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May 20, 2004

SELECTED REFERENCES
Multispectral Imaging Systems & LCTF Components

Applicable to Nuance™ Multispectral Imaging Systems & Maestro™ In-Vivo Imaging Systems

Rajesh Jaganath, B.S.; Cesar Angeletti, M.D., Ph.D.; Richard Levenson, M.D., Ph.D.; David L. Rimm, M.D., Ph.D.; Department of Pathology, Yale University; CRI, Inc.; 2004. Diagnostic Classification of Urothelial Cells in Urine Cytology Specimens Using Exclusively Spectral Information. Cancer (Cancer Cytopathol) 2004;100:000–000. Received November 19, 2003; revision received March 17, 2004; accepted March 24, 2004.

BACKGROUND. Although cytologic evaluation of urine specimens is a standard procedure in the diagnosis and follow-up of bladder carcinoma, its sensitivity and specificity are low. Cytopathologic diagnoses are driven primarily by spatial relations or morphology. Although color enhances the pathologist's perception of the specimen, spectral information plays a minimal role in diagnostic processes. Recently, methods have been developed to capture and analyze spectral information from clinical specimens. In the current study, the authors determined the classification value of spectral information by testing its ability to discriminate between malignant and benign urothelial cells in cytology specimens.

METHODS. Multiple images of benign urothelial cells (n = 39) and urothelial carcinoma cells (n = 35) were collected at serial wavelengths using a liquid crystal tunable optical filter and composited into a mosaic using ENVI (Environment for Visualizing Images) software. Through minimum noise fractionation and principal component analysis, the spectral information in the mosaic was compressed into a 29-dimensional scatter plot. The data generated were analyzed using visual and spectral end member extraction on both the original data set and a second independent data set (test set).

RESULTS. One area of spectral clustering in the scatter plot segmented with carcinoma cells exclusively (100% specific), but was not present in every cell (approximately 50%), which may indicate that these spectral profiles are present in a subpopulation of malignant cells or at specific points of their cell cycle. Using ENVI algorithms, the authors found that a particular classification spectrum (end member 9) and its closest relatives identified malignant cell clusters, with a sensitivity and specificity that reached 82% and 81%, respectively. To validate this mechanism in a test set, a second mosaic comprised of 15 benign and 15 malignant clusters was analyzed using end member 9, resulting in a combined sensitivity and specificity of 73%.

CONCLUSIONS. The results of the current study demonstrated that spectral information, in the complete absence of morphologic or spatial information, allows discrimination of benign and malignant urothelial cells in routine urine cytology specimens. The authors believed that this novel technology, combined with spatial analysis, has the potential to serve as an ancillary test for improved detection of bladder carcinoma.

Richard Levenson, M.D., Ph.D.; Meng Yang; Robert M. Hoffman, Ph.D.; AntiCancer, Inc.; CRI, Inc.; 2004. Whole-body dual-color fluorescence imaging of tumor-host interaction enhanced by spectral unmixing. AACR-04, Permanent Abstract ID: 202. Presented 2004.

ABSTRACT. We have recently developed a new model of tumor-host interaction consisting of red fluorescent protein (RFP)-expressing tumors transplanted to green fluorescent protein (GFP) transgenic mice expressing GFP in all tissues. We have previously shown that this model allows the whole-body imaging of tumor growth and metastasis and the visualization of host cells and structures including blood vessels interacting with the tumor in fresh tissue by dual-color fluorescence microscopy. In the present study, the MDA-MB-435 human breast cancer expressing RFP was orthotopically transplanted to transgenic nude mice expressing GFP in all tissues. Excitation at 470 nm and appropriate >500 nm emission filters visualized the RFP tumor growing in the GFP mice by whole-body imaging. Using the CRI spectral imaging system, we were able to visualize by whole-body imaging the GFP-expressing host vessels vascularizing the RFP-expressing tumor. Initial results indicate that the host vessels in the tumor may have a unique fluorescence spectrum with emission >600 nm, possibly related to interaction of GFP fluorescence with absorbance properties of the blood vessels. The powerful spectral imaging system measures all the spectra present in each pixel and can separate (unmix) any spectrum from the others. This spectral unmixing enabled the whole-body imaging of vessels in the tumor. This new dual-colored tumor-host model and spectral imaging can noninvasively visualize in real-time the onset and progression of angiogenesis in a tumor. Other host tissues in the tumor may also be visualized by spectral imaging.

Xiaohu Gao, Yuanyuan Cui, Richard M. Levenson, Leland W. K. Chung, Shuming Nie; Emory University, Georgia Institute of Technology, CRI, Inc.; 2003. In-Vivo Cancer Targeting and Imaging with Semiconductor Quantum Dots. Article submitted for publication, December 2003.

ABSTRACT. A new class of multifunctional nanoparticle probes based on semiconductor quantum dots (QDs) has been developed for targeting and imaging of cancer cells in living animals. Its structural design involves encapsulating luminescent QDs with an ABC triblock copolymer (MW = 100 kD), and linking this polymer to tumor-targeting ligands such as antibodies and drug-delivery functionalities. In vivo targeting studies of human prostate cancer growing in nude mouse indicate that the QD probes can be delivered to tumor sites by both enhanced permeation and retention (passive targeting) and by antibody binding to cancer-specific cell surface biomarkers such as prostate-specific membrane antigen (PSMA) (active targeting). Using both subcutaneous injection of QD-tagged cancer cells and systemic injection of multifunctional QD probes, we have achieved multicolor fluorescence imaging of as few as 10-100 cancer cells under in vivo conditions. We have further explored the use of spectrally resolved imaging for efficient background removal and for precise delineation of weak spectral signatures in vivo. These results suggest that QD probes and spectral imaging can be combined for multiplexed imaging and detection of genes, proteins, and small-molecule drugs in single living cells, and that this imaging modality can be adopted for real-time visualization of cancer cell metastasis in live animals.

Roy S. Berns, Lawrence A. Taplin, Francisco H. Imai, Ellen A. Day, David C. Day; Munsell Color Science Laboratory, Chester F. Carlson Center for Imaging Science, Rochester Institute of Technology, Rochester, New York, USA; 2003. Spectral Imaging of Matisse's Pot of Geraniums: A Case Study. Presented at the IS&T/SID Eleventh Color Imaging Conference, 2003.

ABSTRACT. The accuracy of color image-acquisition systems is most often evaluated using test targets of uniform color patches imaged under optimal conditions. In artwork imaging, system performance is judged visually, comparing the art with images rendered for display or print. Because the surface properties of the art may not be uniform, the spectral properties of the pigments may be different than the test targets, the sizes may be different, renderings are often metameric to the art, taking and viewing lighting geometries may be different, and the museum observers are more experienced than scientists in judging color accuracy visually, color accuracy as determined on a visual basis may be quite different than target performance. Therefore, an experiment was performed where a spectral-imaging system, designed for scientific purposes under laboratory conditions, was taken to a museum and tested in its photographic and conservation departments. The sensor was coupled with a Cambridge Research & Instrumentation, Inc. liquid-crystal tunable filter (LCTF). 12-bit linearphotometric data were recorded. 31 bands were collected corresponding to wavelength centroids of 400 – 700 nm in 10 nm increments. The work of art evaluated was Henri Matisse's Pot of Geraniums. Spectral and colorimetric comparisons were made between in situ small aperture spectrophotometry and imaging. The average performance was 3.7ΔE00 and 3.1% spectral RMS; this was similar to an independent verification target of typical artist pigments applied to a canvas board. Viewed in close up, this level of accuracy yielded reasonable color matching for images rendered for display and print. Viewed overall, the matching quality worsened, a result of using diffuse lighting during image acquisition. Renderings appeared "flat" and reduced in perceived contrast. This indicates that when creating an image archive for both scientific and visual purposes, it will be necessary to use both directional and diffuse lighting geometries.

E. Michael Attas, Michael G. Sowa, Trevor B. Postumus, Bernard J. Schattka, Henry H. Mantsch, Shuliang L. Zhang; Institute for Biodiagnostics, NRC-Canada; Unilever Research; 2002. Near infrared spectroscopic reflectance imaging: a new tool in art conservation. Vibrational Spectroscopy 28 (2002) 59–66.

ABSTRACT. The application of infrared spectroscopic imaging to non-destructive examination of works of art is described. Its advantages over infrared photography and reflectography are discussed, in particular its ability to provide spectroscopic information, which potentially allows identification of pigments, binders, and other materials. Near-infrared spectra of a selection of brown and black pigments are presented. Results are given of the application of infrared spectroscopic imaging to two works of art in different media: an ink drawing and an oil painting.

Steven C. Gebhart, Wei-Chiang Lin, and Anita Mahadevan-Jansen; Department of Biomedical Engineering, Vanderbilt University; 2002. Characterization of a Spectral Imaging System. Presented at the 2003 SPIE Photonics West/BIOS Conference, January 2003.

ABSTRACT. Complete infiltrating brain tumor margin resection continually eludes neurosurgeons due to inherent limitations of current margin localization techniques. A need exists for an objective, on-site, real-time imaging system that can accurately localize brain tumor margins and therefore be used as a basis for image-guided surgery. Optical biopsy methods are a proven means for successful brain tissue discrimination, indicating promise for spectral imaging to fill such a need. Before testing spectral imaging for surgical guidance, various spectral imaging modalities must be systematically compared to determine the modality most conducive to the clinical setting. A liquid crystal tunable filter spectral imaging system was characterized for field of view, spatial and spectral resolution, and ability to retain spectral features acquired from a clinical single-pixel spectroscopy system.

James R. Mansfield, Michael Attas, Claudine Majzels, Edward Cloutis, Cathy Collins, Henry H. Mantsch; Institute for Biodiagnostics, NRC-Canada; University of Winnipeg; The Winnipeg Art Gallery; 2002. Skin hydration images from near-infrared reflectance spectra. Am Clin Lab 2002:21:32–36.

SYNOPSIS. Light reflected from tissue conveys chemical information, and that information can be interpreted to diagnose a person's health. Digital cameras sensitive to IR light have been fitted with tunable filters and used to collect sets of narrow-band images through the near-IR region. Several vibrational bands in the near-IR reflectance spectrum of tissue can be used as indicators of tissue hydration. The two bands centered at 970 and 1450 nm result from overtones and combinations of OH-bond stretching vibrations. The study of skin hydration is just one example of a biological field in which noninvasive diagnostic tools based on spectroscopic imaging have proven their value. Apparently, surprising results may appear as a result of processing the data in different ways. At this stage of research, the potential applications are limited only by our imaginations.

Richard M. Levenson, Paul J. Cronin, Neal R. Harvey; Los Alamos National Laboratory; CRI, Inc.; 2002. Spectral Imaging and Biomedicine: New devices, New Approaches. AIPR 2002: pp 105-111.

ABSTRACT. The advent of molecular medicine and new demands on pathologists to deliver prognostic and therapy-shaping analyses has created a need for enhanced imaging tools. Spectral imaging coupled with microscopy is a relatively novel and largely unexplored technology that holds out promise of satisfying, at least in part, such a need. New optical methods for spectral discrimination are being combined with powerful software approaches, often originally developed in different fields, to explore and exploit a wealth of information beyond the capabilities of conventional color-based imaging approaches. Some of the new devices and software tools are described and illustrated here. While the results are indeed promising, it must be stressed that this field is in its infancy, and the optimal uses of this technology in the clinical arena still await definition.

Richard M. Levenson, Clifford C. Hoyt; CRI, Inc.; 2000. Spectral Imaging and Microscopy. American Laboratory, November 2000:26–33.

SYNOPSIS. In biomedicine, color is frequently used to increase information content. Traditionally, in the guise of histological stains, color signals the biochemical makeup of different regions of tissue, most typically, nuclei versus cytoplasm. When coupled to more precisely targeted indicators, such as antibodies and nucleic acid probes, colors can allow the detection of multiple, highly specific analytes. However, our native ability to perceive and evaluate color information is somewhat constrained because, by definition, we are limited to the visible range in terms of wavelengths, and because we (and our conventional red, green, blue [RGB] cameras) are suboptimal in terms of spectral resolution. Spectral imaging can provide the necessary spectral resolution to detect and resolve multiple stains.

Charles DiMarzio, Ph.D.; Northeastern University (supported by the National Science Foundation and the General Dynamics Corp.); 2000. Biomedical Hyperspectral Imaging: Guest Lecture at UPRM. Presented November 2000.

SYNOPSIS. Terminology and concepts of hyperspectral imaging with an emphasis on medical imaging. An imaging system developed by Peter Dwyer at Massachusetts General Hospital is discussed. HOSIS uses a liquid crystal tunable filter (LCTF) manufactured by CRI, Inc. and is similar to commercially available systems now sold by CRI, Inc.

Lorenzo Leonardi, Michael G. Sowa, Jeri R. Payette, Henry H. Mantsch; Institute for Biodiagnostics, NRC-Canada; 2000. Near-Infrared Spectroscopy and Imaging: A New Approach to Assess Burn Injuries. Am Clin Lab 2000:19:20–22.

SYNOPSIS. A need exists for a reliable, nonsubjective, and easy-to-handle technique to evaluate burn injury themodynamics in the early postburn period that provides diagnostic as well as prognostic information on the severity of the injury. Near-infrared (NIR) reflectance spectroscopy and imaging provides a noninvasive means of assessing the balance between oxygen delivery and oxygen utilization in tissue. The principal benefit of using NIR spectroscopy and imaging is that regional variations in tissue themodynamics can be discerned objectively.

Applicable to VariSpec™ Liquid Crystal Tunable Filter (LCTF) components

Brent D. Johnson, 2002. Spectral Imaging Finds a Place on the Farm. Photonics Spectra Magazine (2002: January issue).

SYNOPSIS. With the lower cost of components—and the increased pressures of globalism—remote spectral imaging is becoming a viable agricultural tool. Sophisticated airborne and space-based imagers from NASA, such as Aviris, Hyperion and Advanced Land Imager, are enabling precision agriculture. As improvements in software, automation and sensor technology continue to make remote sensing more accessible, multispectral and hyperspectral remote imaging will play a greater role in agriculture. This is significant for a farmer seeking to compete in today's global markets.

Roy S. Berns, Lawrence A. Taplin, Francisco H. Imai, Ellen A. Day, David C. Day; Munsell Color Science Laboratory, Chester F. Carlson Center for Imaging Science, Rochester Institute of Technology, Rochester, New York, USA; 2003. Spectral Imaging of Matisse's Pot of Geraniums: A Case Study. Presented at the IS&T/SID Eleventh Color Imaging Conference, 2003.

ABSTRACT. The accuracy of color image-acquisition systems is most often evaluated using test targets of uniform color patches imaged under optimal conditions. In artwork imaging, system performance is judged visually, comparing the art with images rendered for display or print. Because the surface properties of the art may not be uniform, the spectral properties of the pigments may be different than the test targets, the sizes may be different, renderings are often metameric to the art, taking and viewing lighting geometries may be different, and the museum observers are more experienced than scientists in judging color accuracy visually, color accuracy as determined on a visual basis may be quite different than target performance. Therefore, an experiment was performed where a spectral-imaging system, designed for scientific purposes under laboratory conditions, was taken to a museum and tested in its photographic and conservation departments. The sensor was coupled with a Cambridge Research & Instrumentation, Inc. liquid-crystal tunable filter (LCTF). 12-bit linearphotometric data were recorded. 31 bands were collected corresponding to wavelength centroids of 400 – 700 nm in 10 nm increments. The work of art evaluated was Henri Matisse's Pot of Geraniums. Spectral and colorimetric comparisons were made between in situ small aperture spectrophotometry and imaging. The average performance was 3.7ΔE00 and 3.1% spectral RMS; this was similar to an independent verification target of typical artist pigments applied to a canvas board. Viewed in close up, this level of accuracy yielded reasonable color matching for images rendered for display and print. Viewed overall, the matching quality worsened, a result of using diffuse lighting during image acquisition. Renderings appeared "flat" and reduced in perceived contrast. This indicates that when creating an image archive for both scientific and visual purposes, it will be necessary to use both directional and diffuse lighting geometries.

Amanda E. Lowell, Kah-Siew Ho, Robert A. Lodder, Ph.D.; Department of Chemistry, Advanced Science and Technology Center, University of Kentucky; 2002. Remote Hyperspectral Imaging of Endolithic Biofilms Using a Robotic Probe. Contact in Context, SETI League, 2002.

ABSTRACT. Many scientists on Earth have concentrated their searches for extraterrestrial life on robotic probes sent to nearby planets and moons. These robotic probes are able to analyze conditions on the planets and transmit data back to Earth. Hyperspectral imaging can be used to identify astrobiologically interesting sites from a distance. The rover can then drive up to the site and conduct further sampling. In this study, reflectance measurements made by a visible - near-IR / IR imager mounted on a battery-powered robot were used to detect the growth of Gloeocapsa cyanobacterial colonies on a prepared limestone surface at a distances up to 20 meters. Hyperspectral imaging at higher energies (9090-15385 cm-1) was accomplished with a liquid crystal tunable filter (CRI, Woburn, MA) and Si CCD (Sharp) camera with zoom lens. Data were collected at 20 different wavenumbers evenly spaced over the spectral range. The camera and filter system operated at ambient temperature. The distance from the biofilm samples to the robot was twenty meters.

Nahum Gat, Ph.D.; Jim Buss; 2002. Full Stokes Vector Extraction with Imaging Spectro-Polarimetry Using a Liquid Crystal Variable Retarder and a Liquid Crystal Tunable Filter. Detection & Classification of Difficult Targets; US Army Aviation & Missile Command; Redstone Arsenal, Alabama. September 25—26, 2002.

SYNOPSIS. For the past several years OKSI has been building hyperspectral imaging (HSI) sensors based on the liquid crystal tunable filter (LCTF) device from Cambridge Research & Instrumentation, Inc. (CRI). The LCTF is a Lyot filter made of birefringent LC materials. The LCTF is electronically controlled and can be commanded to switch wavelengths practically instantaneously. The LCTF principle of operation is discussed in a subsequent section, and it can be seen that with modifications the concept lends itself to also capturing polarization information. The images and data processing chain demonstrate the feasibility of building a LC based imaging spectro-polarimeter.

E. Neil Lewis, John E. Carroll, Fiona Clarke; Spectral Dimensions Inc.; Cadrai; Pfizer Central Research, UK; 2001. A near infrared view of pharmaceutical formulation analysis. NIR Imaging, Vol. 12 No. 3 (2001).

SYNOPSIS. Pharmaceutical dosage forms consist of a mixture of ingredients combined to provide desirable characteristics. Called the pharmaceutical formulation, the dosage form is most often a tablet or capsule. The scale-up process that yields the most desirable dosage form is called formulation development. It is critical that the formulation be robust and consistent, any tablet or capsule produced anywhere in the world must have the same therapeutic characteristics. Spectral Dimensions offers complete NIR imaging systems utilizing liquid crystal tunable filters (LCTFs) manufactured by Cambridge Research & Instrumentation, Inc. (CRI). With these instruments, the spatial relationship and chemical composition of complex matrices, such as pharmaceutical blends, can be rapidly determined.

Sofya Poger and Elli Angelopoulou; Stevens Institute of Technology; 2001. Multispectral sensors in Computer Vision. CS Report, 2001-3.

ABSTRACT. Abstract: The majority of color work in machine vision has been based on a trichromatic (and specifically RGB) color representation. In reality, color is a continuous univariate function of wavelength which can be quantized into an arbitrary number of dimensions. The capture of reflectance information in spectrally higher dimensions will improve image analysis. To acquire spectrally and spatially highdimensional images, one has to employ specialized image acquisition devices. This paper is a survey of the currently available technologies for this type of imaging systems. Electronically tunable filters offer the fastest, most accurate and flexible color filtering techniques that are currently available. We provide an overview of this type of filters and present a set of criteria for selecting the appropriate device depending on the specific application requirements.

Eugenia J. Robinson; Foundation for the Advancement of Meso-American Studies, Inc.; 2001. Multispectral Imaging of La Casa de las Golodrinas Rock paintings. Report Submitted to FAMSI, October 16, 2001.

SYNOPSIS. La Casa de las Golondrinas (The House of the Swallows), located in the Antigua Valley, Guatemala, is the largest rock art site in the Guatemalan Highlands. Like other painted rock art sites in the highlands, the site is at a sacred location near water. Many of the 105 paintings recorded at the site so far, based on stylistic and thematic criteria, appear to pertain to late in the Postclassic period. Numerous abstract and fantastic motifs, however, have uncertain themes and styles admitting to the possibility that they date to earlier times. Multispectral imaging is a non-invasive preservation technique that can enhance faded details and differentiate between pigments used in paintings. In several cases, the multispectral images revealed details not easily seen by eye. Professor Gene Ware of Brigham Young University utilized LCTFs manufactured by Cambridge Research & Instrumentation, Inc. (CRI) to gather multispectral imaging data on location and subsequently process his data.

Jon Y. Hardeberg, Francis Schmitt, Hans Brettel; Ecole Nationale Superieure des Telecommunications, Paris, France; 1999. Multispectral image capture using a tunable filter. SPIE Proc. Vol. 3963, pp. 77-88.

ABSTRACT. In this article we describe the experimental setup of a multispectral image acquisition system consisting of a professional monochrome CCD camera and a tunable filter in which the spectral transmittance can be controlled electronically. We have performed a spectral characterization of the acquisition system taking into account the acquisition noise. To convert the camera output signals to device-independent data, two main approaches are proposed and evaluated. One consists in applying regression methods to convert from the K camera outputs to a device-independent colour space such as CIEXYZ or CIELAB. Another method is based on a spectral model of the acquisition system. By inverting the model using a Principal Eigenvector approach, we estimate the spectral reflectance of each pixel of the imaged surface.

Dimitra N. Stratis, Kristine L. Eland, J. Chance Carter, Samuel J. Tomlinson, S. Michael Angel; University of South Carolina; 1999. Comparison of Acousto-optic and Liquid Crystal Tunable Filters for Laser-Induced Breakdown Spectroscopy. Applied Spectroscopy, Volume 55, Number 8, 2001, pp. 999-1004.

ABSTRACT. In this paper, we report the first time-resolved laser-induced plasma images acquired using a liquid crystal tunable filter (LCTF). We also compare the use of LCTFs and acousto-optic tunable filters (AOTFs) for time-resolved plasma imaging applications in terms of resolution, out-of-band rejection, and image quality. Application of tunable filter technologies to plasma imaging is unlike other spectroscopic imaging methods because of the intense and spectrally broad background generated by a laser-induced plasma. High quality images of the distribution of atomic emission within a laser-induced plasma can be achieved using both AOTFs and LCTFs. However, additional filters are needed for rejection of wavelength outside the tuning ranges of the devices. Both devices exhibited superior resolution in the lower working range of the filters (~500 nm) with the LCTF exhibiting superior spectral resolution to the AOTF.

Eric T. Baumgartner; Jet Propulsion Laboratory, California Institute of Technology; 2000. In-Situ Exploration of Mars Using Rover Systems. American Institute of Aeronautics and Astronautics, AIAA-2000-5062.

ABSTRACT. This paper will describe a NASA/JPL rover system that has been focused on developing technologies required for the in-situ exploration of Mars. In particular, JPL has been developing a class of rovers that carry significant science payloads that address geological exploration and discovery along with the ability to acquire samples from soils and rocks. The aim of this work is to validate mission concepts and to gain valuable experience related to the operation of rovers on Mars so that improved mission operations and scientific return can be realized during future flight missions. FIDO's remote sensing suite located on the mast includes a multi-spectral, narrow field-of-view PanCam stereo imaging system, a monochromatic, wider field-of-view NavCam stereo imaging system, and the optics for a near-infrared point spectrometer that operates in the 1200–2500 nanometer wavelength region. The multi-spectral capability associated with the PanCam system is realized using a Liquid Crystal Tunable Filter (LCTF) manufactured by Cambridge Research & Instrumentation, inc. (CRI) that is tuned to the three near-IR wavelengths of 650, 750 and 850 nanometers.

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