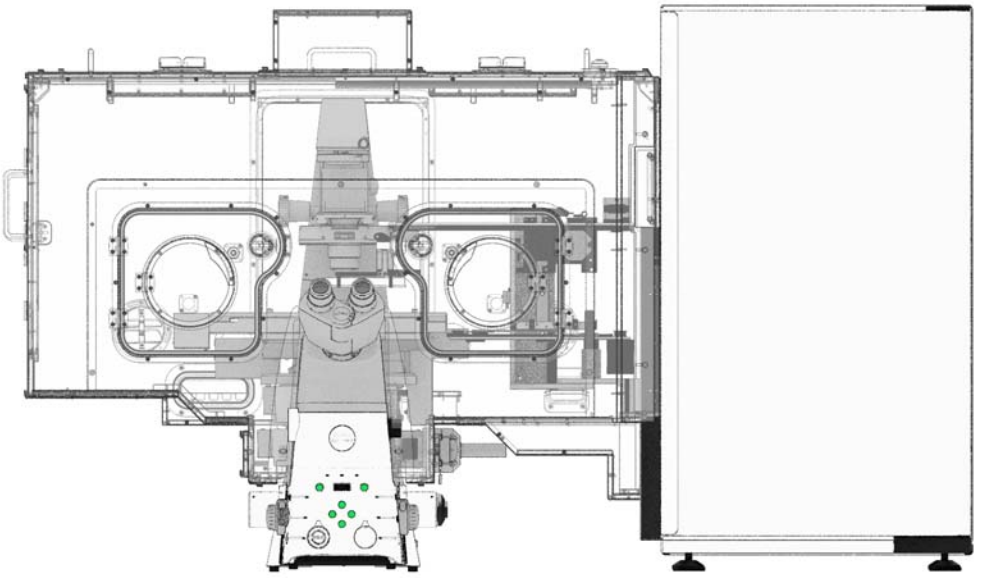
Plate Incubator Specifications

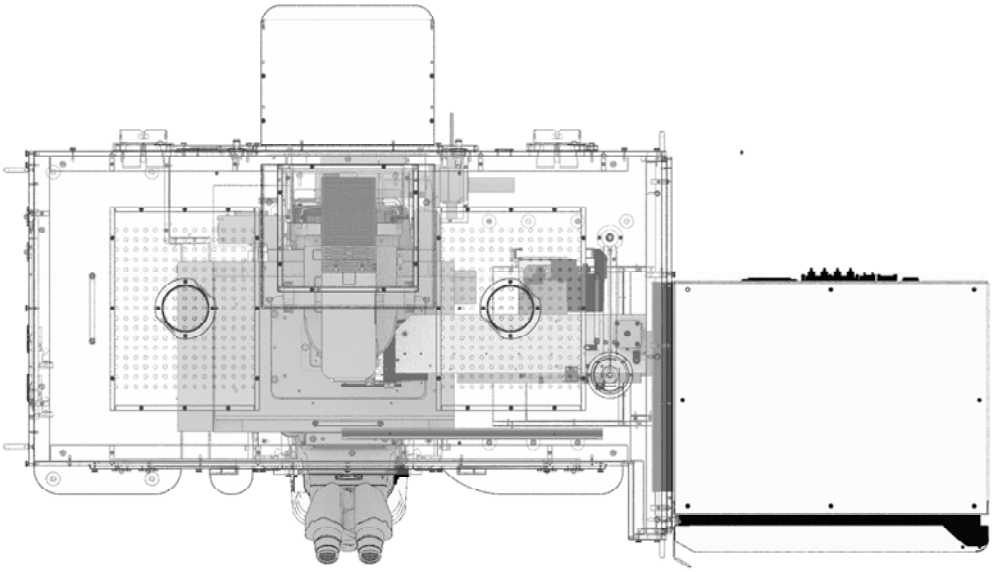
Application	Incubation
Capacity	44 plates (128mm x 85mm x 14mm standard) in any format (e.g., 6, 12, 96, 384)
Barcode Format	Code 128
Robotics	Internal shovel robot and external grabber robot
Robotics Speed	3 speed settings for robotic movement acceleration and maximum speed
Temperature Range (HT)	33.50 (70) °C
Temperature Deviation	+/- 0.2 °C
Relative Humidity	Maximum 95%
Communication	RS232 or USB virtual COM port
Power Requirements	100V / 50Hz 115V / 60Hz / 240V / 50Hz ; switchable
Power Consumption	450W

Server Specifications

Rack Size	22U
Processor	Intel Xeon Silver 412 2.6 GHz
OS	Windows Server
RAM	128 GB
Storage Type	SAS
Storage Capacity	200TB
Network	12x 10GBase-T + 4x 1Gbit/10Gbit SFP+
Support	3 year Foundation Care Service and Support
Power Consumption	600W (average) – 1300W
Options	Tape Backup, 144TB Expansion
Physical Dimensions	(W x D x H) 90.00 x 129.20 x 151.00 cm

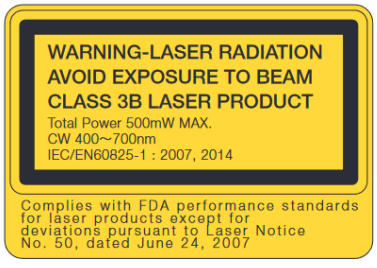


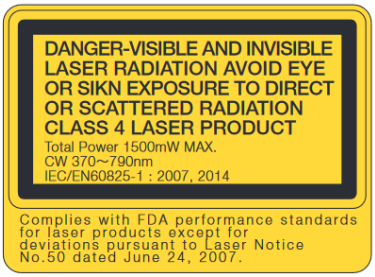




Specifications and equipment are subject to change without any notice or obligation on the part of the manufacturer.

⚠ WARNING	TO ENSURE CORRECT USAGE, READ THE CORRESPONDING MANUALS CAREFULLY BEFORE USING YOUR EQUIPMENT.





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