Applied Spectral Imaging

Bringing Details to Light

GenASIs HyperSpectral

HyperSpectral Imaging Solutions for Biomedical Applications

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Diagnosis Made Simple

www.spectral-imaging.com

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GenASIs Platforms

Designed to Meet the Requirements of Any Laboratory - Large and Small

ASI's scalable and modular platform can grow to meet your future laboratory needs. As your caseload increases, so can your lab by upgrading your single slide workstations to 9-slide or 81-slide scanning stations, additional workstations, dedicated servers, and modular LIS/LIMS connection to automate your workflow. GenASIs platforms allow you to process more cases, quicker and with better clinical results.

GenASIs Capture & Analysis platform is a high-end computer aided diagnostic system with multiple assay support. This versatile solution may be adapted to a plurality of pathology, cytogenetics and research applications. The system is designed to work with a manual or automated microscope and includes a dedicated, high powered microscope camera combined with state-of-the-art image analysis software for clinical and research oriented image analysis.

GenASIs Scan & Analysis platform is a top-of-the-line, automated computer aided slide scanning diagnostic platform. This modular platform enables automation of a wide range of laboratory selected slide-based assays for various applications. This flexible solution may be adapted to the advanced automation and workflow needs of any laboratory or research institution. The system includes a fully automated, computer-controlled microscope, motorized 9-slide stage and a high powered microscope-camera. This platform also comes with a variety of additional components, such as an oil dispenser, automated fluorescent illumination control and state-of-the-art image analysis software for clinical and research oriented image analysis and automation.

High Throughput Scanning platform is a robotic slide loading system, enabling high-throughput automated slide analysis for a wide range of applications. This platform, combined with the GenASIs Scan & Analysis platform, provides a true "walk-away" functionality, scanning up to 81 slides consecutively, without human intervention. Moreover, slides can be replaced while the system is scanning. These scanning capabilities, presented with the GenASIs High Throughput platform, offer the most efficient and cost-effective way to optimally use the scanning and analysis system for uninterrupted scanning.

GenASIs Analysis & Review platform is an advanced analysis platform with full case review capability. This versatile platform supports the analysis and review of a wide range of pathology, cytogenetic and research applications. The platform allows users to review, analyze, sign-out and generate reports for case data, captured using the GenASIs Scan & Analysis and Capture & Analysis platforms. Case data may be accessed from any network location.

GenASIs HyperSpectral platform is based on a cutting-edge, dual-mode optical device, which allows both interferometer-based image capture for hyperspectral imaging and direct view mode for high-resolution CCD image capture. The HyperSpectral data reveals the spectrum of every pixel in the image, and provides advanced analysis tools to extract quantitative and hidden information from within a sample. In Direct View mode, the system records image details under extremely low intensities and provides a finely detailed high-resolution and high-definition image.

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GenASIs HyperSpectral

Insights Into the Molecular and Structural Content of Images

Spectral imaging represents an enabling technology for a spectrum of applications in biomedical imaging and remote sensing. In all of the applications, the foundation technology remains virtually identical, thereby providing tremendous technology leverage.

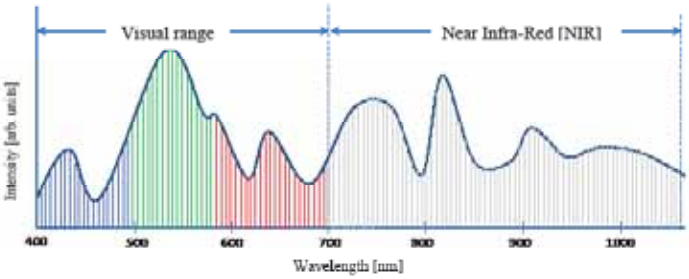
Spectral Imaging describes image acquisition and analysis method which combines spectroscopy, multi-dimensional imaging and computing to delineate the way light reacts with a sample in order to quantify and analyze information that might otherwise be hidden. The underlying principle is the simultaneous measurement of the detailed spectrum of every point of a given area (surface), or more specifically, of each pixel of a given CCD array. Spectral Imaging can be used to obtain fluorescence or brightfield spectra, such as absorption, transmission, or reflection.

The spectral image allows you to precisely locate chemical constituents providing unique and unparalleled insights into the molecular origin, formulation and phase of the observed living entity.

GenASI's HyperSpectral platform is considered an extensive enhancement of the famous Fourier Transform Infrared Spectroscopy (FTIR). While FTIR measures a single IR spectrum by using an interferometer, the GenASIs HyperSpectral platform uses the same principle to simultaneously measure many spectra, one for each point in the image, in the visual and low-near infrared (NIR) range. The system can be attached to a microscope, telescope, lens or any other fore optics.

The sensitivity range of the spectral image measurement follows the sensitivity of the camera CCD and allows measurements between 400 and 1000 nm, thus covering the whole visible range as well as low near infrared range of electromagnetic radiation. A maximum spectral resolution, comparable with ~3 nm at short wavelengths and increasing to ~20 nm towards the near infrared range, is achieved.

GenASIs HyperSpectral



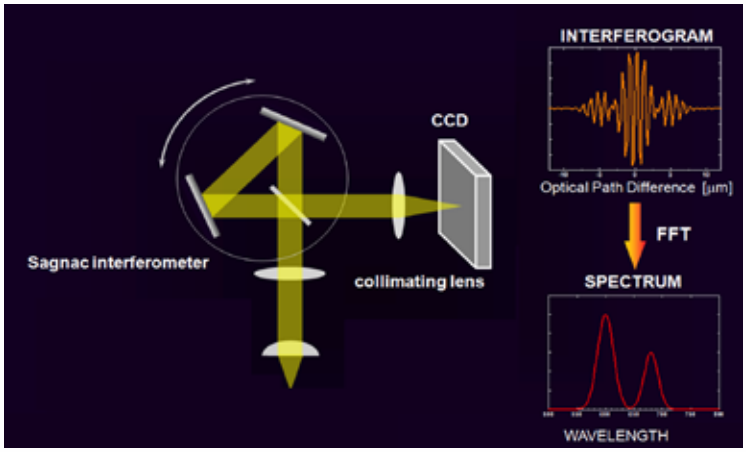
All the information in a single scan

GenASIs HyperSpectral

Insights Into the Molecular and Structural Content of Images

The unique design of GenASIs HyperSpectral platform with SpectraView allows the simultaneous processing of the entire input image without the need for sequential spatial or wavelength scanning of the sample or the sample illumination.

The core of the HyperSpectral platform is a common path Sagnac interferometer, mounted on a rotatable disk, to which a CCD camera is coupled. The light beam which enters the triangular interferometer, is split into two beams (a transmitted and a reflected beam), which travel in opposite directions, but in the same path in space (common-path interferometer). They reach the CCD with controlled Optical Path Difference (OPD) and form an interference pattern that is affected by the spectral content of each point in the image. A sequence of images is captured, each with different OPD, to form an interferogram at each pixel. A Fourier-analysis methodology is applied to extract the hyperspectral image of the sample.



Optical Design and Analysis Flow

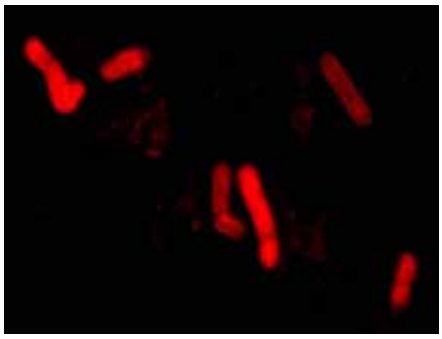
GenASIs SpectraView running under the GenASIs HyperSpectral platform, harnesses the way light reacts with a sample to quantify and analyze information that might otherwise be hidden.

ASI's GenASIs SpectraView enhances your capabilities when analyzing samples enabling :

- Imaging a spectral range twice as wide as the visual range, revealing hidden information
- Un-mixing multiple colors, resolving co-localized image components
- Removing background signals, in bright field or auto-fluorescence, and enhancing cluttered signals

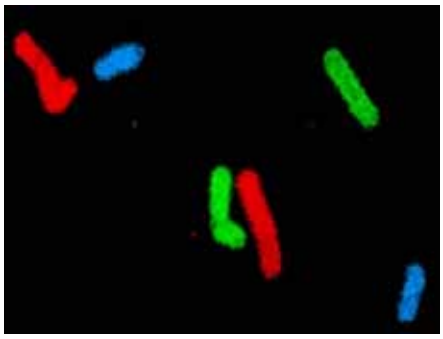
This system allows the user to investigate samples and identify the true physical and component characteristics.

One can distinguish between different materials even if they look identical by conventional imaging tools. On the left, one cannot differentiate between the chromosomes based on color only, as they are all dyed red. In the image on the right, the three dyes are classified by GenASIs SpectraView and then displayed in unique colors. The software reveals crucial information that cannot be detected without hyperspectral imaging.



Color Image as it looks to the human eye

Three types of red dyes were used to stain these chromosomes



Color image after GenASIs SpectraView

With the GenASIs HyperSpectral, each dye is displayed as a unique color

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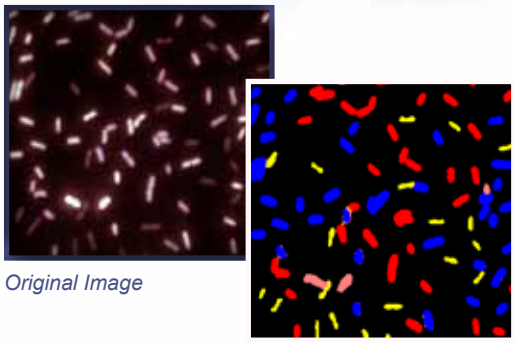
GenASIs SpectraView Capabilities

Addressing the Needs in Microscopy and Cell Biology

Differentiate

Uncover chemically similar areas hidden to the eye. Create color-coded maps of chemical similarities and differences. Compare the chemical makeup of components between different images.

Choose a region with the qualities you want to analyze, GenASIs SpectraView automatically finds all the other similar regions in the image



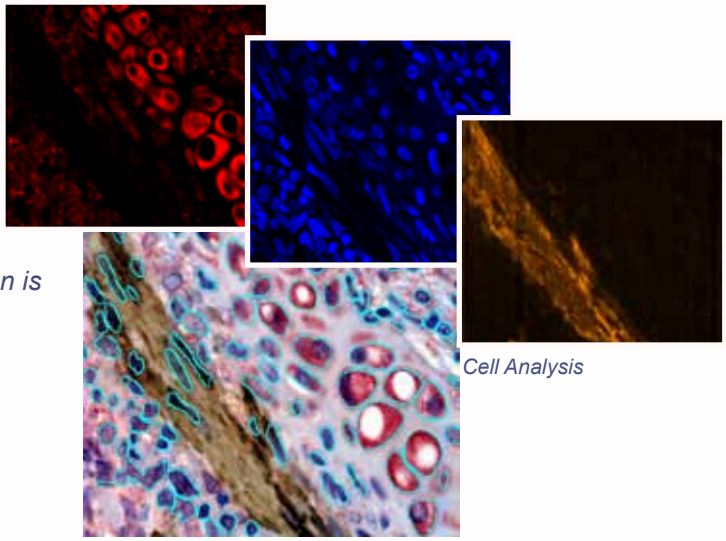
Original Image

Classified Image

Separate

Separate spectral components to view them as individual image layers.
Automatically detect objects and classify them based on quantitative morphological and spectral content.

Each layer is displayed as a separate image so no information is obscured

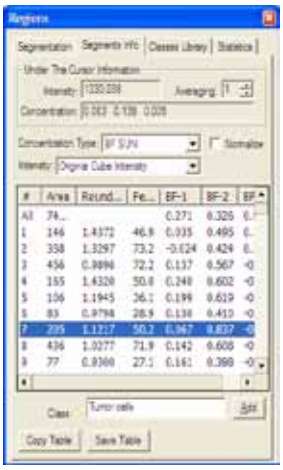


Cell Analysis

Quantify

Un-mix spectral components and remove background, providing accurate, quantitative, spectral content at each pixel.

Extract information from the selected regions to quantify dye concentration, intensity, size and shape



Region Quantification

Document

Enhance images automatically with brightness and contrast tools and provide customized reports, including images and notes. Connect with ASI's Advanced Data Manager System, Case Data Manager, and export the information in common spreadsheet formats.

Case Data Manager - CDM

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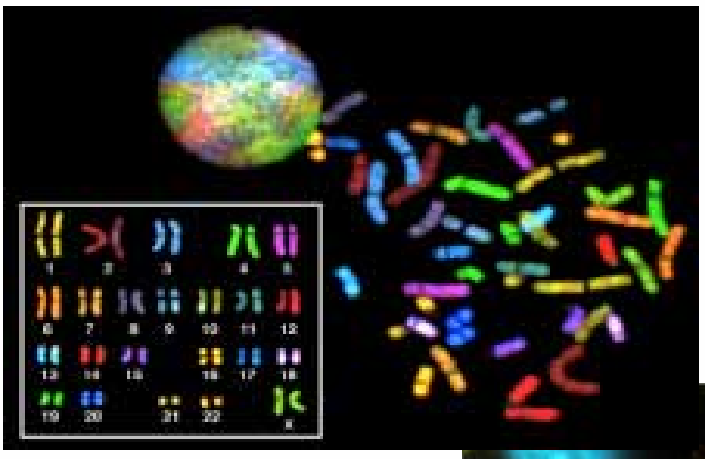
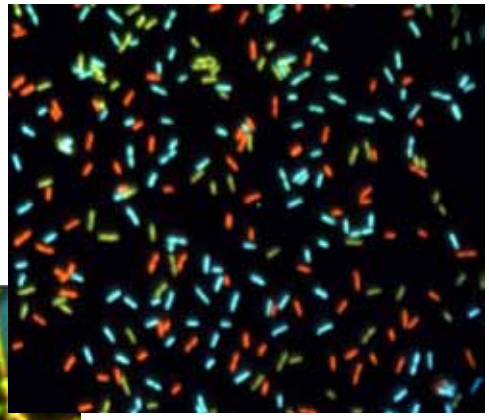
GenASIs SpectraView Specifications

Addressing the Needs in Microscopy and Cell Biology

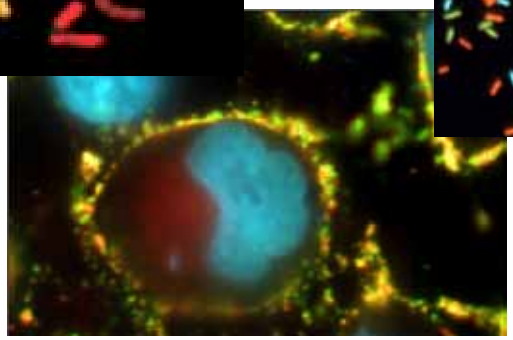
- Spectral range: 400-1000 nm, covering the entire visual range and the low NIR range
- User defined spectral resolution is 6 nm at 400 nm, with capability for improved spectral resolution up to 3nm with the high resolution setup option
- Dual mode enables both hyperspectral capture and regular monochromatic imaging on the same system
- The system maintains the polarization of the measured light
- Transmission efficiency is higher than 80% for the entire visual spectral range, making GenASIs SpectraView suitable for fluorescence and other faint applications
- 16 bit spectral data per pixel
- Simultaneous measurement of all wavelengths with full image alignment between layers
- Compatible with both cooled (-20 degrees Celsius) as well as non-cooled 12 bit digital cameras (1.3M pixels, ~70% peak Quantum Efficiency)
- Advanced database for research and clinical applications



Spectral Karyotyping 24-Color



Bacteria Multiplexing



Drug Discovery - Liposomes

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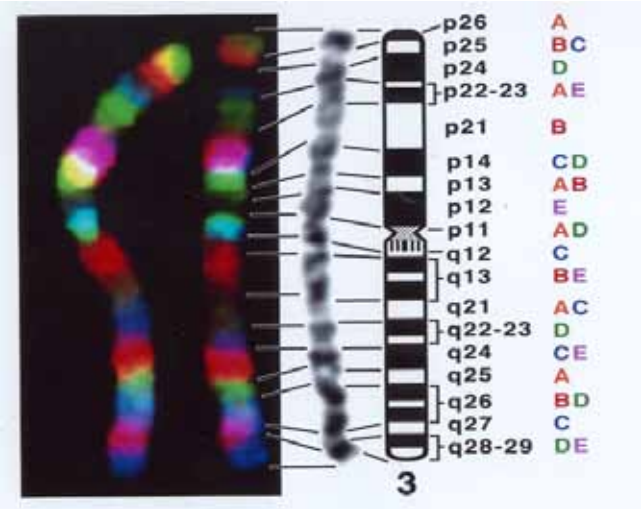
GenASIs SpectraView for Spectral Karyotyping

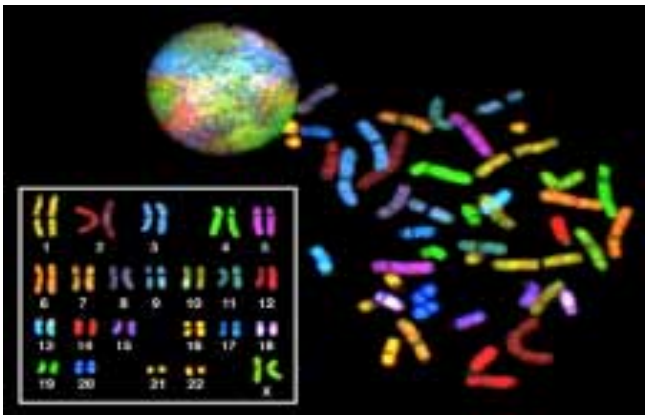
Spectral Karyotyping - SKY

Utilizing its high spectral resolution, the GenASIs HyperSpectral platform detects and identifies a plurality of colors simultaneously. Spectral Karyotyping (SKY) is an example, in which each of the 24 chromosomes is identified based on a unique color combination. The GenASIs HyperSpectral System HiSKY is widely used in cancer research and in pre- and post-natal analysis.

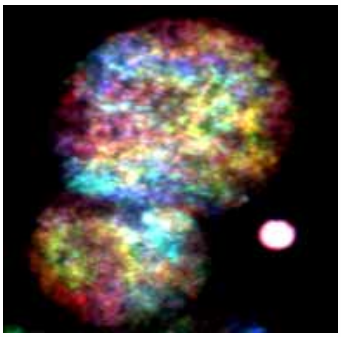


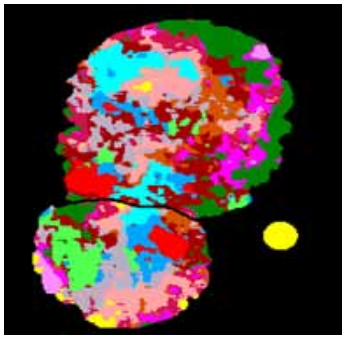
Color Banding *G-Banding* *Dye Combination*

N. Kakazu, T.Abe (2006)
Multicolor banding technique, spectral color banding (SCAN): new development and applications.
Cytogenetic and Genome Research 114 : 250-256



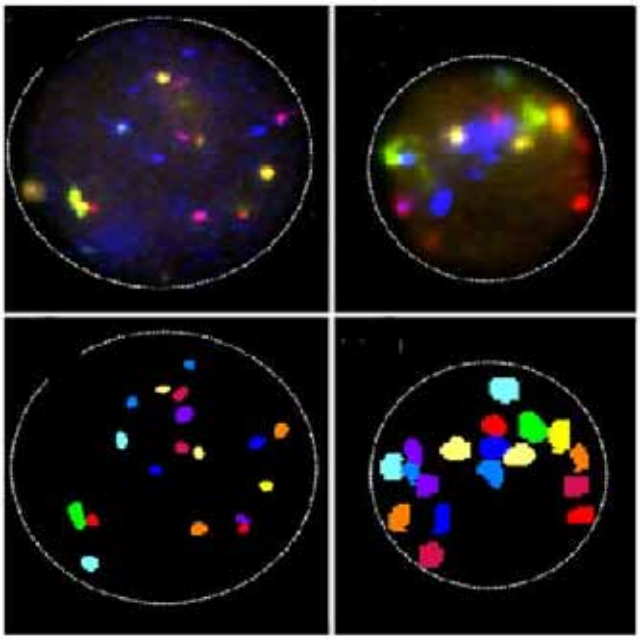
24-color HiSKY combination





Micronuclei Analysis by HiSKY

Courtesy of C. Jackson-Cook and N. Tszine Virginia Commonwealth Univ.



Multilocus Genetic Analysis - 10 and 11 Probe Interphase FISH

J. Fung, H.-U.G. Weier, J.D. Goldberg, R.A. Pedersen (2000)
Multilocus genetic analysis of single interphase cells by spectral imaging. Hum Genet. 107: 615-622.

GenASIs SpectraView for Pathology

Spectral Un-mixing with Fluorescence and Bright Field for Cell Identification

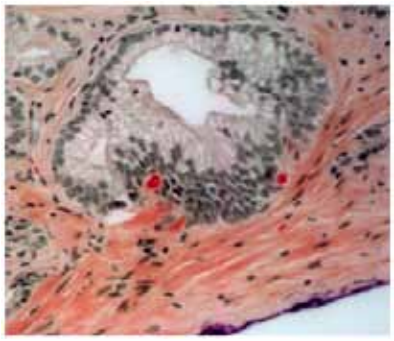
The detailed spectral information enables performing accurate spectral un-mixing, extracting a set of images corresponding to the pure colors from which an image is constructed. The physical meaning of this operation varies between fluorescence and brightfield.

In fluorescence each un-mixed pure image corresponds to any of the following:

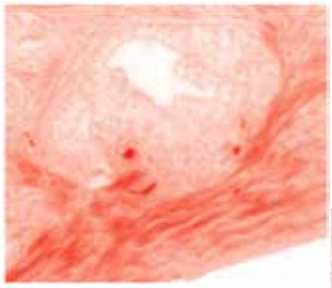
- A single dye that is included in the sample
- An auto-fluorescence image
- Unwanted background that is caused either by residual of specific dyes or by auto-fluorescence

As a result of the un-mixing operation, each dye can be viewed independently and any auto-fluorescent material or background can be removed.

In brightfield, un-mixing is performed in order to extract pure images of each of the absorbing chromophores included in the sample. These chromophores may originate in the sample itself (e.g. Melanin) or can be added to the sample in order to improve differential visualization of entities (e.g. Hematoxylin, Eosin, DAB etc.)

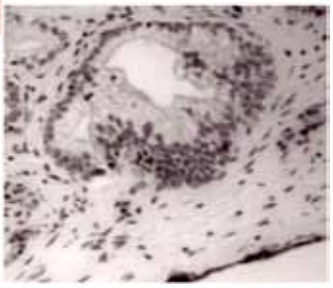


Original Image

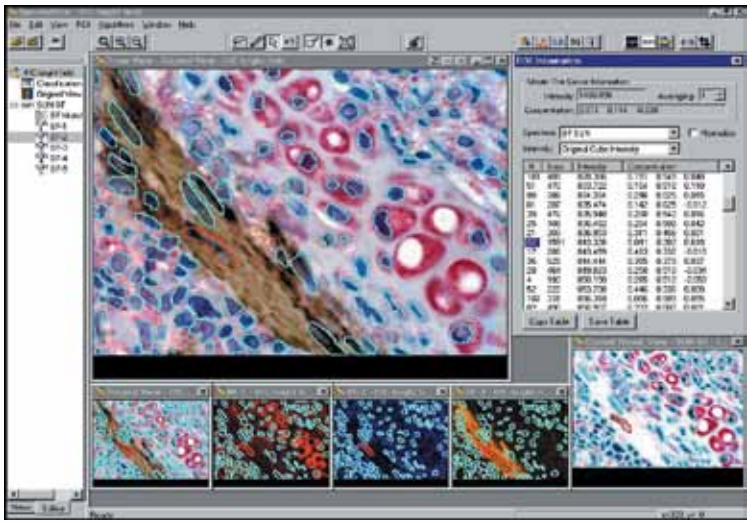


Eosin Layer

H & E stained prostate tissue
GenASIs SpectraView separates to two pure images, of Hematoxylin and Eosin content, enabling quantitative analysis



Hematoxylin Layer



Three-color separation in brightfield

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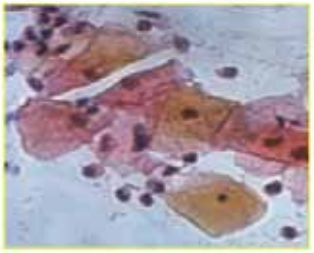
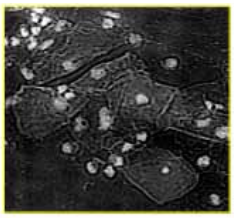
GenASIs SpectraView for Pathology

Spectral Un-mixing in Bright Field and Cell Identification

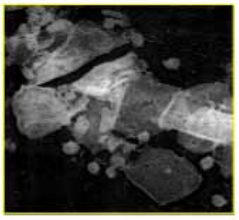
Pap-Smear Analysis

Quantitative analysis of Pap-stained slides. The image of the smeared cells is measured in bright field. Each component of the Pap-stained slide has a different spectrum. These spectra are used to identify the different entities. SUN algorithm is used for the analysis.



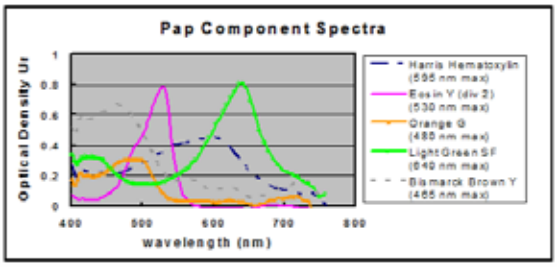


Hematoxylin



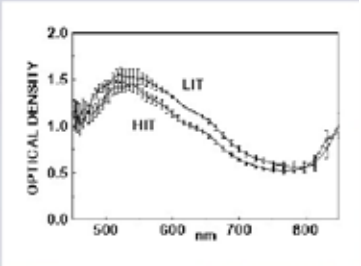
Eosin Y

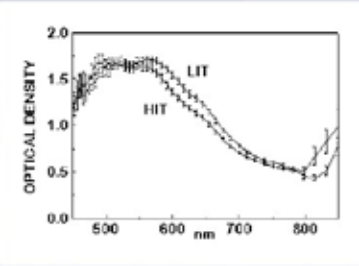
Orange G

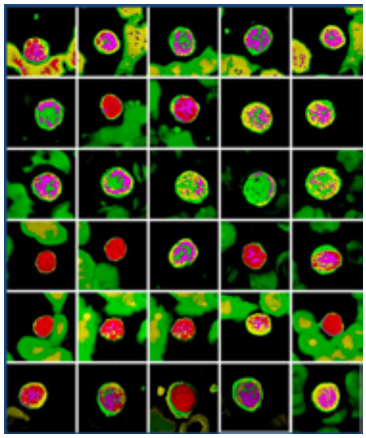


Chronic Lymphatic Leukemia (CLL)

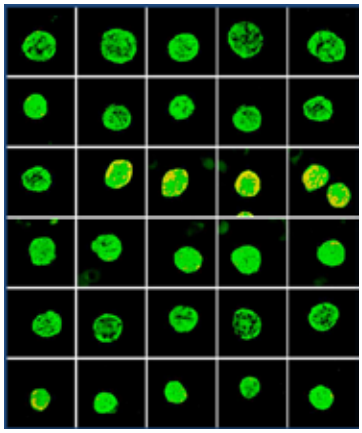
Normal and CLL cells have different spectral signatures. These spectra were used to classify the images on the right (classified colors)







Normal Lymphocytes



CLL

Z. Malik et al, Spectral morphometric characterization of B-CLL cells versus normal small lymphocytes. J. Histochem. Cytochem. 46: 1113-1118, 1998.

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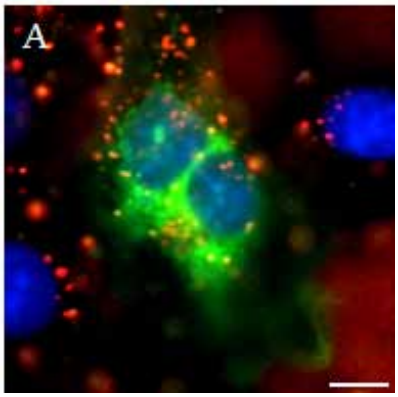
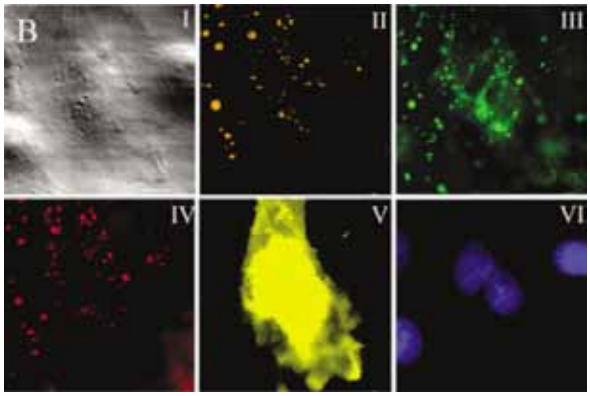
GenASIs SpectraView for Cell Biology

Multiplexing Colors for Parallel Analysis

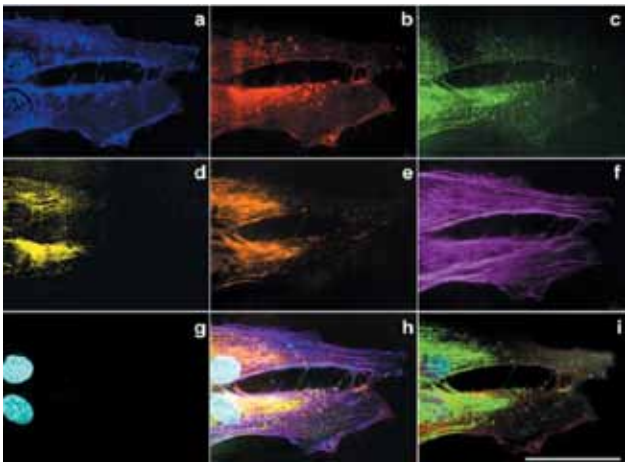
Intracellular Fate of Liposomes

Multicolor study with five dyes and COS-7 cells: (A) original view, (BI) brightfield image of the same group of cells, (BII-VI) spectrally decomposed single-color images: (II) LysoTracker Red, (III) FITC-dextran, (IV) Rh-PE, (V) Vybrant DiO, and (VI) DAPI.





Ulrich Huth, et al. Fourier Transformed Spectral Bio-Imaging for Studying the Intracellular fate of Liposomes Cytometry Part A 57A:10-21 (2004)



Matggias Schieker, et al. Human Mesenchymal Stem Cells at the Single Cell Level: Simultaneous Seven-Color Immunofluorescence J. Anat. (2007) 210, pp.592-599

Stem Cell Identification

Multicolor immunofluorescence of human mesenchymal stem cells.
(a-g) Six-color immunofluorescence plus DAPI nuclear staining with spectral image aquisition. Spectral image after linear unmixing:

(a) CD44/AMCA,
(b) Endoglin (CD105/TexasRed),
(c) VCAM-1 (CD106/FITC),
(d) Collagen -IV/Alexa546 (pseudo-colored yellow),
(e) Fibronectin/Cy2 (pseudo-colored brown),
(f) F-actin/Alexa633 (pseudo-colored violet),
(g) DAPI nuclear staining

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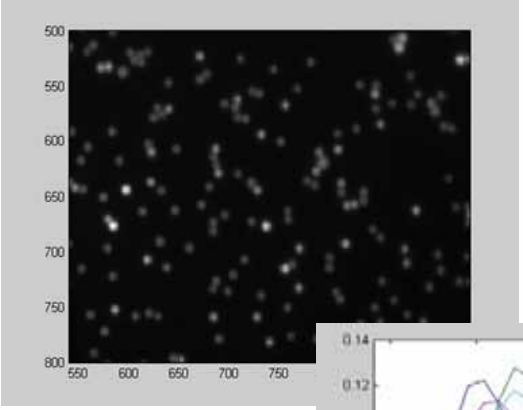
GenASIs SpectraView for Biomedical Research

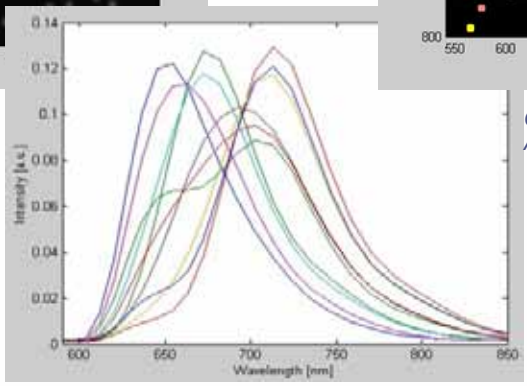
Catering to General Research Needs

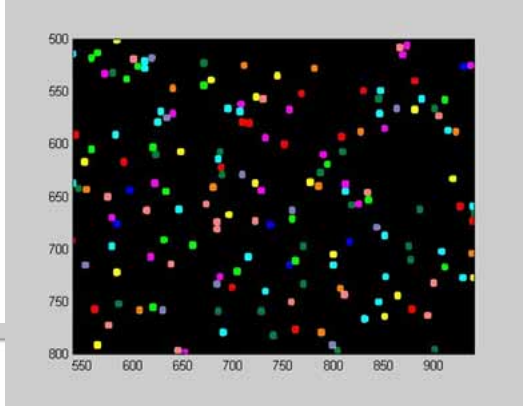
Polystyrene Beads

5 nm beads, coded to 10 classes by fluorescent dyes (combinatorial stained) are spread over a slide or titer-plate membrane. To each group of beads a specific Single Nucleotide Polymorphisms (SNP) is attached. The detection of the SNPs is done by a fluorescent reporter molecule that emits in a different spectral range than the color beads. Beads are imaged with GenASIs SpectraView and classified based on their spectral signature. The attachment of SNPs to the coded beads is detected by the monochrome reporter image.



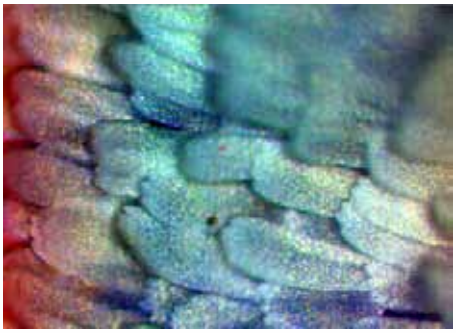
Black and white image of fluorescent beads. There are 10 different color beads. Cytometry Part A 57A:10-21

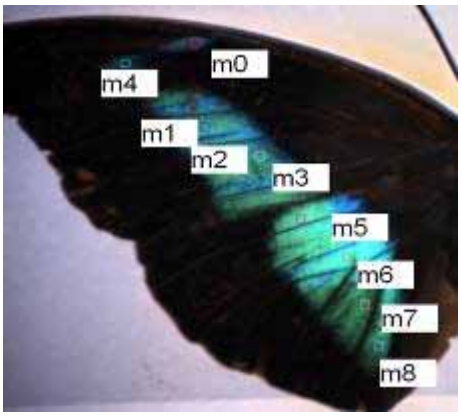




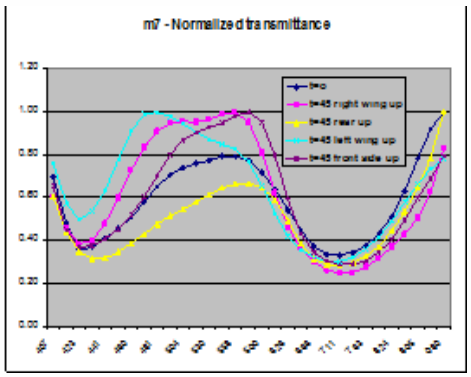
Classified beads after spectral analysis. All beads are red to the human eye.

Butterflies- Color Analysis



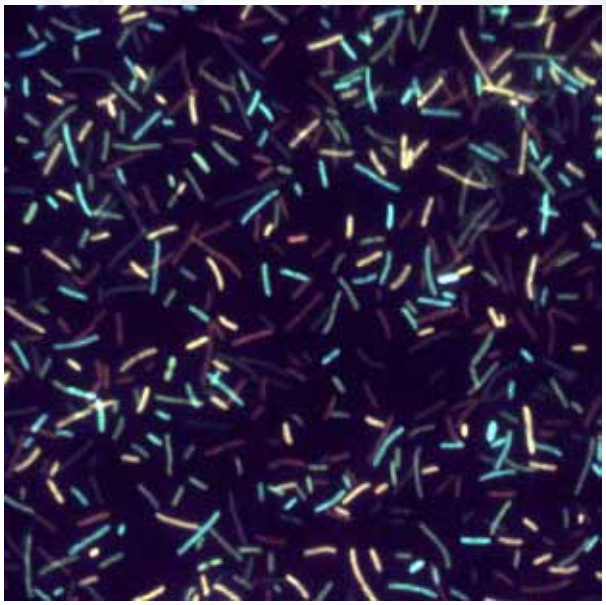


Nanometric structure of butterfly wings contributes to the conceptual color as a function of the viewing angle.

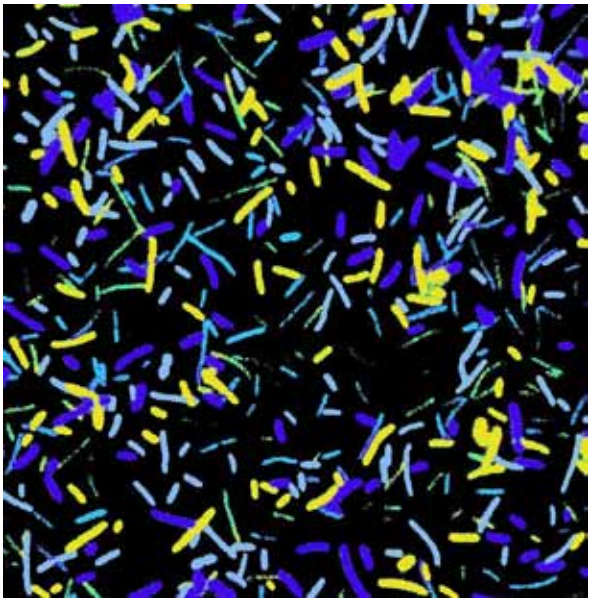


GenASIs SpectraView for Bacteriology

Bacterial Combinatorial Staining



Multi-color (5 green probes), combinatorial fluorescence staining of bacteria.
Each bacteria is stained with multiple DNA fluorescent-probes, thus resulting in a different color that can be classified and grouped by the SpectraView.



Spectral un-mixing and classification of bacteria after background removal.

Note that the bacteria were coded according to their specific spectra, depending on various DNA, with fluorescent probes attached to each of them.

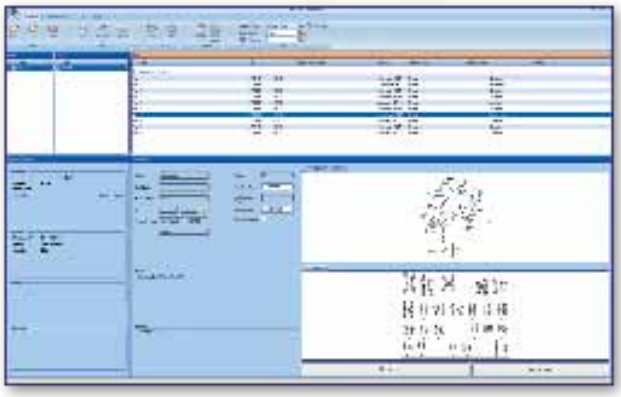
GENASIS
Diagnosis Made Simple

GenASIs Case Data Manager - CDM

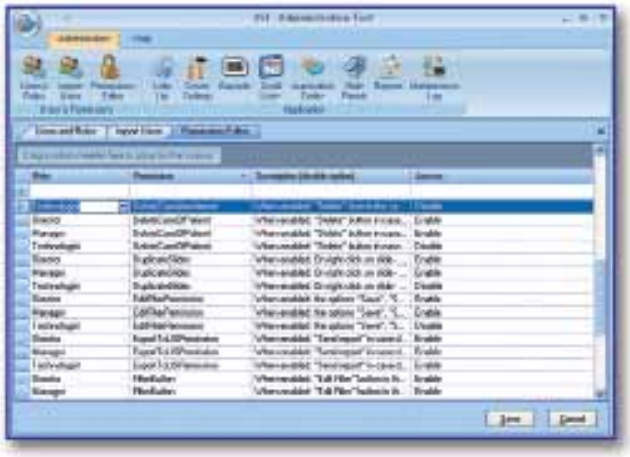
Unified Patient Data Management and Reporting for All GenASIs Applications

GenASIs Case Data Manager (CDM) is the central portal and database for the entire GenASIs suite. CDM is designed to support the modern 'paperless laboratory'. An integrated multi-application microscopy imaging database with advanced search and reporting capabilities offers statistical analysis and cross-case comparison.

CDM features simple, multi-site data management with real-time case summary and the ability to produce comprehensive reports ensuring comprehensive case analysis.



CDM Interface



Administration Tool

Security Maintenance

Laboratory administrators can set access rights for each user and lab, to accommodate data access policies based on the lab's and the organization's protocol.

Data Integrity – Archiving and Backup

Data integrity is strictly preserved by allowing archiving and backup of all clinical data to any storage media. The flexibility CDM allows in the selection of archiving and backup media ensures a simple and quick solution for maintaining data integrity. Import and export utilities facilitate easy access to archived material and storage of external data.

Robust and Flexible Reporting

Multiple reports may be defined in CDM and are available in multiple languages. CDM's advanced reporting tools support customization according to the user's needs with the ability to select which fields, images and format are used in each report.

- Physician reports are automatically generated with data from key fields
- Statistics reports may be easily created, including multi-application summary reports reviewing all sample types in a case
- A freehand report using a choice of annotation styles may include any information or image across multiple cases

Highlights:

- Integrated, clinical utilities for multi-application support for pathology and cytogenetics
- Flexible data management and storage options may be adapted to the needs of any size laboratory or multiple laboratories.
- Multi-site laboratory support with seamless connectivity for remote clients
- Advanced multiple-user access and user permission management mechanism
- Real time connectivity to LIS systems
- Advanced design supporting the 'paperless laboratory', including automated count-sheet update

The Company

Bringing Details to Light

Applied Spectral Imaging (ASI) makes patient care better through advanced biomedical imaging.

The GenASIs Automated Imaging Platforms for Genetic and Pathological Analysis are the foundation of ASI's offering. With superior imaging and analysis capabilities, ASI provides state-of-the-art diagnostic aids, offering cytogeneticists and pathologists accurate analysis. GenASIs enables automated tissue analysis for primary diagnostics, with reproducible and reliable results. GenASIs Hyperspectral with HiSKY® Probes adds a new dimension to biomedical image analysis.

GenASIs is FDA cleared for FISH clinical applications such as UroVysion, HER2/neu, CEP XY and Karyotyping. ASI complies with major regulatory requirements and international quality standards.

ASI is the industry's leading microscopy imaging solution provider since 1993, with over 30 registered patents in the US, Europe and Japan and over 2,500 systems deployed worldwide. With worldwide offices in the US, Europe and Asia, ASI has built a global network of over 50 distributors.

Quality and Regulatory Compliance

ASI conforms to ISO 9001:2008 and ISO 13485:2003 quality standards for medical devices and is fully conversant with HIPAA, Health Insurance Portability and Accountability Act requirements for patient privacy and security.

ASI is FDA cleared for in-vitro diagnostic procedures of detection of the following:

- GenASIs BandView® to be used for karyotyping with real time microscope images from stained metaphases, for Cytogenetics.
- GenASIs FISHView® to be used for karyotyping with real time microscope images from cultured and stained cell specimens in their metaphase. In addition, FISHView is intended as an aiding tool for digitally visualizing, processing, counting and classifying stained cells and storing FISH multi-dye images.
- GenASIs UroVysion designed for the microscopic imaging and analysis of chromosomal abberations using fluorescence in situ hybridization (FISH) in urine specimens from persons suspected of having bladder cancer.
- GenASIs CEP XY to assess the effectiveness of bone marrow transplantation in opposite-sex transplants.
- GenASIs HER2/neu FISH for in-vitro diagnosis as an aid to the cytogeneticist/pathologist in the deletion, classification, and counting of cells of interest.

GenASIs SpotScan was cleared to be used as an adjunctive automated enumeration tool for all the above products.

All other applications are intended For Research Use Only.

Applied Spectral Imaging
Bringing Details to Light

ASI is proud to have a worldwide network of business and service partners

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