

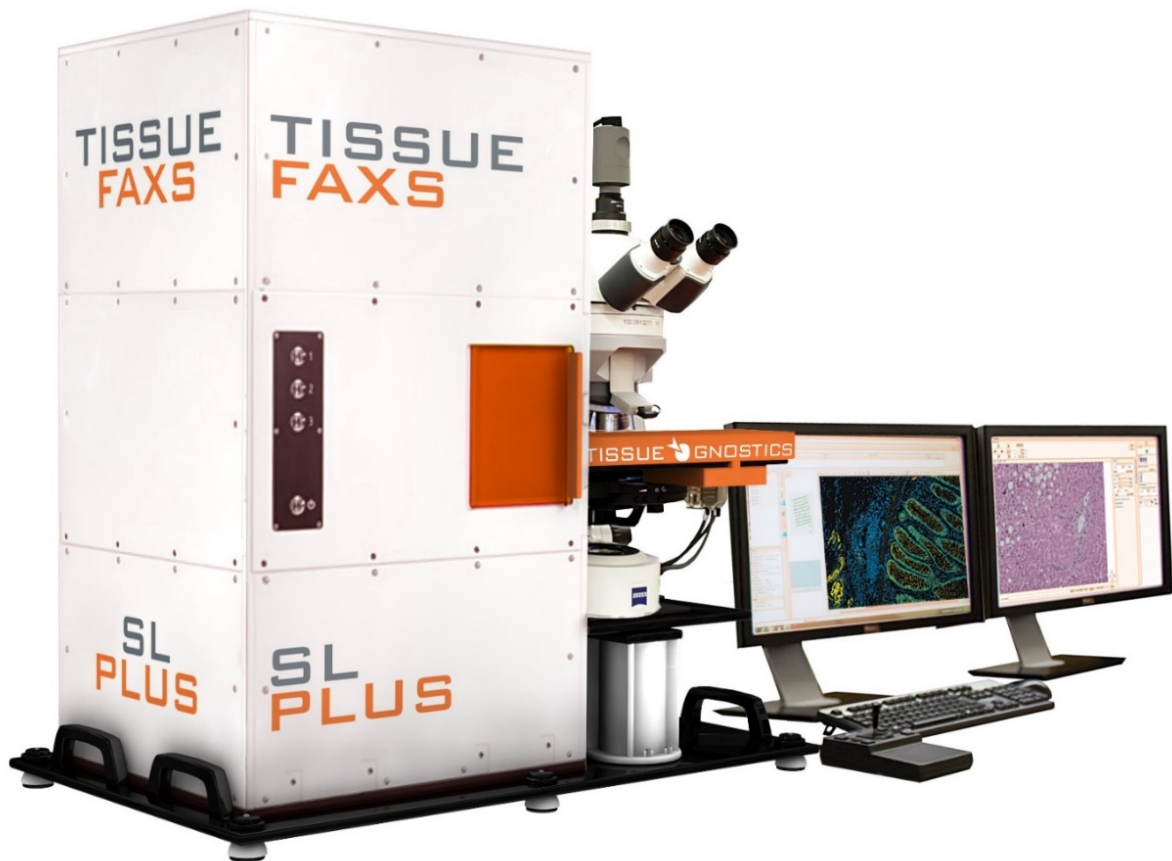
TissueFAXS SL PLUS

Hardware Configuration

Automated Slide Loader

Märzhäuser Slide Express

TissueFAXS SL PLUS is designed to automatically scan up to 120 brightfield and fluorescence slides and TMAs. The application supports up to 4 colors in IHC and 8 fluorescence channels.



TissueFAXS SL is TissueGnostics' solution for automated high throughput scanning.

The TissueFAXS slide loader includes a slide robot, integrated, high-performance scanning stage, holds four slide magazines, and optionally includes a barcode scanner. The slide loader also has a priority loading position to quickly load samples for immediate imaging.

Each slide magazine holds 30 standard slides (76mm x 26mm) and holders for large format slides (76mm x 52mm) are available. Slide magazines hold slides securely and protect them from breakage during transportation and storage.

TissueFAXS SL PLUS is has a small system footprint and can fit on a standard lab bench.

TissueFAXS SL PLUS

Hardware Configuration

Microscope stand:

Zeiss AxioImager.Z2

Upright optical system – for slides stained in immunofluorescence and immunohistochemistry.

Equipped for the analysis of:

- Standard slides
- Chamber Slides
- Paraffine sections
- Cryocut sections
- Biopsies
- Tissue Microarrays (TMA)
- Smears
- Cytospins

Objectives

Motorized Nosepiece

System default objectives include 2.5x, Plan-Apo 10x, Plan-Apo 20x, Plan-Apo 40x.

Additional objectives available upon request

- Up to 7 objectives
- The system is calibrated for each objective, providing for the calculation of sample area and cell count per mm²

Fluorescence

- Motorized Cube Turret, 10 positions for fluorescence applications
- Quadband filter: DAPI, Cy2, Cy3, Cy5
- Quadband filter: Alexa 430, Alexa 514, Alexa 594, Alexa

All filters are hard-coated and pixel-shift free

TissueFAXS SL PLUS

Hardware Configuration

Fluorescence Imaging – High Sensitivity

Hamamatsu ORCA flash 4 V3 for microscopy (16 bit)

The Orca Flash 4 is the default camera solution for TissueFAXS fluorescence imaging. The camera is well suited for:

- Direct immunofluorescence
- Indirect immunofluorescence
- Fluorescence In-Situ Hybridization (FISH)

Color Imaging - High-speed

Pixelink M4 OEM

- 4.2MP Color Camera
- 5.5µm CMOSIS CMV4000 sensor
- 90fps

Illumination

VIS-LED brightfield LED light source

- 4.2MP Color Camera
- 5.5µm CMOSIS CMV4000 sensor
- 90fps

Fluorescence Lighting System

Spectra III – LED Light Engine with 8 colours

Excitation wavelengths :

COLOR	Exc. Filters	Dye Name	Dye Excitation Interval	Dye Emission interval
VIOLET	390/22	DAPI	300 – 410 nm (max 357)	390 – 600 nm (max 457)
BLUE	434/21	Alexa 430	300 – 510 nm (max 434)	480 – 710 nm (max 541)
CYAN	475/34	Cy2, Alexa 488, FITC	425 – 515 nm (max 492)	480 – 580 nm (max 510)
GREEN	555/28	Cy3, PE, Alexa 555, Alexa 568	450 – 580 nm (max 550)	540 – 640 nm (max 570)
YELLOW	585/35	TR, Alexa 594	500 – 630 nm (max 590)	580 – 730 nm (max 617)
RED	640/30	Cy5, APC, Alexa 647	550 – 680 nm (max 650)	625 – 770 nm (max 665)
nIR	730/40	Cy7, Alexa 750	590 – 800 nm (max 749)	725 – 820 nm (max 775)

- Fully integrated light source control
- Liquid-filled optical light guide

Boosts the scanning speed by 40% in comparison with the standard 120PC Q system due to higher switching speed between wavelengths.

TissueFAXS SL PLUS

Hardware Configuration

High-performance PC for microscope control and analysis

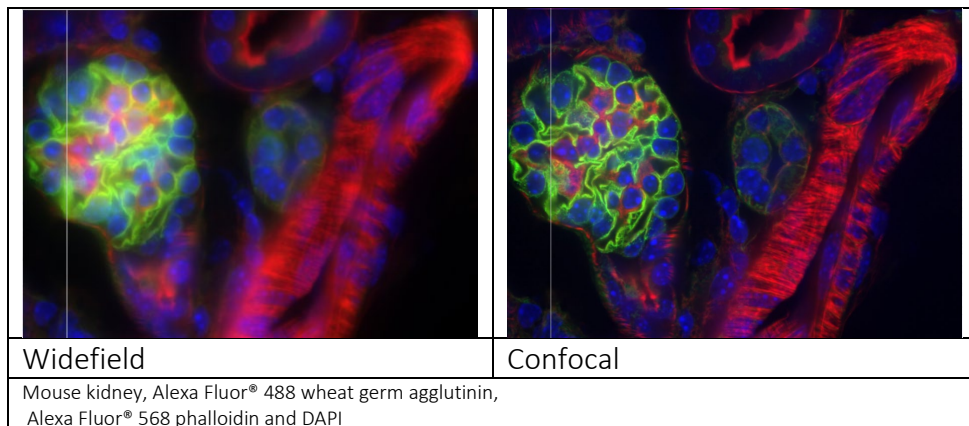
- HP Z4 G4 workstation, incl. Windows 10 Pro 64-bit
- RAM: HP 32GB
- 2 x 2 Terabyte hard disks in RAID system
- 2 TB SSD
- Two Dell 24 inch UltraSharp PremierColor TFT screens



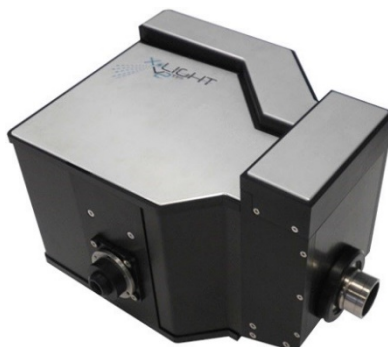
OPTIONAL:

Spinning Disc Confocal with 60 μm pinhole size

The Crest X-Light high speed spinning disk improves image contrast and optical sectioning without limiting system throughput or exposure time. This option improves axial specificity of imaging and enable segmentation and analysis and can be added to any upright or inverted TissueFAXS system



- Large FOV: up to 22mm diagonal
- 15000 RPM
- Motorized
 - 5 position Dichroic wheel
 - 8 position emission wheel
 - widefield bypass
- Multiple disc options available to match any objective
- Robust and accessible



TissueFAXS SL PLUS

Hardware Configuration

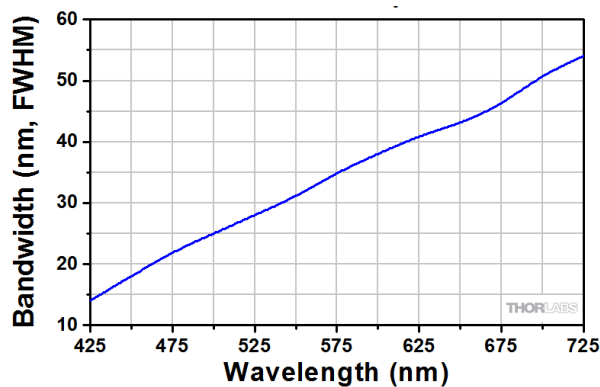


OPTIONAL: Multi-Spectral Imaging Upgrade

Liquid Crystal Tuneable Filter with:



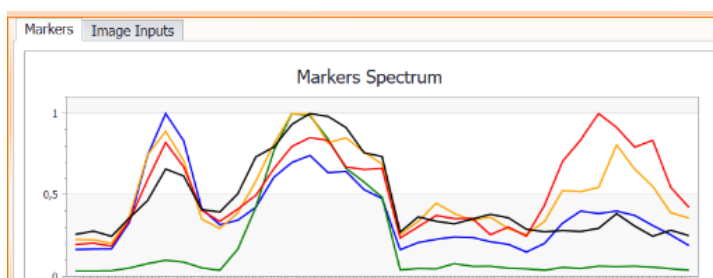
- Spectral range from 420 nm to 730 nm
- Spectral bandwidth (detection interval per single image); 35 nm FWHM* at 550 nm



- Spectral incremental step size: 1 nm
- Switching speed <40 ms
- Tuning Accuracy: \pm FWHM / 10

* FWHM = Full Width at Half Maximum is the width of a spectrum curve measured between those points on the y-axis which are half the maximum amplitude and here describes the “sharpness” of the spectral signal.

TissueFAXS Multi-Spectral *lambda-stack* acquisition mode produces a stack of images for any FOV and focal plane in which each image represents a single spectral band. Spectral unmixing of the *lambda-stack* based upon the spectral signature of each fluorochrome produces precisely separated channels and eliminates autofluorescence.



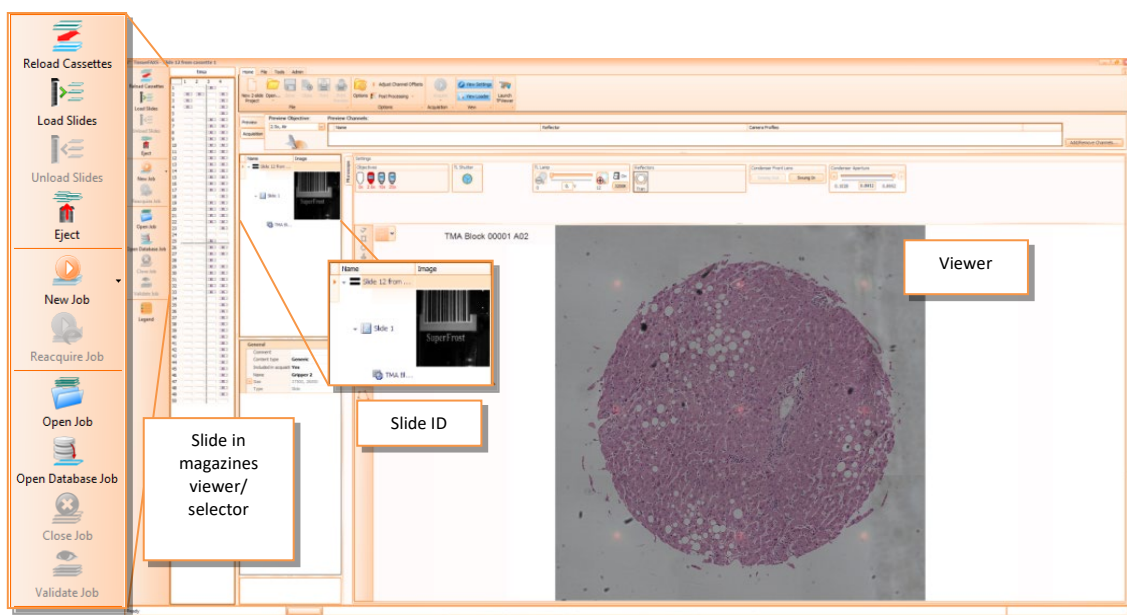
TissueFAXS SL PLUS

Software (acquisition)

TissueFAXS SL PLUS

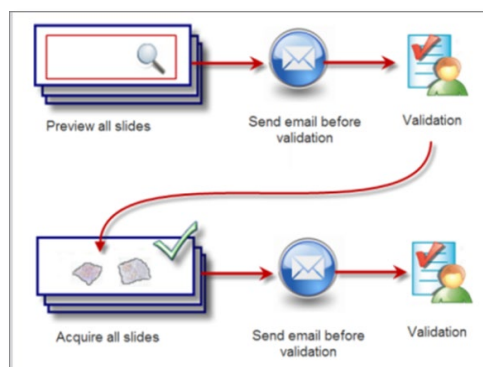
TissueFAXS SL PLUS software automates slide preview and high throughput slide scanning for all TissueGnostics slide loader based systems. TissueFAXS SL PLUS includes the ability to create a queue of “jobs”, each of which define blocks of slides with distinct acquisition parameters or “templates”.

TissueFAX SL PLUS can also be configured with an optional bar code reader to read slide alphanumeric slide labels or barcodes for inclusion into slide names or metadata.



TissueFAXS 120 Main interface, with sample viewer, slide ID display, magazine viewer/slide selector and main toolbar.

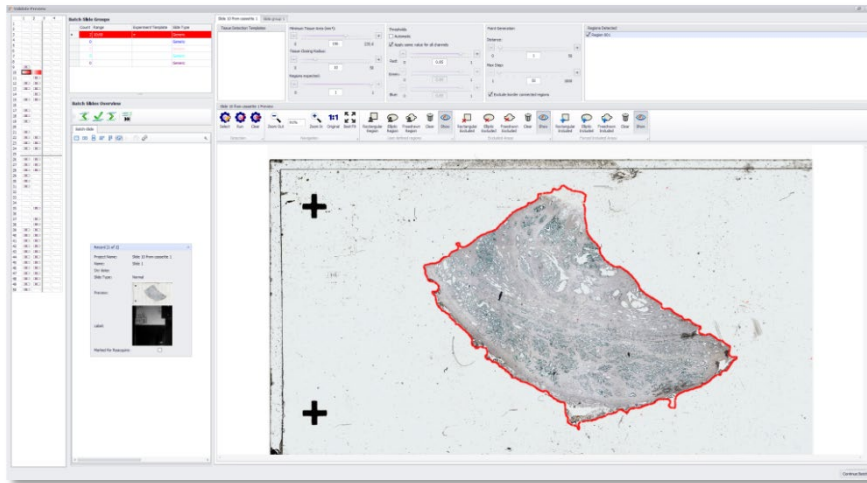
TissueFAXS Scanning software enables users to validate the tissue overviews prior to batch scanning. During validation users can review tissue overview scans to determine whether all tissues sections have been properly identified and to make any necessary corrections before scanning proceeding with scanning.



E-mail notification options are available when major workflow steps are done.

TissueFAXS SL PLUS

Software (acquisition)



Tissue detection validation/correction window.

TissueFAXS SL PLUS Feature list:

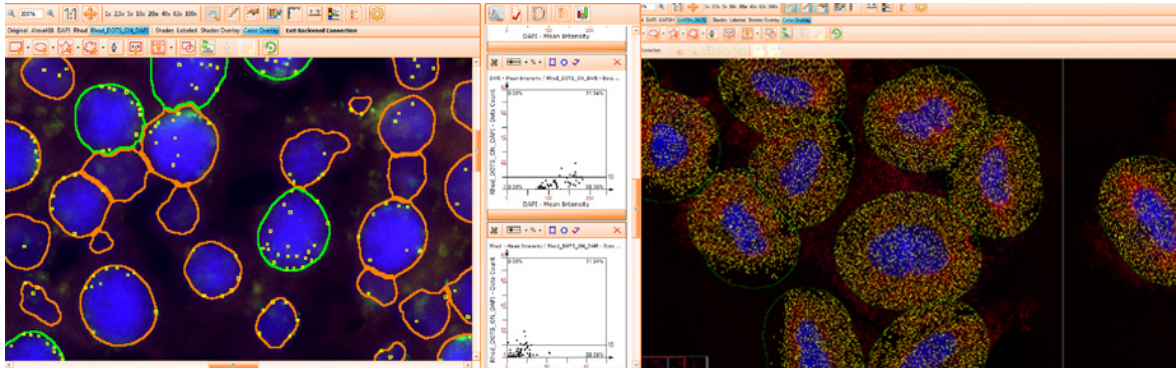
- 2.5x preview Scan for fluorescence and brightfield imaging
- Automatic tissue detection
- Automatic tiling and stitching of digital slide
- User definable acquisition templates and autofocus profiles
- Autofocus profiles adapt automatically to changes in magnification
- Support for air and immersion objectives
- Manual drawing tools for high magnification scan area definition
- Z-Stack acquisition
- Detects and scans TMA slides in brightfield and fluorescence
- Generates and exports user definable composite overviews
- Image viewer for easy display and navigation of digital slides

TissueFAXS SL PLUS

Software (Cytometry)

TissueQuest

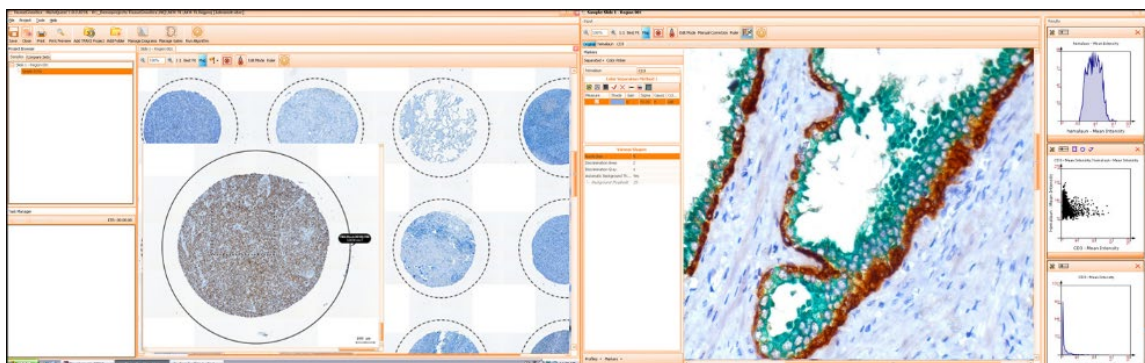
Analysis of single cells in fluorescence



TissueQuest is designed for cytometric analysis of Fluorescence imaging and can be applied to tissues, cultures, and smears. TissueQuest identifies and segments single cells according to nucleus and cytoplasm, and quantifies them across 18 attributes. The application is designed to facilitate the segmentation and quantitation of cellular populations and is intended for fluorescence imaging only.

HistoQuest 6.0

Analysis of single cells in color transmission



HistoQuest is designed for brightfield imaging and the colorimetric analysis of immunohistochemically stained tissue sections. HistoQuest is applied to tissues, cultures, and smears. HistoQuest identifies and segments single cells according to nucleus and cytoplasm, and quantifies them across 18 attributes. The application is designed to facilitate the segmentation and quantitation of cellular populations and is intended for Brightfield imaging only.

Detection

- Single cell Detection of **populations in sections**
- Single cell Detection of **adherent populations in culture**
- Single cell Detection of **dense or confluent populations**

TissueFAXS SL PLUS

Software (Cytometry)

- Segmentation and identification of nuclei, ring structures and cytoplasm

Population Segmentation and Data Display

- Create dynamic plots and histograms across 18 measured attributes
- Assign **gates** and **cut-offs** to any data display
- Define **positive and negative cutoffs** for any population
- Use **reverse gating** to show targeted cell populations in source images
- Project gated sub-populations into detailed single cell **subpopulation analysis**
- Use **forward gating** of image data shows cells as they occur in scattergrams
- Visualize “Dots per Cell” in multiple color channels
- Propagate analytical protocols to within and between projects

Measurement

- Option to analyze within ROIs for **analysis of virtual slides**
- Single cell - **nuclear and cytoplasmic measurements across 18 parameters**
- Characteristic chromogen-mediated cellular staining patterns
- Cell counts – cells/area as read-out% of negative/positive cells
- “total stained area” per sample or region of interest

Measurement (Continued)

- Analyze of **nuclear and cytoplasmic coexpression** (dots, etc.)
- Structural quantitation of
 - Nuclei
 - Cytoplasmic
 - **Dots** (RNA)
 - Globular stains (**FISH analysis**)

Data Export

- **Export statistic and raw data to MS Excel**
- Automatically **create PDF analysis reports**
- Image and plot clipboard **copy/paste to other applications**

Licensure

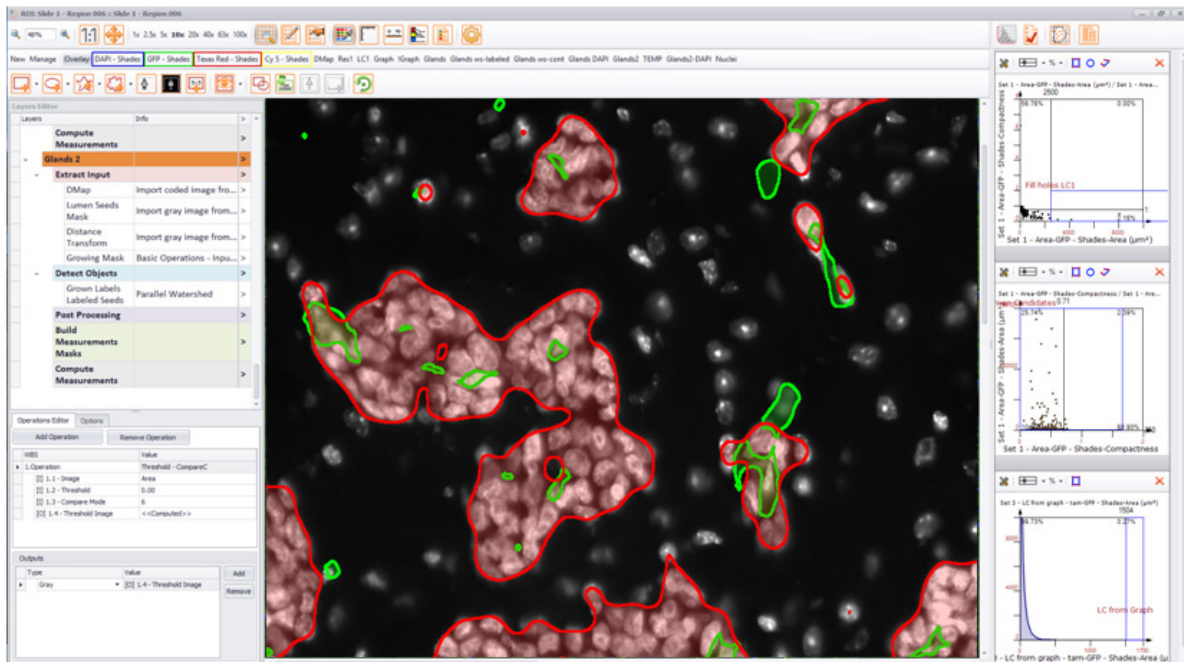
- Single-site license

TissueFAXS SL PLUS

Support, Maintenance and Upgrades

StrataQuest PLUS –

Biomedical Image Analysis and Application Development



StrataQuest PLUS is TissueGnostics 6th generation of image analysis software for multi-layer biomedical image analysis.

The StrataQuest **CORE** image processing engine is a stack of virtual image layers built from the original scanned image. Each successive virtual layer is *driven* by an algorithm or set of algorithms and provides specific segmentation or analytical features useful to accomplish the overall analytical goal.

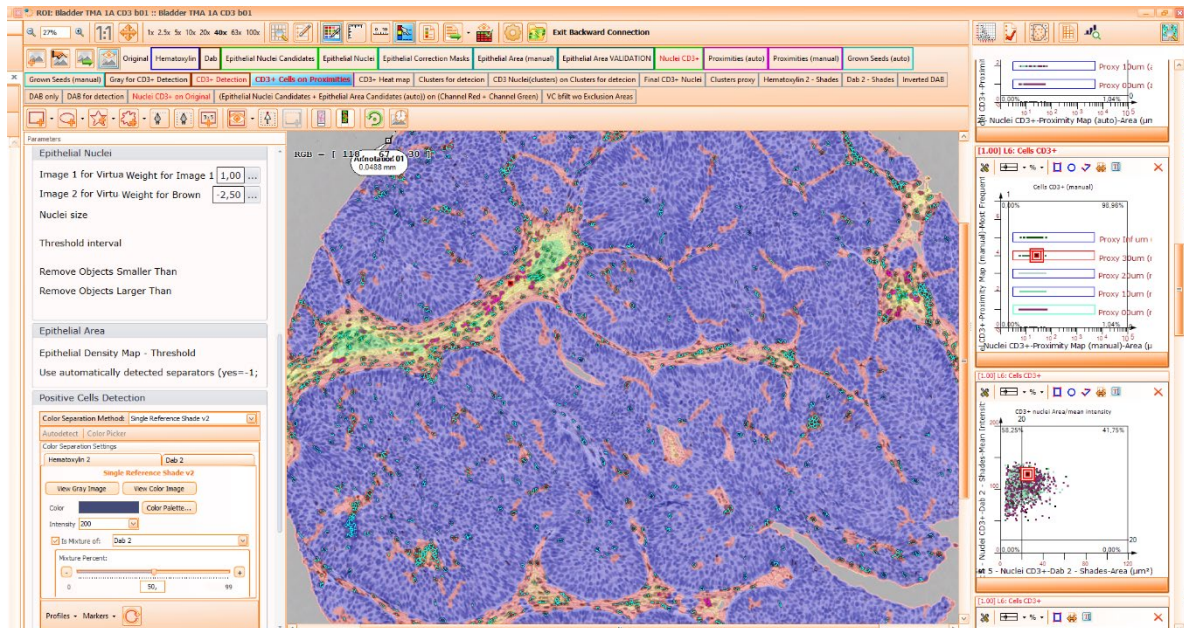
A StrataQuest solution is generated when layers are combined to achieve the desired analytic goal. Once completed, the solution can be saved and distributed for use by other StrataQuest users.

StrataQuest supports both fluorescence and brightfield immunohistochemistry image analysis as well as an unlimited number of acquired channels and computed virtual channels. StrataQuest software is unique in its approach toward morphological analysis that combines the features of population segmentation and gates and cutoffs common to flow cytometry analysis.

As a development tool for research laboratories and core facilities StrataQuest is a powerful resource for applications development that can be used to create easily distributed image processing applications that can be run within StrataQuest or in the stand-alone StrataQuest engine as a static application.

TissueFAXS SL PLUS

Support, Maintenance and Upgrades



StrataQuest PLUS Features

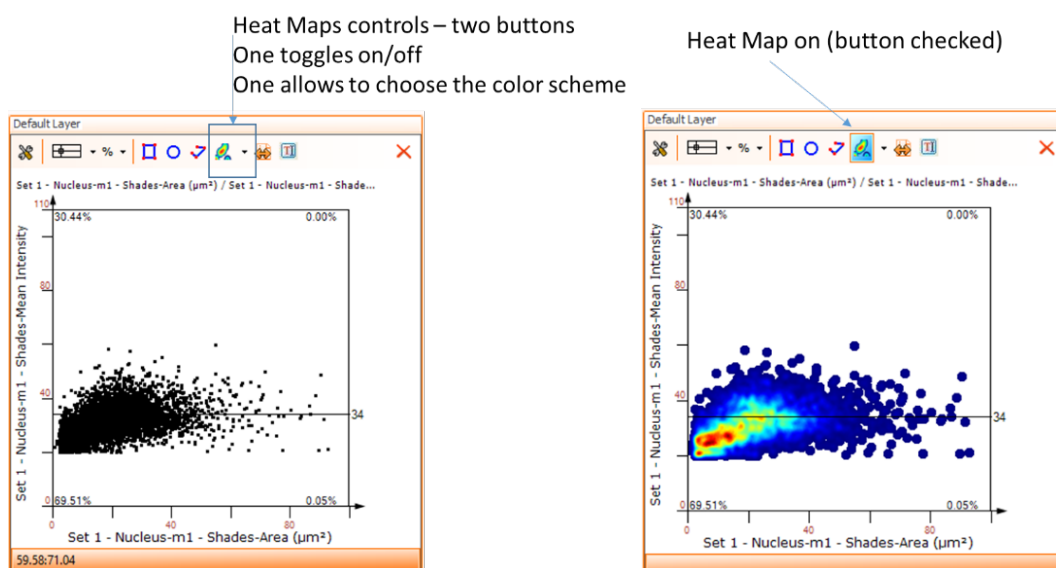
- Unlimited number of detection algorithms run simultaneously (i.e. for dot-like objects, nuclei, cytoplasm, membrane, whole cells, fat cells, small clusters like tumor budding, blood vessels, epithelial structures, or even more complex structures like glomeruli)
- High definition of contour detail even for large structures by running at original pixel resolution (no downscaling), e.g. for the correct detection of thin stromal areas even within dense tumor centers
- Multi-layer visualization tools for overlaying and highlighting any combination of original images, artificially enhanced channels, processing masks, automatically detected contours and manual correction input with customizable contours (color, line, transparency)
- Manual correction of detection results is done on defined layers and can be reapplied on all subsequent analysis runs.
- New measurements like intercellular distance or distances between cells and tissue structures provide new measurement possibilities on both cellular and higher tissue structure level.
- Tools for detection of small objects as little as 1-2 pixels

TissueFAXS SL PLUS

Support, Maintenance and Upgrades

StrataQuest PLUS 6.0 – New Features

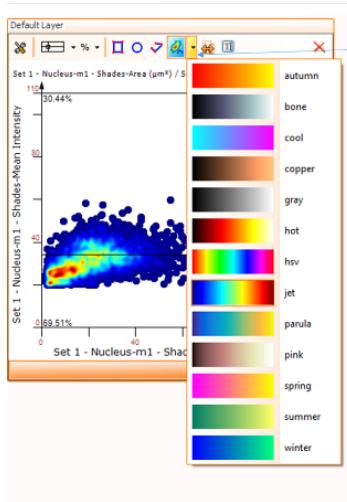
- Tools for detection of large structures as big as the entire digital slide, segmenting each object and merging its fragments that may be in different image tiles
- Fast analysis due to multi-threading analysis engines taking advantage of modern multi-core processors
- New containment-type measurements like number of positive cells within each of the selected glands/structures
- New relational-type measurements like distance from each cells to nearest blood vessel or distance of each immune cell to nearest tumor structure
- Normalization features based on integration of both directly measured parameters as well as calculated ones
- New statistic data types extracted from manual or automatically detected Regions of Interest
- Improved automation through analysis profile reuse
- Multi-profile capabilities allowing analyzing digital slides with different staining protocols in the same analysis project (i.e. patient based projects, where each patient has several slides stained with different markers)
- NEW Heat-Map diagrams :



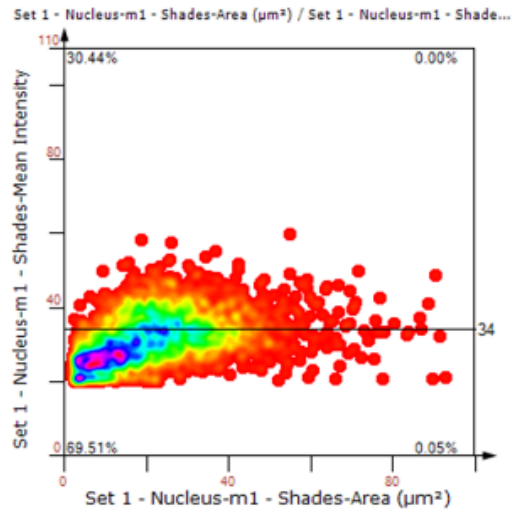
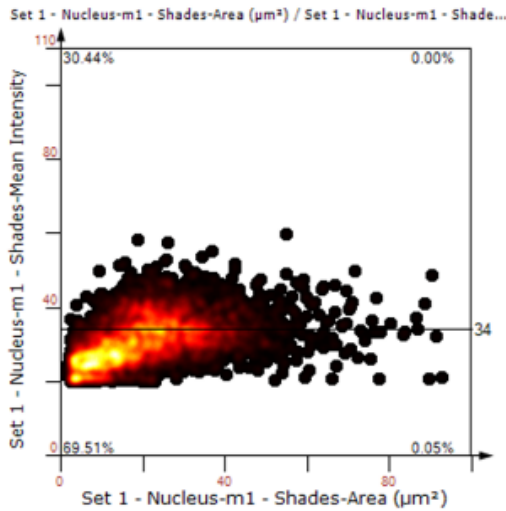
TissueFAXS SL PLUS

Support, Maintenance and Upgrades

- NEW Heat-Map diagrams (Continued)



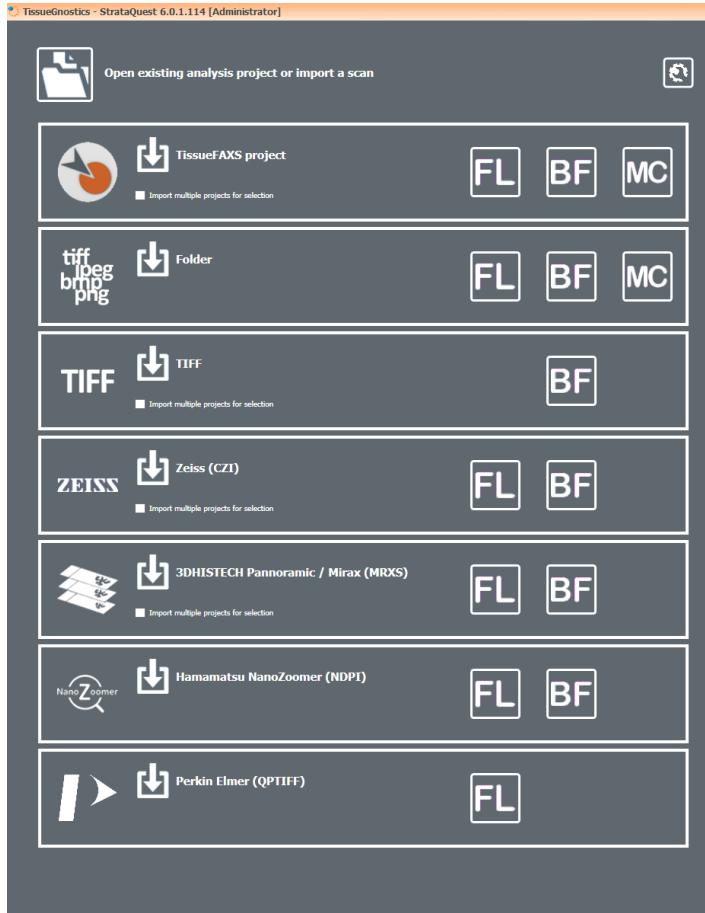
Heat Map options
Color scheme is per scattergram
Default is "jet" as in this image.
Color schemes are standard from Matlab



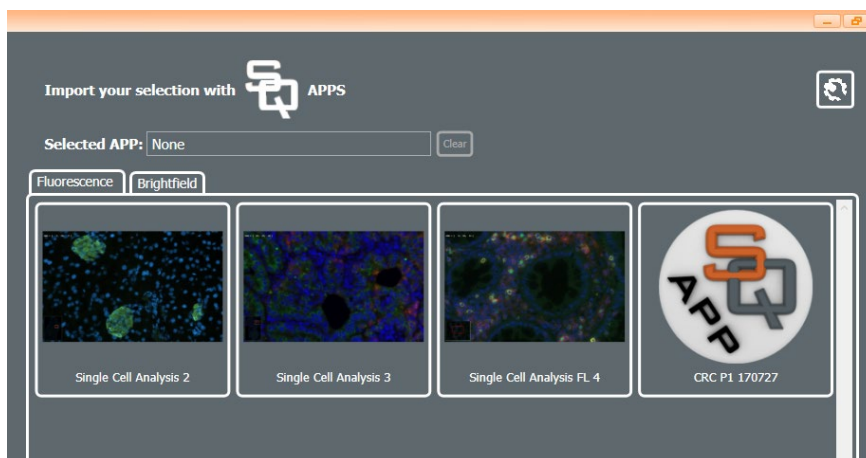
TissueFAXS SL PLUS

Support, Maintenance and Upgrades

- NEW file import wizard at application launch:



- NEW Built-in and user-defined groups with SQ Apps



TissueFAXS SL PLUS

Support, Maintenance and Upgrades

StrataQuest FLUO

Fluorescence only analysis configuration of StrataQuest limited to the analysis of immunofluorescent markers and their morphology.

This configuration of StrataQuest contains analysis features comparable to the current TissueQuest versions, as well as a set of predefined multilayer analysis macros enabling the user to quickly develop new solutions for many analysis tasks.

Upgrading to higher versions and solutions: StrataQuest FLUO can be upgraded to StrataQuest PLUS to allow the creation or addition of any immunofluorescent or immunohistochemical analytical solution

StrataQuest HISTO

Color Brightfield only analysis configuration of StrataQuest limited to the analysis of immunohistochemical markers and their morphology.

This configuration of StrataQuest contains analysis features comparable to the current HistoQuest versions, as well as a set of predefined multilayer analysis macros enabling the user to quickly develop new solutions for many analysis tasks.

Upgrading to higher versions and solutions: StrataQuest HISTO can be upgraded to StrataQuest PLUS to allow the creation or addition of any immunofluorescent or immunohistochemical analytical solution

StrataQuest PLUS

StrataQuest PLUS supports the analysis of both images of immunohistochemical and immunofluorescent markers.

It contains analysis features comparable to the current TissueQuest and HistoQuest versions, as well as a set of predefined multilayer analysis macros enabling the user to flexibly develop solutions for many different analysis tasks.

Any solution for immunofluorescent or immunohistochemical marker analysis can be added to StrataQuest PLUS.

StrataQuest SOLUTIONS

StrataQuest SOLUTIONS contains the **CORE** engine necessary to run stand-alone StrataQuest solutions developed by other users. The application will run pre-defined Apps only and cannot be used to develop new applications for distribution. It comes preconfigured with one StrataQuest solution from the solutions library.



TissueFAXS SL PLUS

Support, Maintenance and Upgrades

StrataQuest SOLUTIONS (Continued)

More solutions can be added to the StrataQuest **CORE**

StrataQuest SOLUTIONS comes in three price levels (SOL-I to SOL-IV) according to the complexity of the solution that is envisaged. Solutions more complex than SOL-III are priced individually after assessment by the TissueGnostics sales and development teams

Upgrading to higher versions and solutions: StrataQuest SOLUTIONS can be upgraded to any other SQ version. Any solution for immunofluorescent or immunohistochemical marker analysis can be added.

TissueFAXS SL PLUS

Support, Maintenance and Upgrades

Yearly Support

TissueGnostics' team of experts will answer your application questions. Your regional TissueGnostics representative is your first contact for all issues, and depending upon the nature of your request your local support representative may choose to connect you with TissueGnostics remote support. The Tissue Gnostics remote support team is generally available between 3AM and 8PM EST.

Yearly support contracts include 12 hours of remote support per year. Additional hours can be added into the contract upon request for a regular rate per hour.

Annual Maintenance

Maintenance of the microscope hardware and the PC:

- Disassembly and cleaning of components
- Optical paths cleaned of dust
- Removal of glass splinters
- Check of coated glass surfaces (damaged elements can be exchanged at cost)
- Check of function and cleaning of visual tube
- Check of cameras, cleaning of chips, Cleaning and alignment of the C-mount adapter, check of motorized functions
- Check of the complete lighting system for function and adjustment, replacement of illuminants as necessary (at cost)
- Check of light guide and replacement if necessary (at cost)
- Check and cleaning of filter blocks, scanning stage, and insert
- Check of all connectors and cables and replacement as necessary at cost, dust removal
- Check of cables, slots and ventilators for good connection and function
- Replacement of damaged components as necessary at cost
- Defragmentation of hard disks

TissueFAXS SL PLUS

Support, Maintenance and Upgrades

Annual Maintenance (Continued)

Service and recalibration of the TissueFAXS PLUS system

- Adjustment of objective parfocality.
- Calibration of field of view for all cameras and all objectives.
- Adjustment of scanning stage.
- Check of objective alignment and final check of aligned system.

Yearly upgrades

The yearly upgrade service for TissueFAXS PLUS consists of at least one performance enhancement (=new features) of the software packages for each calendar year, and will include version upgrades when they occur. Bug fixes/patches are free of charge.