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Themed issue: Optical Diagnosis

CRITICAL REVIEW
David I. Ellis *et al.*
Illuminating disease and enlightening biomedicine: Raman spectroscopy as a diagnostic tool

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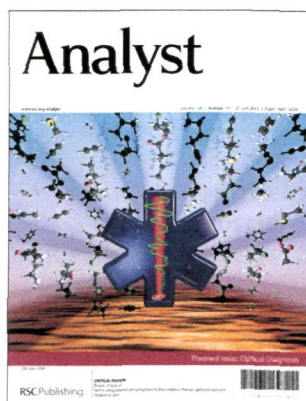
Cover
See David I. Ellis *et al.*,
pp. 3871–3884.
Image reproduced by permission
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2013, **138**, 3871.

EDITORIALS

3871

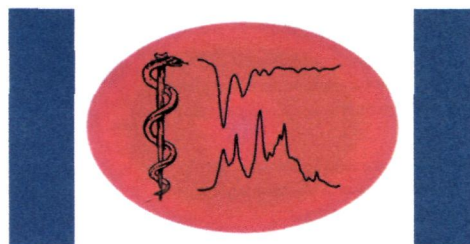## Illuminating disease and enlightening biomedicine: Raman spectroscopy as a diagnostic tool

David I. Ellis,* David P. Cowcher, Lorna Ashton, Steve O'Hagan and Royston Goodacre

An introduction to some of the more exciting recent advances and dynamic current areas of development in biomedical Raman spectroscopy.
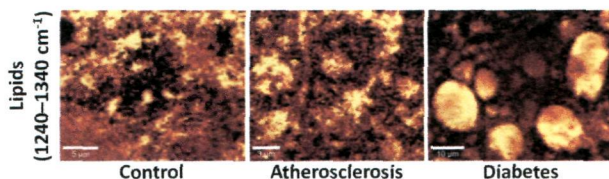
3885

Pathological changes in the biochemical profile of the liver in atherosclerosis and diabetes assessed by Raman spectroscopy

Kamila Kochan, Katarzyna M. Marzec, Katarzyna Chruszcz-Lipska, Agnieszka Jasztal, Edyta Maslak, Hanna Musiolik, Stefan Chłopicki and Malgorzata Baranska*

Raman microspectroscopic imaging has been utilized for the investigation of pathological changes in the liver induced by diabetes and atherosclerosis.

3891

Synchrotron Fourier transform infrared (FTIR) analysis of single living cells progressing through the cell cycle

Donna R. Whelan, Keith R. Bambery, Ljiljana Puskar, Don McNaughton and Bayden R. Wood*

Synchrotron FTIR spectroscopy was employed to investigate living cells as they progress through the cell cycle. A principal components analysis scores plot showed general clustering of the different phases that were related to changes in nucleic acids, lipids and proteins.
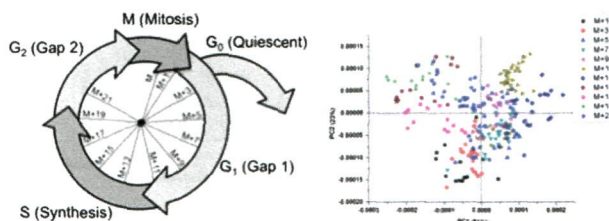
3900

## Discrimination between benign, primary and secondary malignancies in lymph nodes from the head and neck utilising Raman spectroscopy and multivariate analysis

Gavin Rhys Lloyd, Linda E. Orr, Jonathan Christie-Brown, Keith McCarthy, Simon Rose, Michael Thomas and Nicholas Stone*

Raman spectra provide a characteristic spectral fingerprint of the biochemical state of the tissue which can be exploited for cancer diagnosis.
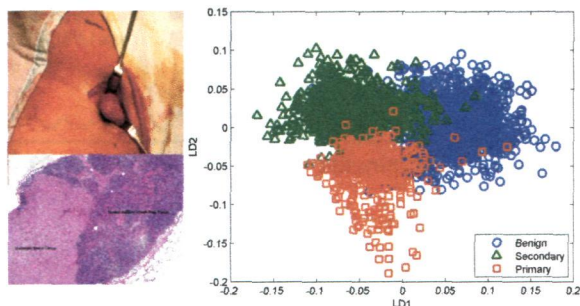
3909
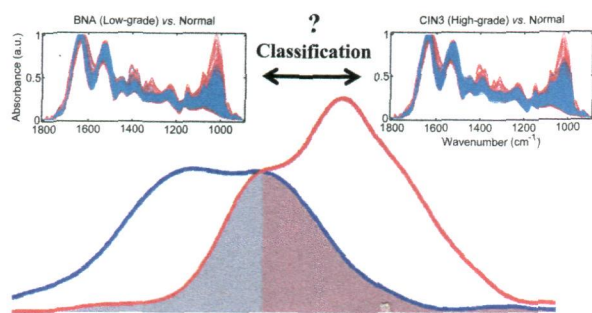
Biospectroscopy insights into the multi-stage process of cervical cancer development: probing for spectral biomarkers in cytology to distinguish grades

Nikhil C. Purandare, Imran I. Patel, Júlio Trevisan, Noel Bolger, Ronan Kelehan, Günther von Bünau, Pierre L. Martin-Hirsch, Walter J. Prendiville and Francis L. Martin*

Spectral classification based on imperfect conventional screening: probing the apparent crossover between classes.

3917
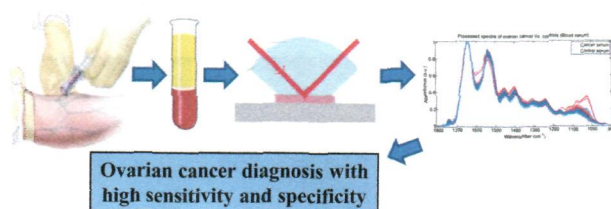
Fourier-transform infrared spectroscopy coupled with a classification machine for the analysis of blood plasma or serum: a novel diagnostic approach for ovarian cancer

Ketan Gajjar, Júlio Trevisan, Gemma Owens, Patrick J. Keating, Nicholas J. Wood, Helen F. Stringfellow, Pierre L. Martin-Hirsch and Francis L. Martin*

A classification machine for vibrational spectroscopy data derived from plasma or serum to screen for ovarian cancer in a well-population.
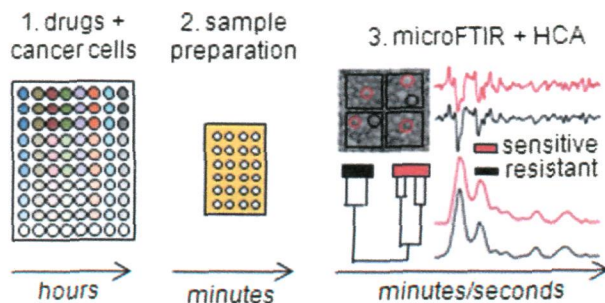
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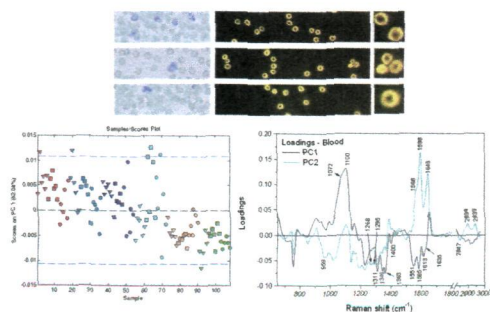
Raman spectroscopic analysis of malaria disease progression *via* blood and plasma samples

Alison J. Hobro, Aki Konishi, Cevayir Coban and Nicholas I. Smith*

Raman spectroscopy can detect early changes in the blood and plasma of malaria infected individuals, predominantly the appearance of hemozoin.

3934

Rapid recognition of drug-resistance/sensitivity in leukemic cells by Fourier transform infrared microspectroscopy and unsupervised hierarchical cluster analysis

Giuseppe Bellisola,* Gianfelice Cinque, Marzia Vezzalini, Elisabetta Moratti, Giovannino Silvestri, Sara Redaelli, Carlo Gambacorti Passerini, Katia Wehbe and Claudio Sorio

MicroFTIR + HCA is an accurate, robust, and reliable method to identify drug-resistance/sensitivity in leukemic cells.

3946

Raman spectroscopic mapping for the analysis of solar radiation induced skin damage

S. M. Ali,* F. Bonnier, K. Ptasinski, H. Lambkin, K. Flynn, F. M. Lyng and H. J. Byrne

The effects of simulated solar irradiation of an artificial skin model have been examined using Raman spectroscopy and the results are compared with cytotoxicological and histological profiling.
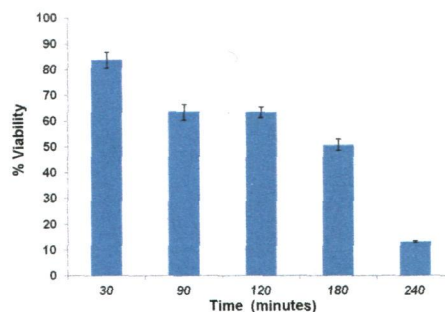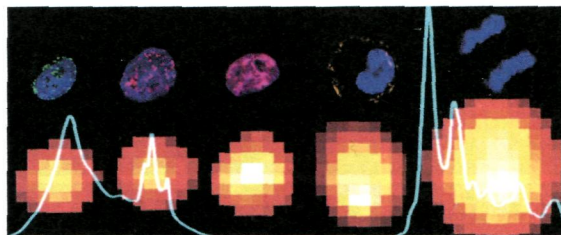
3957

Exploring the spectroscopic differences of Caki-2 cells progressing through the cell cycle while proliferating *in vitro*

M. Jimenez-Hernandez, C. Hughes, P. Bassan, F. Ball, M. D. Brown, N. W. Clarke and P. Gardner*

An illustration of the importance of separating chemical from morphological changes in IR spectra of cells progressing through the cell-cycle.
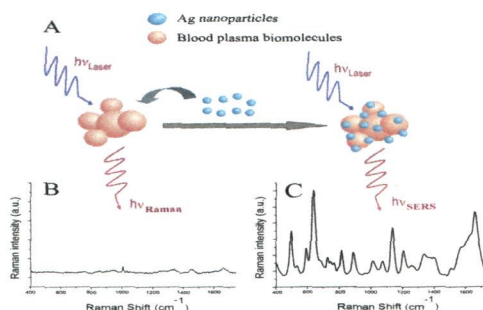
3967

Blood plasma surface-enhanced Raman spectroscopy for non-invasive optical detection of cervical cancer

Shangyuan Feng, Duo Lin, Juqiang Lin, Buhong Li, Zufang Huang, Guannan Chen, Wei Zhang, Lan Wang, Jianji Pan, Rong Chen and Haishan Zeng*

Cervical cancer detection based on blood plasma surface-enhanced Raman spectroscopy and multivariate analysis.
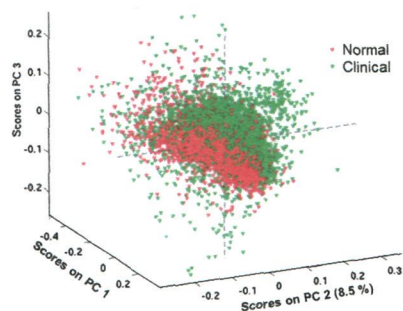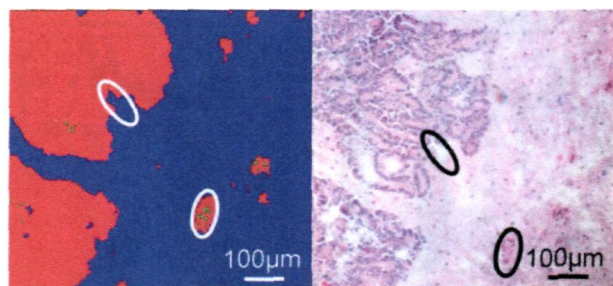
3975

Spectral cytopathology: new aspects of data collection, manipulation and confounding effects

Miloš Miljković, Benjamin Bird, Kathleen Lenau, Antonella I. Mazur and Max Diem*

Spectral cytopathology can distinguish individual cells from normal and clinical patients based on inherent infrared spectral signatures.

3983

Tumor margin identification and prediction of the primary tumor from brain metastases using FTIR imaging and support vector machines

Norbert Bergner, Bernd F. M. Romeike, Rupert Reichart, Rolf Kalff, Christoph Krafft* and Jürgen Popp

Two level support vector machines identified carcinoma in FTIR images and used this subset to determine the primary tumor.

3991
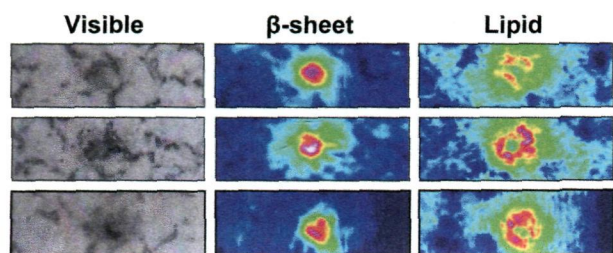
Synchrotron FTIR reveals lipid around and within amyloid plaques in transgenic mice and Alzheimer's disease brain

Catherine R. Liao,* Margaret Rak,* Jillian Lund, Miriam Unger, Eric Platt, Benedict C. Albensi, Carol J. Hirschmugl and Kathleen M. Gough

Diffraction-limited FTIR images of brain tissue obtained at the IRENI beamline (Synchrotron Radiation Center, Madison WI) reveal intimate integration of membrane and aggregated amyloid plaque at 1 μm length scale.
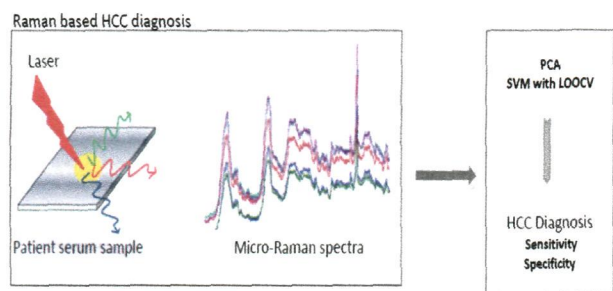
3998

all on the same cells
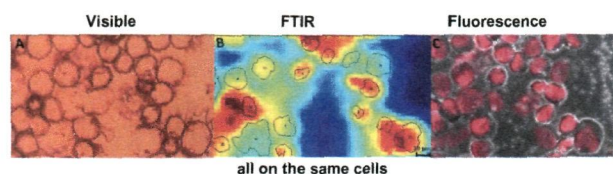
FTIR spectral signature of anticancer drug effects on PC-3 cancer cells: is there any influence of the cell cycle?

Allison Derenne, Alix Mignolet and Erik Goormaghtigh

The same cells are imaged successively by visible, FTIR and fluorescence imaging techniques.

4006

Diagnosis of hepatocellular carcinoma in cirrhotic patients: a proof-of-concept study using serum micro-Raman spectroscopy

I. Taleb, G. Thiéfin, C. Gobinet, V. Untereiner, B. Bernard-Chabert, A. Heurgué, C. Truntzer, P. Hillon, M. Manfait, P. Ducoroy and G. D. Sockalingum*

This study demonstrates the potential of Raman microspectroscopy coupled with advanced chemometrics for discriminating sera from patients with and without hepatocellular cancer (HCC).

4015

Determination of cell cycle phases in live B16 melanoma cells using IRMS

Diana E. Bedolla, Saša Kenig, Elisa Mitri, Paolo Ferraris, Alessandro Marcello, Gianluca Grenci and Lisa Vaccari*

New silicon modified BaF$_2$ microfluidic devices were used for the assessment of cell cycle stages of live B16 melanoma cells by using label-free IRMS. Spectroscopic results were cross-checked with flow cytometry data showing a good agreement between these techniques.

B16 cell cycle phase assessment by FC and IRMS in microfluidic devices
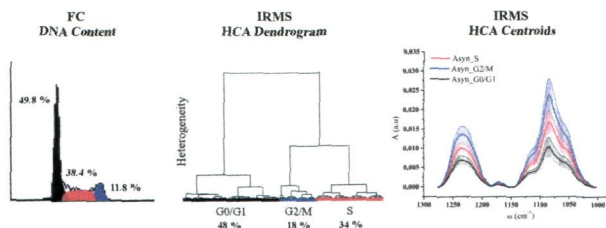
4022

Reagent-free monitoring of multiple clinically relevant parameters in human blood plasma using a mid-infrared quantum cascade laser based sensor system

Markus Brandstetter, Tamara Sumalowitsch, Andreas Genner, Andreas E. Posch, Christoph Herwig, Andreas Drolz, Valentin Fuhrmann, Thomas Perkmann and Bernhard Lendl*

QCL based mid-infrared point-of-care sensor for reagent-free multianalyte detection in human blood plasma.
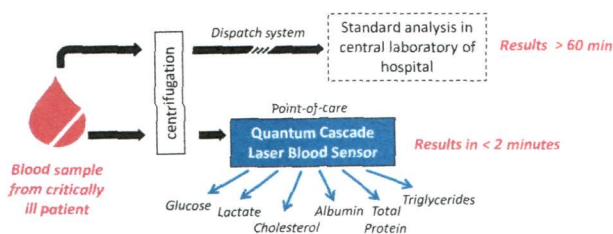

4029

Optical fibre probe NIR Raman measurements in ambient light and in combination with a tactile resonance sensor for possible cancer detection

Morgan Nyberg, Kerstin Ramser and Olof A. Lindahl*

First measurements on a combined instrument with a thin fibre optic Raman probe mounted inside a hollow tactile resonance sensor have been performed in ambient light on porcine tissue.
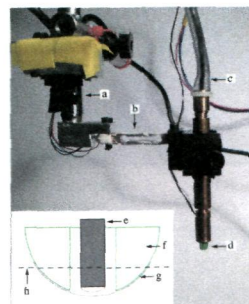

4035

Spectral histopathology of colon cancer tissue sections by Raman imaging with 532 nm excitation provides label free annotation of lymphocytes, erythrocytes and proliferating nuclei of cancer cells

Laven Mavarani, Dennis Petersen, Samir F. El-Mashtoly, Axel Mosig, Andrea Tannapfel, Carsten Kötting and Klaus Gerwert*

This article presents label-free detection of p53 active areas in colon cancer tissue sections and classification of the surrounding tissue components by Raman imaging.

4040

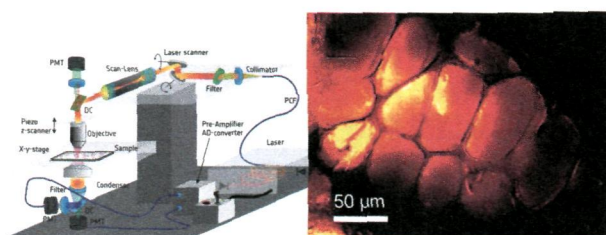Visible   ν(CH) ~2900 cm⁻¹   Amide II ~1545 cm⁻¹
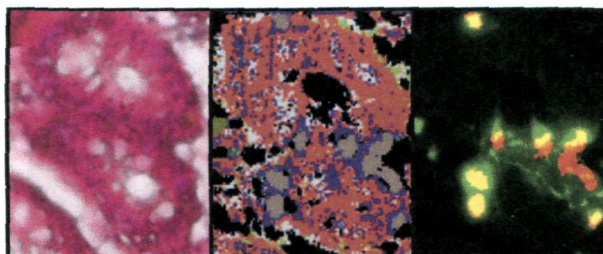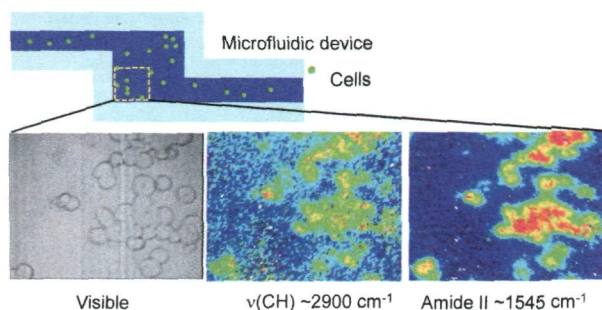
Aberration-free FTIR spectroscopic imaging of live cells in microfluidic devices

K. L. Andrew Chan and Sergei G. Kazarian*

FTIR spectroscopic images of live cells in aqueous solutions and in droplets in microfluidics have been obtained without optical aberrations.

4048

A compact microscope setup for multimodal nonlinear imaging in clinics and its application to disease diagnostics

Tobias Meyer, Martin Baumgartl, Thomas Gottschall, Torbjörn Pascher, Andreas Wuttig, Christian Matthäus, Bernd F. M. Romeike, Bernhard R. Brehm, Jens Limpert, Andreas Tünnermann, Orlando Guntinas-Lichius, Benjamin Dietzek, Michael Schmitt and Jürgen Popp*

Realization of a high performance small-sized and simple-to-use instrument for molecular imaging in clinical settings.
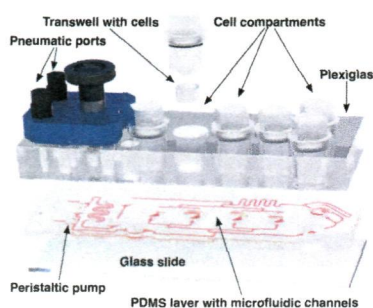
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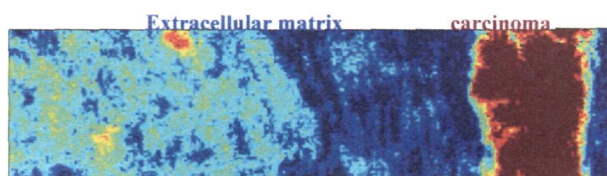
Change in the microenvironment of breast cancer studied by FTIR imaging

S. Kumar, C. Desmedt, D. Larsimont, C. Sotiriou and E. Goormaghtigh*

Depletion of a collagen component near the tumor (in red). Intensity of the second derivative of the scaled spectra at 1632 cm⁻¹.

4066

Fluorescent optical fiber sensors for cell viability monitoring

Ilia Sergachev, Alexander Rusanov, Evgeny Trushkin, Dmitry Sakharov,* Uwe Marx and Alexander Tonevitsky

A new simple method for non-invasive cell culture viability monitoring based on vital fluorescent stains is introduced, and its efficiency for long-term experiments on cells is demonstrated.

4070

A new dimension for cell identification by FTIR spectroscopy: depth profiling in attenuated total reflection

A. Gaigneaux and E. Goormaghtigh*

Modulation of penetration depth in ATR improves cell type discrimination.
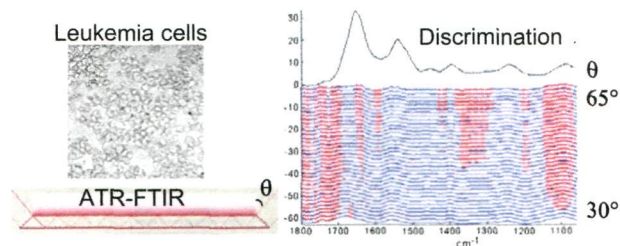

4076

Improving the classification accuracy for IR spectroscopic diagnosis of stomach and colon malignancy using non-linear spectral feature extraction methods

Sanguk Lee, Kyoungok Kim, Hyeseon Lee,* Chi-Hyuck Jun, Hoeil Chung* and Jong-Jae Park

Non-linear feature extraction recognizes minor spectral difference between normal and malignant tissues, and improves accuracy of diagnosis based on IR spectroscopy.
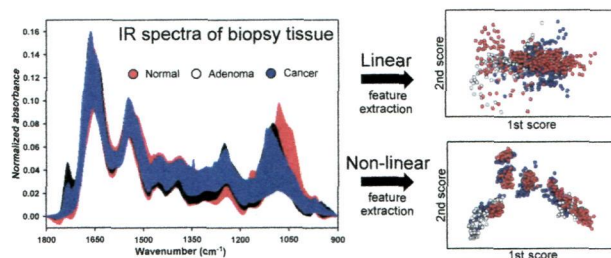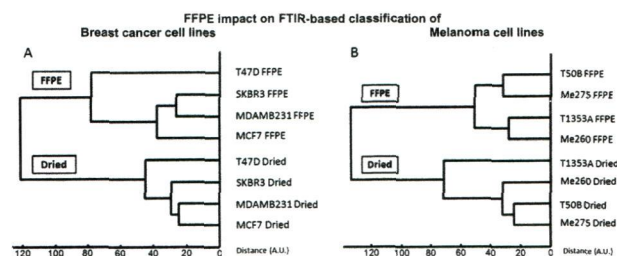

4083

Breast cancer and melanoma cell line identification by FTIR imaging after formalin-fixation and paraffin-embedding

M. Verdonck, N. Wald, J. Janssis, P. Yan, C. Meyer, A. Legat, D. E. Speiser, C. Desmedt, D. Larsimont, C. Sotiriou and E. Goormaghtigh*

Closely related cancer epithelial cell lines are still successfully identified by FTIR spectroscopy after FFPE processing.
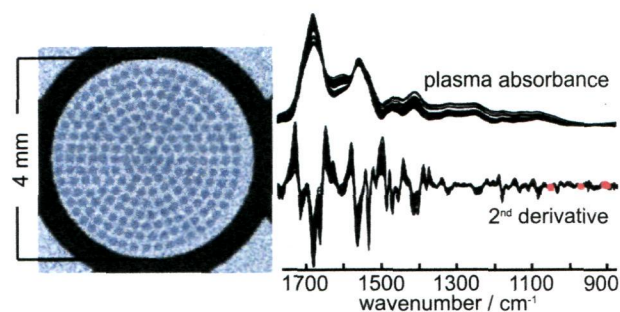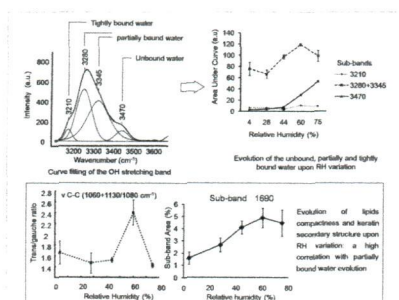

4092

FTIR spectroscopy of biofluids revisited: an automated approach to spectral biomarker identification

Julian Ollesch,* Steffen L. Drees, H. Michael Heise, Thomas Behrens, Thomas Brüning and Klaus Gerwert*

Infrared spectra of films from printed patterns of sub-nanoliter blood volumes are evaluated for disease pattern recognition of bladder cancer.

4103

Effects of atmospheric relative humidity on Stratum Corneum structure at the molecular level: *ex vivo* Raman spectroscopy analysis

Raoul Vyumvuhore, Ali Tfayli,* Hélène Duplan,
Alexandre Delalleau, Michel Manfait
and Arlette Baillet-Guffroy

Partially bound water plays an important role in the optimal physical properties and physiological functions of the skin.
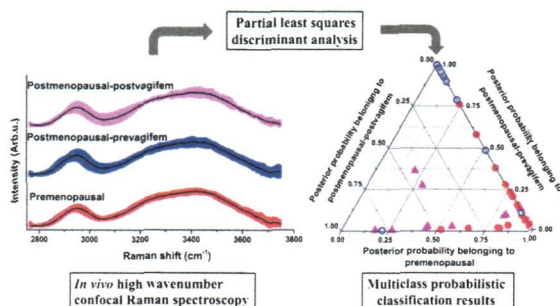
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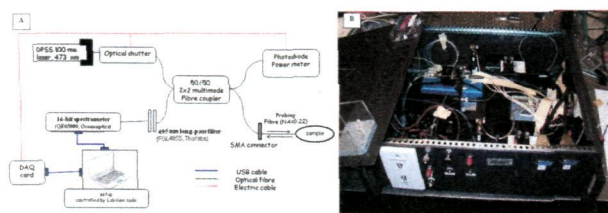
Total viable bacterial count using a real time all-fibre spectroscopic system

E. Bogomolny, S. Swift and F. Vanholsbeeck*

In the present work, we have developed a novel all-fibre spectroscopic optical setup for sensitive and near real time bacterial enumeration in the aquatic environment.

4120

Non-invasive analysis of hormonal variations and effect of postmenopausal Vagifem treatment on women using *in vivo* high wavenumber confocal Raman spectroscopy

Shiyamala Duraipandian, Wei Zheng, Joseph Ng,
Jeffrey J. H. Low, A. Ilancheran and Zhiwei Huang*

High wavenumber confocal Raman spectroscopy for non-invasive monitoring of hormonal/menopausal variations in women.

4129
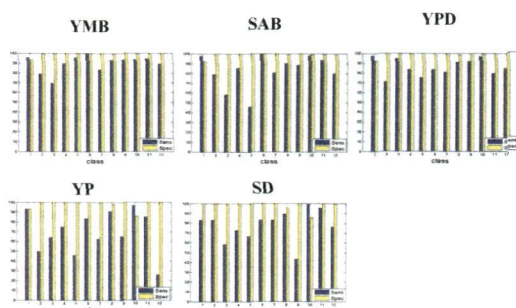
FTIR spectroscopic characterization of differently cultivated food related yeasts

V. Shapaval,* B. Walczak, S. Gognies, T. Møretrø,
H. P. Suso, A. Wold Åsli, A. Belarbi and A. Kohler

A high-throughput micro-cultivation protocol based on micro-cultivation and several cultivation media increases the discrimination ability of yeasts in FTIR spectroscopy.

4139

Substrate contributions in micro-ATR of thin samples: implications for analysis of cells, tissue and biological fluids

Paul Bassan, Ashwin Sachdeva, Joe Lee and Peter Gardner*

Experimental and theoretical results demonstrating that low-e IR-reflective slides do not prevent spectral contamination from the underlying glass layer during micro-ATR spectroscopy.
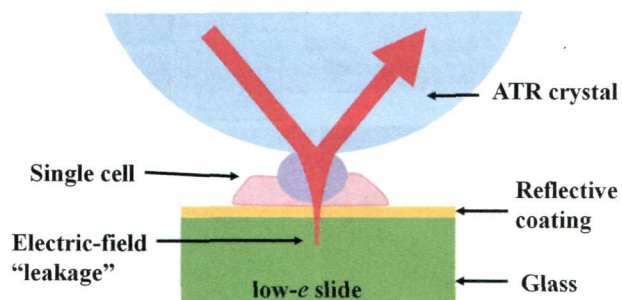

4147

Fourier transform infrared microspectroscopy reveals that tissue culture conditions affect the macromolecular phenotype of human embryonic stem cells

Julie Cao, Elizabeth S. Ng, Don McNaughton, Edouard G. Stanley, Andrew G. Elefanty, Mark J. Tobin and Philip Heraud*

We showed that FTIR microspectroscopy could detect phenotypic changes in human embryonic stem cells and their differentiated progeny induced by the cellular environment.
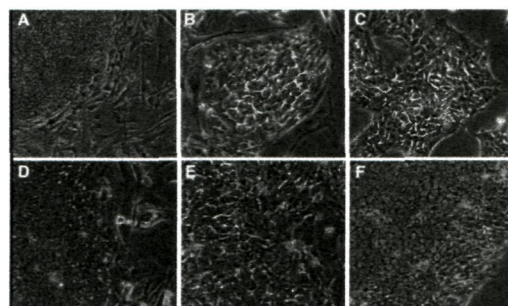
4161

Raman spectroscopy of serum: an exploratory study for detection of oral cancers

Aditi Sahu, Sharada Sawant, Hitesh Mamgain and C. Murali Krishna*

The proposed oral cancer detection method shows the advantage of offering an objective, real-time and minimally invasive detection as a complementary diagnostic tool which may have the potential to improve the efficiency of screening procedures for oral cancers.
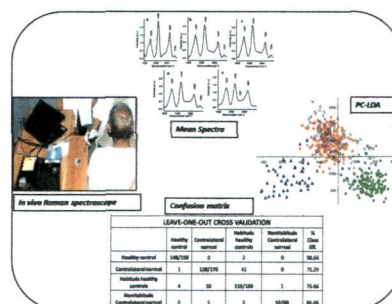

4175

In vivo Raman spectroscopy of oral buccal mucosa: a study on malignancy associated changes (MAC)/ cancer field effects (CFE)

S. P. Singh, Aditi Sahu, Atul Deshmukh, Pankaj Chaturvedi and C. Murali Krishna*

Raman spectroscopic approach for identification of MAC/ CFE in oral cancers: A. Raman spectroscope, B. Mean spectra, C. Scatter plot, D. leave-one-out cross validation.

4183
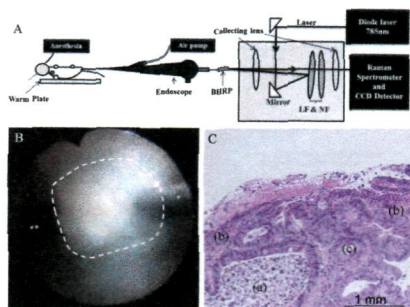
Raman endoscopy for the *in situ* investigation of advancing colorectal tumors in live model mice

Akinori Taketani, Retno Hariyani, Mika Ishigaki, Bibin B. Andriana and Hidetoshi Sato*

This paper describes an application study of a novel technique, miniaturized Raman endoscopy for mice. It can observe tumor development continuously in a single live subject, which is difficult for human patients. We observed the molecular changes in advancing tumor and also in shrinking tumor. The Raman observation suggests that the shrunk tumor is changed in type into a flat tumor.

4191
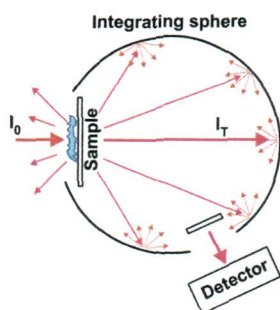
Minimising contributions from scattering in infrared spectra by means of an integrating sphere

Alexandre Dazzi, Ariane Deniset-Besseau and Peter Lasch*

In this paper it is demonstrated that scatter-induced distorted mid-infrared spectral line shapes can be minimised by using an integrating sphere unit.