

SYNENREC

**YF-SOFTWARE
ECOSYSTEM**

SYNENTEC provide the most versatile high-throughput cell imagers in the market. All instruments can be equipped with full fluorescence capability. This allows an extensive range of applications ranging from single cell cloning, apoptosis studies, through to transfection efficiency, toxicity studies and ultra-high throughput cell counting with viability determination. The instruments are compatible with a wide range of SBS format plate types and have a built in automation interface enabling integration into automation platforms.

SYNENTEC's team of engineers, software developers and biologists have developed automated, high throughput cell culture microscopes with fast and easy to use image analysis software.

The CELLAVISTA, a fully automated high throughput cell imager, was launched in June 2007 and has been continuously developed ever since. It was joined by the NYONE range of instruments in 2014, further extending the versatility of SYNENTEC's products. The instruments are used throughout the industry for applications varying from CLD, drug discovery, stem cell research, gene editing and cell and gene therapies through to viral infectivity studies and spheroid monitoring in various settings.



ABOUT YT-SOFTWARE ECOSYSTEM

What started as YT-Software has diversified into a whole ecosystem of possibilities to optimize throughput, reliability and precision as well as customization. The YT-Software ecosystem consists of separate building blocks that can be used to generate processes tailored for our customers' requirements. All systems are cross-compatible to perform the exact task in the exact right time in lightning speed and with highest accuracy.

YT-Software itself is a complete package having 65 different image processing algorithms and imager operation built in. High resolution 4K images can be displayed extremely fast as well as analyzed in instant. Speed and precision of image analysis is paramount for process performance - in case it is slower than the high throughput imaging, it can be outsourced to the Batch Processing Suite to increase throughput of manually operated imagers or fully automated workstations.

SYNENTEC'S automation suite with the Automation Server enables external control by third party automation software and is well known within the automation industry. SYNET.scheduler enables automation control of SYBOT-1000 without programming knowledge and automation experience.

GxP suite is an essential requirement for assays run in advanced regulatory settings and is SYNENTEC's plug and play solution to validated imaging and data integrity monitoring.

All individual components of the YT-Software ecosystem can be run in conjunction orchestrating ultra-high throughput validated imaging using SYNENTEC's imagers in full walk-away automation.



YT-SOFTWARE

PAGE 4

Image acquisition, device controlling as well as image and data analysis software for our portfolio of automated imaging systems.



BATCH PROCESSING SUITE

PAGE 6

Batch processing solutions providing the highest claims in plate throughput.



AUTOMATION SUITE

PAGE 8

Take advantage of SYNENTEC'S high throughput automation with additional features for high throughput applications.



AI-SUITE

PAGE 10

AI-based image processing workflow with the NYONE and CELLAVISTA.



GxP SUITE

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Audited Imaging Requirements - 21 CFR part 11 compliant imaging and image processing.



AUDIT Server

PAGE 14

AUDIT Server supports multi-device audit trailing in automation including batch processing.



SYNENTEC brings the latest standard in image acquisition, device controlling and image and data analysis software in the field of automated imaging systems.

YT-SOFTWARE

- + Imaging
- + Evaluation
- + FL Viewer

The YT-software offers a complete tool - from experimental set-up and automatic high throughput image acquisition with precise image analysis, through to the storage, handling and processing of data for documentation and presentation purposes. The high-resolution, stored images mean your results can be tracked over years to come.

Data generation in CELLAVISTA and NYONE is conducted using one of SYNENTEC's 65 proprietary image processing algorithms that can be used for a variety of applications. The high quality images are analysed for specific properties, for example cells or cell features, and the results are visualised using overlays in YT-software.

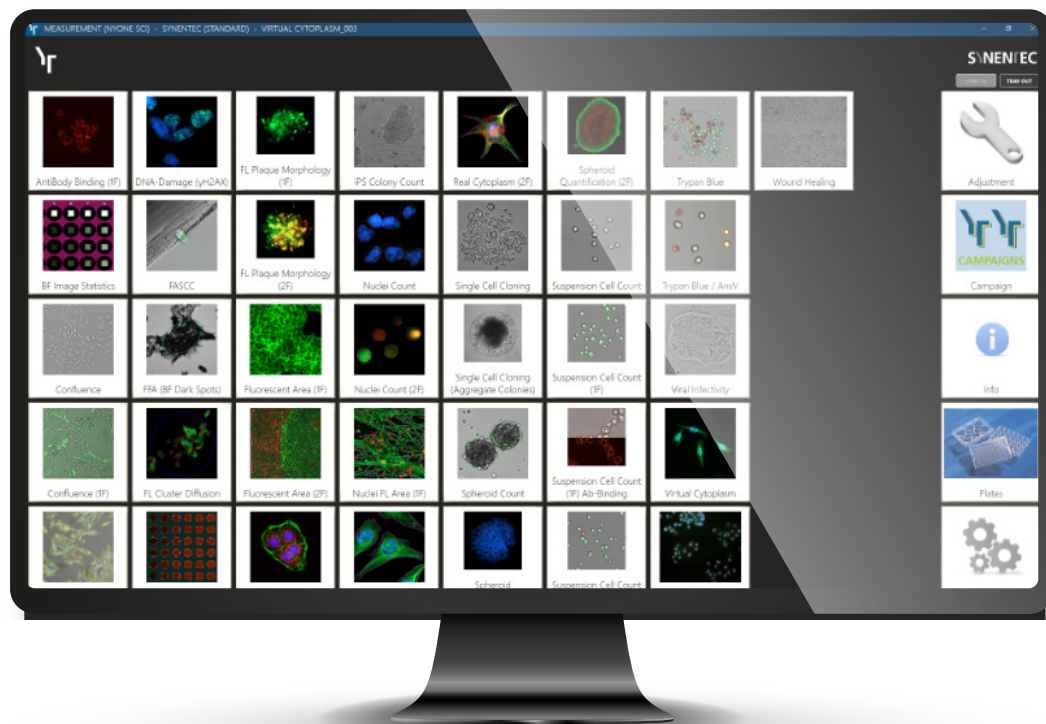
The software also evaluates the results generated in a per-well manner to readily display the data obtained in a comprehensive form. These well-based results can be exported in a machine-readable format to be incorporated in well-based decision making, for example, in binding studies or response analyses like cytotoxicity or hitpicking in a CLD or drug discovery setting. All parameters for a specific assay, including imaging, image processing and export variables, can be stored in templates, which enables hands-off operation in semi-automated processes.

THE BENEFITS

- ✓ Intuitive workflow to set up your experiment.
- ✓ Performing automated, high-quality image acquisition in parallel with accurate, reliable image analysis.
- ✓ Automated, customizable data and image export function for report creation, documentation and regulatory approval.
- ✓ Supporting automation interfaces.
- ✓ Available data batch-processing solutions for highest claims in plate throughput.
- ✓ Further software licenses in combination with an imaging system independent evaluation mode of the software reduces workstation blocking during data review.

HIGH THROUGHPUT IMAGING General method of operation





SUPPORTS ALL THE COMMON APPLICATIONS NEEDED TO RUN R&D PROCESSES IN HIGH THROUGHPUT

Cell Line Development

Including: Single Cell Cloning, CRISPR/Cas9 Tracking, Transfection Efficiency, Cell Viability Monitoring, PAIA Protein Titer Measurements, PAIA Glycosylation Measurements, PAIA Aggregation Assays, Fluorescent Activated Single Cell Cloning (FASCC).

Cancer Research & Drug Discovery

Including: Imaging of 3D Spheroids, Toxicity Testing, IC₅₀ studies, Cell Expansion Tracking, Cell Cycle/ Mitosis, CD-Marker Analysis, Apoptosis Monitoring, Nucleus Characterization, Antibody Binding & Internalisation, Wound Healing and Scratch Assays.

Stem Cell Research

Including: Colony Count on Feeder Layer, Fluorescent Pluripotency Studies, Validation of Proliferation and Cell Migration, Cell Differentiation Analysis, Recombinant Lectin Probes.

Immunology

Including: B-Cell and T-Cell Studies, Cytotoxic T-Lymphocyte Testing, Evaluation of Helper T-Cells and Subsets, Performing Cell Death Studies.

This user-friendly software interface provides the choice of either using a predefined set-up from a list of established assays, or defines your own work flow protocol and store this into a customised template.

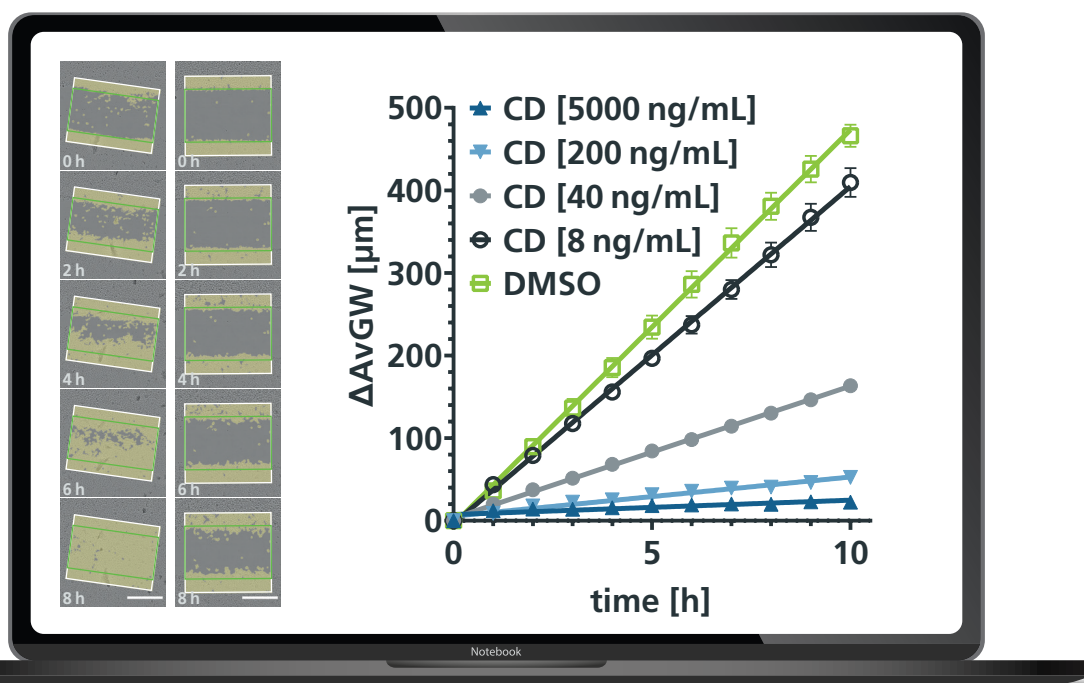
Both imaging systems run on the same software platform which makes it easy to transfer your process, in case of upgrading, from NYONE for higher throughput to CELLAVISTA.



The SYNENTEC data batch processing solutions provide the highest claims in plate throughput.

BATCH PROCESSING SUITE

- + Software only (Client & Server)
- + Hardware (optional)



PROCESSING DATA USING BATCH PROCESSING SERVER

- ✓ Enables highest plate throughput and automated data handling.
- ✓ Automatic, sequential, and complete processing of all data contained in one or more input files.
- ✓ Completely independent image processing (e.g. over night).
- ✓ API enabling external access for third party software, e.g. automation scheduling software integration.
- ✓ Massive parallel data processing for multiple experiments and runs.
- ✓ Modification or changes of image processing algorithm.
- ✓ Automatic export of data and images.

EXPORT CAPABILITIES

Save it, sort it,
show it, store it!

EXPORTABLE SETTINGS

Experimental Settings

Image Processing Settings

EXPORTABLE DATA

Result Table

High Content Object Data

Histogram

EXPORTABLE IMAGES

Clone Gallery for SCC

Plate Overview & Plate Heat Map

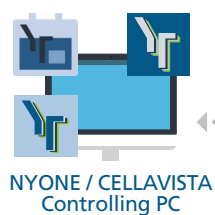
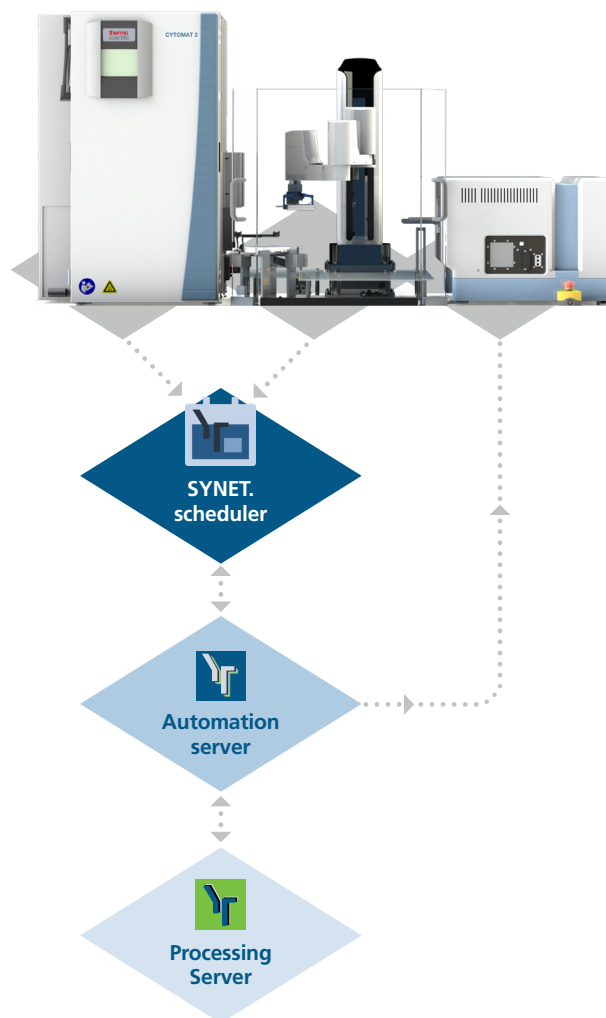
Well Channels & Well Overlay

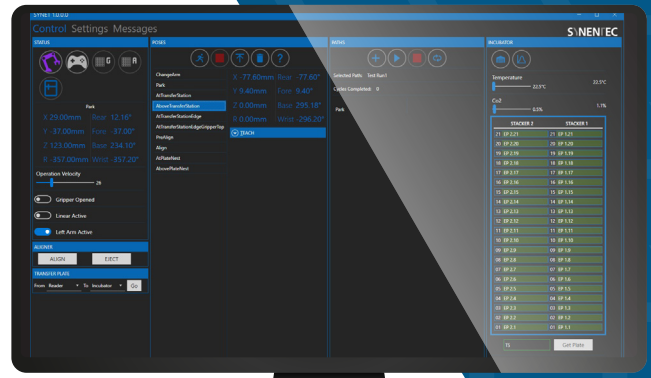
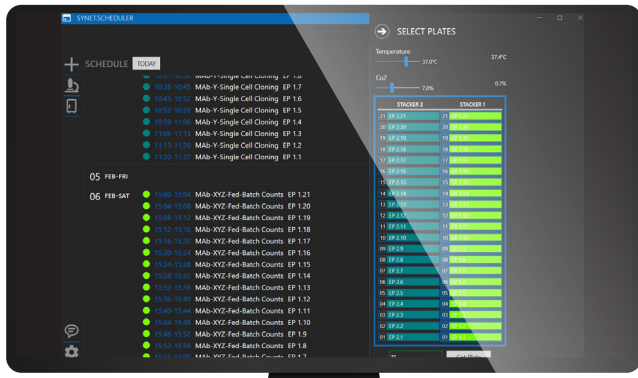
All taken Raw-Images as

ZIP-container

Add Brightness, Contrast and
Normalisation Settings to Image

AUTOMATED BATCH PROCESSING SYBOT-1000 Automation & BPS

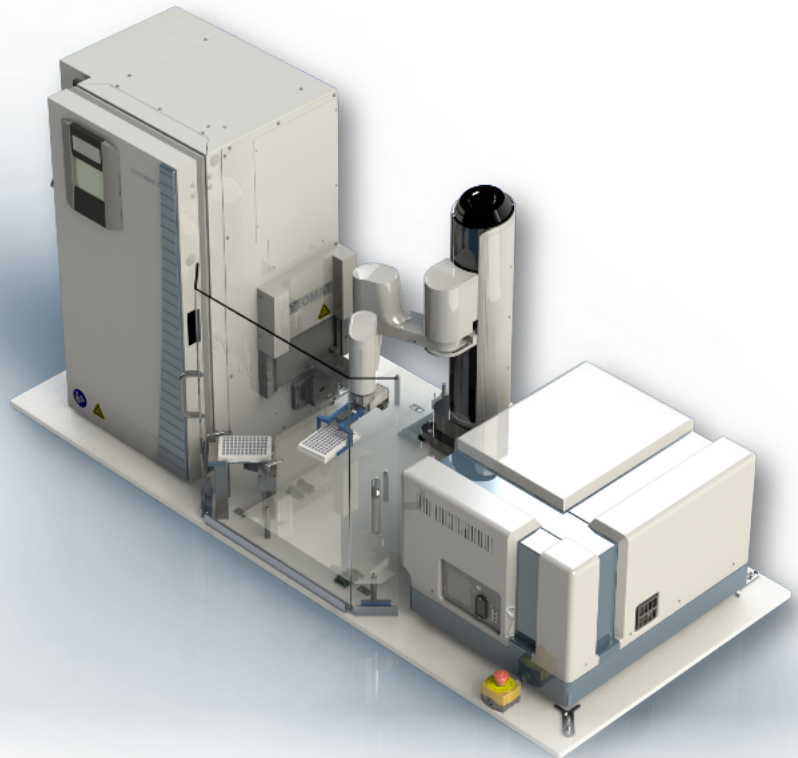




Take advantage of SYNENTEC'S high throughput automation with additional features for high throughput applications.

AUTOMATION SUITE

- + Automation Server
- + SYNET.scheduler



SYNENTEC INTEGRATION

SYBOT-1000 & Cytomat 2-C LiN

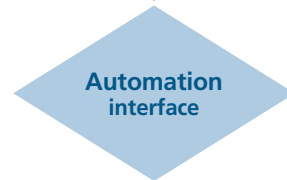
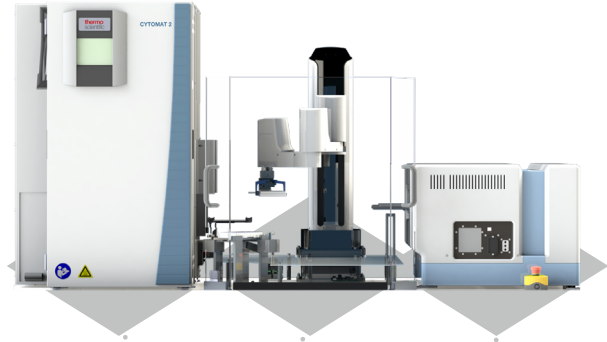
- ✓ Safe to operate
- ✓ Fits regular benchtop
- ✓ 188 cm x 80 cm x 92 cm (w/d/h)
- ✓ Easy access for servicing (modular)
- ✓ Easy to use software suite SyNET
- ✓ Accessible scheduling (no „coding“)
- ✓ SYBOT-1000 and Cytomat 2-C LiN control software SyNET

SyNET

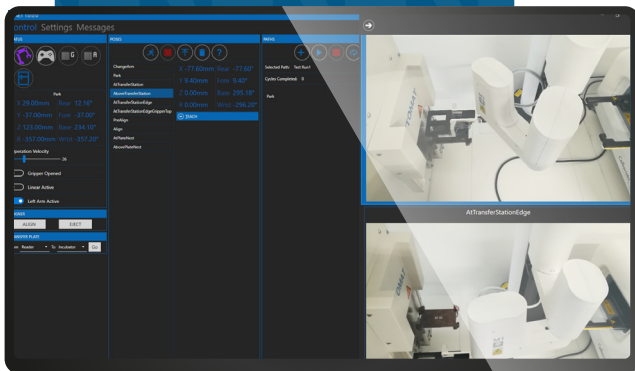
- ✓ User interface is easy to overlook
- ✓ Provides teaching aids for each position
- ✓ Uses X-Box Elite controller for teaching
- ✓ Uses calendar and project-based scheduling
- ✓ Uses barcode reader within incubator for rapid scheduling
- ✓ Schedules complex measurements rapidly and visually aided
- ✓ Live modeling of Automation for remote setups



WALK AWAY SOLUTION SYBOT-1000 Automation



NYONE / CELLAVISTA
Controlling PC



ADDITIONAL BENEFITS

- ✓ Years of experience in integration into robotic systems
- ✓ Increasing throughput using Batch Processing Suite
- ✓ Interchangeable stackers in incubator
- ✓ Low level entry for easy onboarding of new lab members



AI-based image processing workflow using NYONE and CELLAVISTA.

AI SUITE

- + AI-STUDIO+
- + AI-SERVER

In recent years the requirements for image processing have changed significantly. Customers require individual image processing solutions which are sometimes uniquely adapted to specific cells and workflows. Some image processing algorithms on the other hand are used throughout industry and academia, while the need for more detailed analyses of existing data is found ubiquitously.

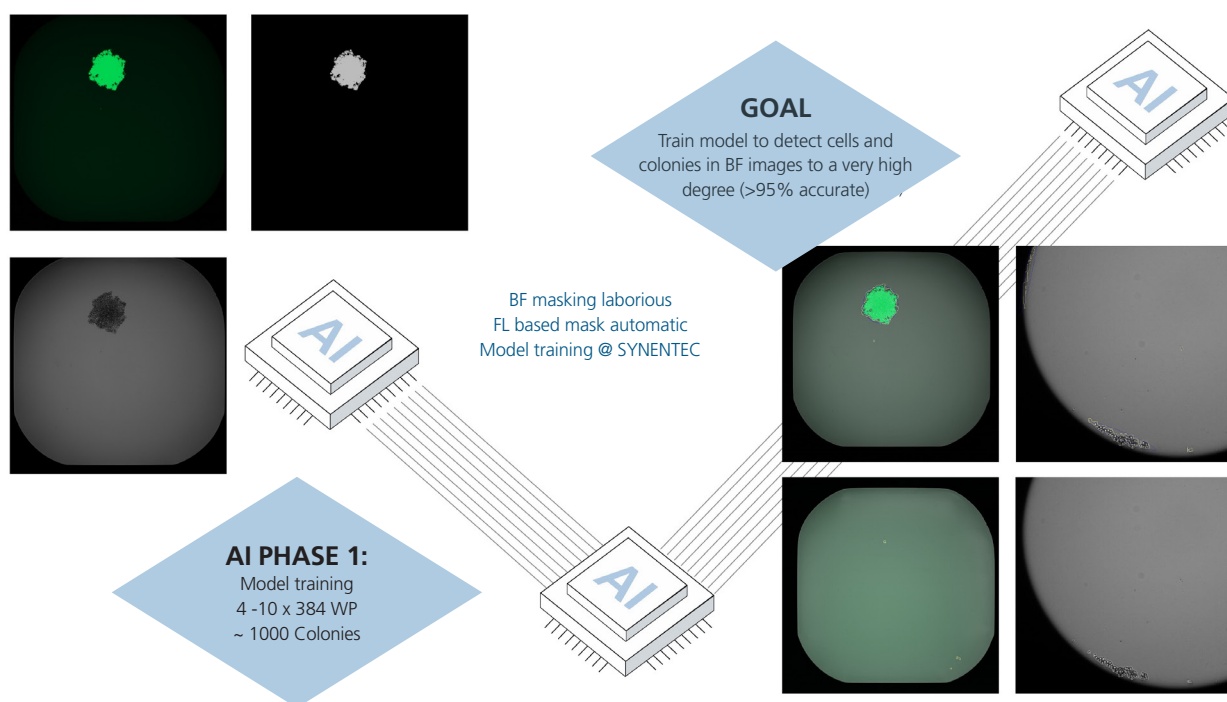
SYNENTEC has developed AI-STUDIO+ and AI-SERVER to address these challenges and requirements by bringing AI-based model training and AI-based image processing to NYONE and CELLAVISTA.

AI-STUDIO+ uses image data generated in high throughput by NYONE and CELLAVISTA and enables the user to conveniently label objects to be detected and define how results are going to be reported. These images and the labels are used to train a model dedicated to the exact requirements of the users. Once validated, the model can be used on the AI-SERVER responsible for image processing with the model. This processing can be included in any manual or automated imaging process.

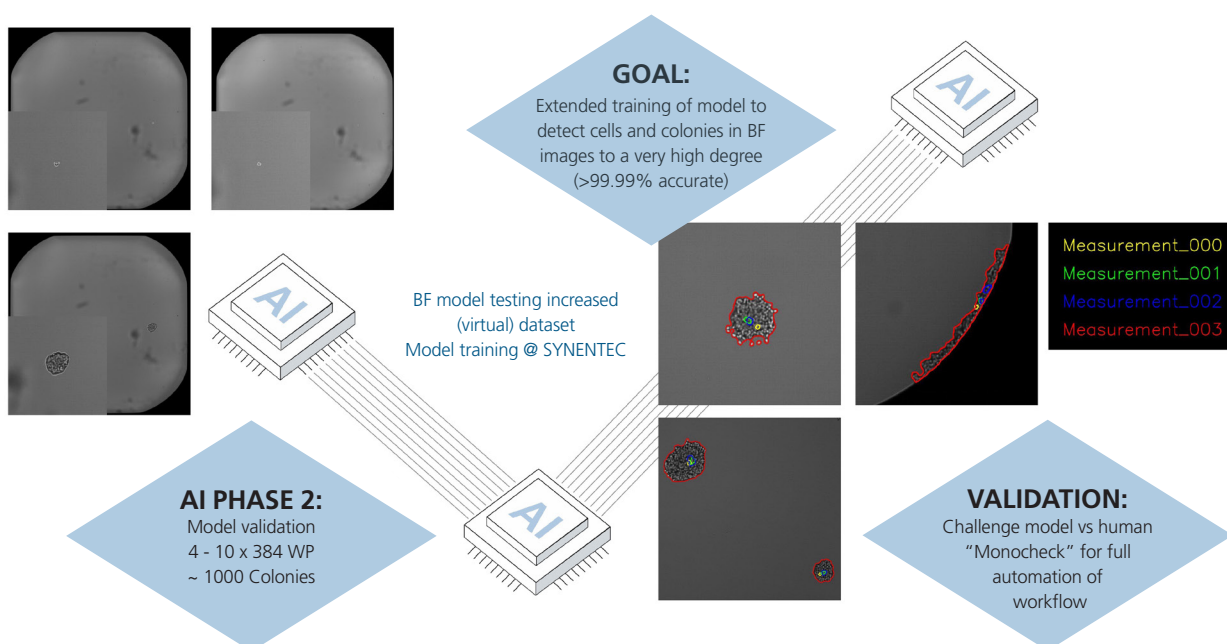
AI-SUITE

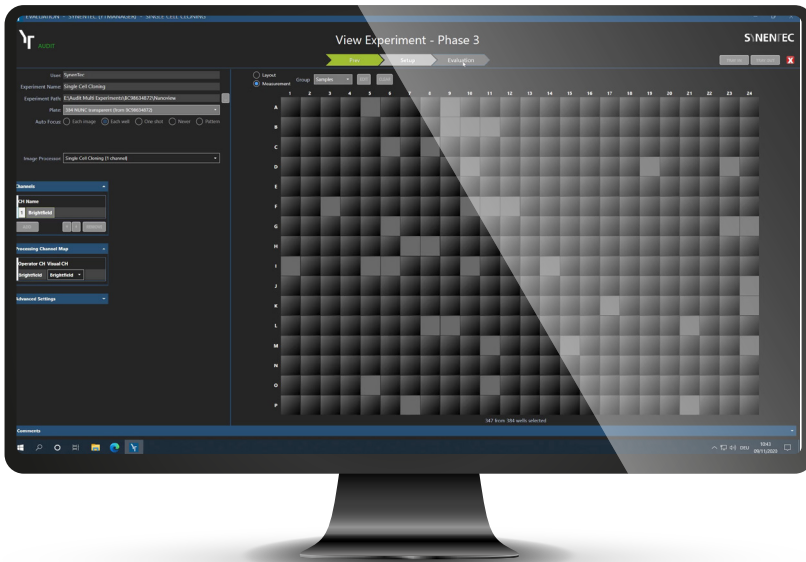
- ✓ Easy to operate
- ✓ Highly customizable
- ✓ High content screening made simple
- ✓ Brightfield
- ✓ Fluorescence
- ✓ Multiplex brightfield & fluorescence
- ✓ Custom cell and feature detection

AI-BASED SINGLE CELL DETECTION Brightfield & Fluorescence Imaging



AI-BASED SINGLE CELL DETECTION Brightfield Imaging





21 CFR part 11 compliant imaging and image processing.

GxP SUITE

- + Standalone in YT-Audit
- + Automated with Audit Server
- + Always includes Audit Browser



AUDITED IMAGING REQUIREMENTS

Database

- Locally stored
- Aviation grade
- Fast
- Up to 281 TB size
- Audit Trail

Digital Fingerprints

- SHA1 (160 bit file protection)
- Storage with data
- Data integrity check
- Error Rate = 8.2×10^{-20}

Did you know...
Human Fingerprint is 1.56×10^{-14}

AUDITED ENVIRONMENT IS HIGHLY AUTOMATED

Setup/ Maintenance of YT-Audit Environment

YTManager

- ▶ Plate definition
- ▶ Template development
- ▶ Saving of validated templates
- ▶ Import of standard templates

YTUser

- ▶ Template testing

IT

- ▶ Group management in Win OS
- ▶ Setting up routine backups

Use of YT-Audit

YTUser

- ▶ Measurements using validated templates

YTManager

- ▶ Measurements using validated templates
- ▶ User remarks in case of experimental change

IT

- ▶ Backup integrity check

Auditing

YTManager

- ▶ Data review and validation

YTAuditor

- ▶ Data review and auditing
- ▶ .pdf-reporting

WHY 21 CFR PART 11 COMPLIANT IMAGING AND IMAGE PROCESSING?

Vaccine Production

- Efficacy testing

Cell Line Development

- Proof of Monoclonality / Assurance of Monoclonality
- CDMO work for external projects

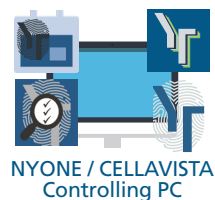
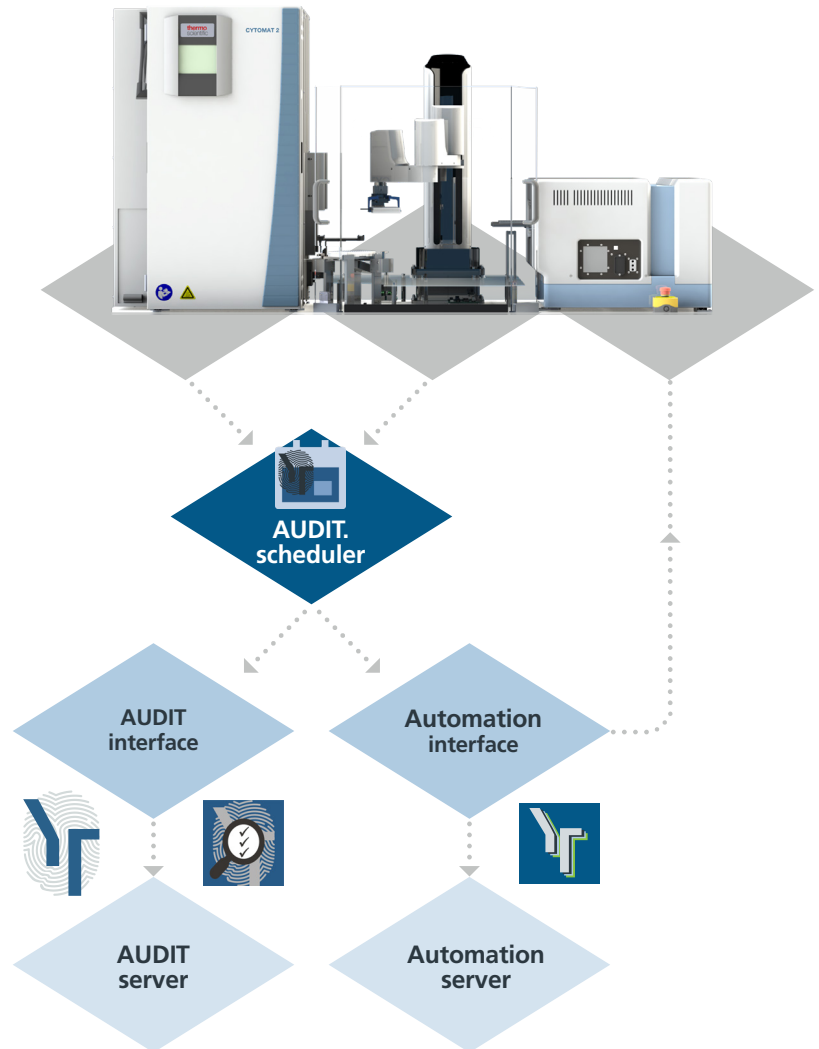
Gene Therapy

- Proof of Monoclonality
- Working with primary cells
 - Efficacy testing

Cell Therapy

- Proof of Monoclonality
- Working with primary cells
 - Efficacy testing

AUDITED AUTOMATION SYBOT-1000 Automation & YT-Audit



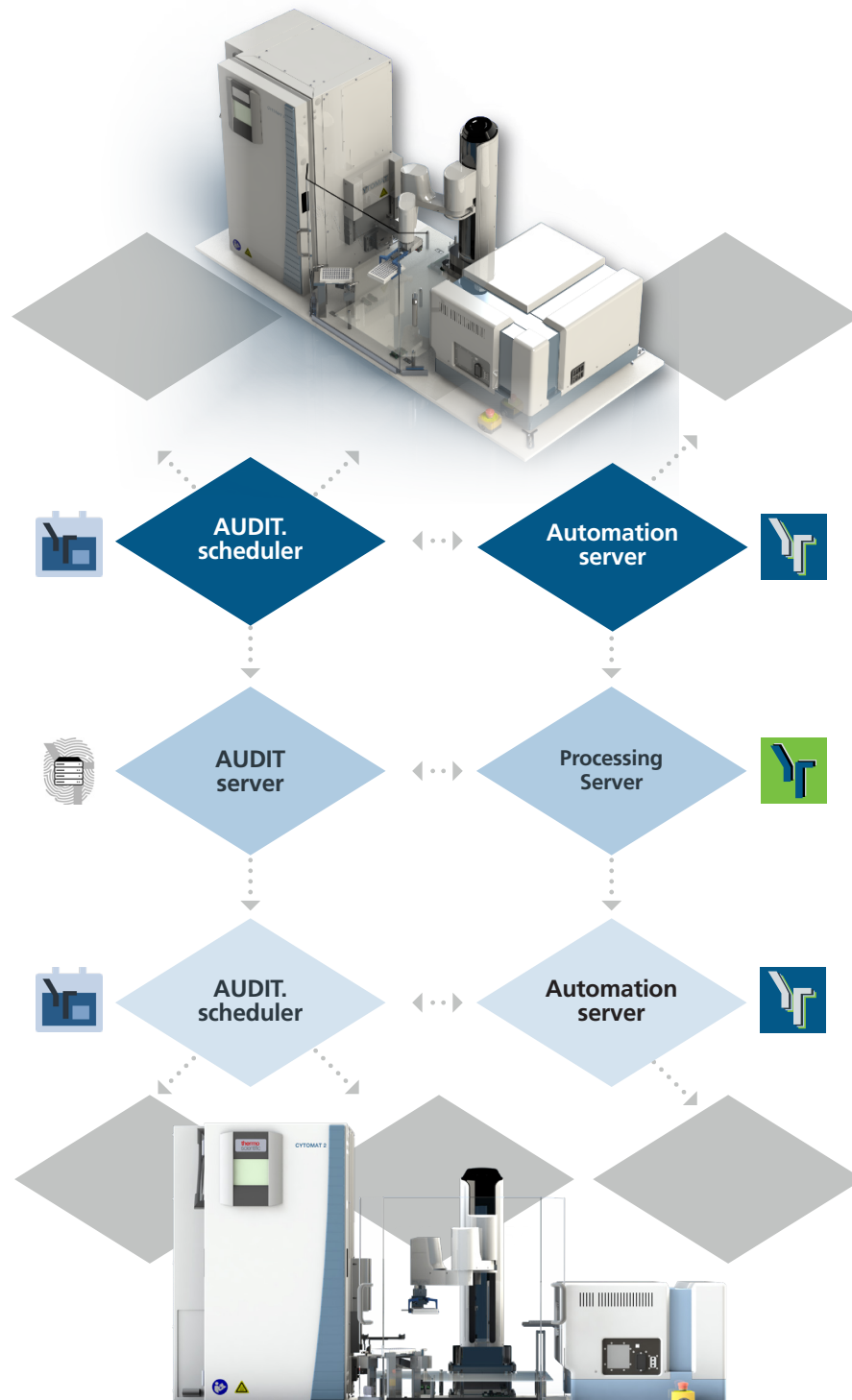
BENEFIT FROM
Full Traceability
Validation procedure
Audit procedure





AUDIT Server

AUDIT Server supports multi-device Audit trailing in Automation including Batch Processing.



This automation scheme shows two SYBOT-1000 automations with CELLAVISTA 4K High End and Cytomat 2-C LiN. All processes including the Batch Processing are audited completely and result in a 21 CFR part 11 compliant imaging processes. Using AUDIT Server enables fully flexible usage of the imaging systems even providing a continuous audit trail even when an experiment is imaged on different imagers at different points in time. This feature can also be applied to third party automation workcells involving multiple imaging systems.



