2007

UNIVERSITY OF LIVERPOOL

Programme and Abstracts for Multidisciplinary Workshop on "Image Processing Techniques and Applications"

Wednesday, 28th November 2007
at Math Sciences Building

http://www.liv.ac.uk/~cmchenke/imagew/

Under the auspices of
"Centre for Mathematical Imaging Techniques"

Supported by the Faculty of Science

Organized by

Ke Chen, Department of Mathematical Sciences (Comp Math Group)
Colin Baker, School of Health Sciences (Division of Medical Imaging)
Andy Cossins, School of Biological Sciences (Biocomplexity Institute)

UNIVERSITY OF LIVERPOOL

http://www.liv.ac.uk/~cmchenke/imagew/

Multidisciplinary Workshop Programme for 28 November 2007

"Image Processing Techniques and Applications"

Venue: Maths Sciences Building (Precinct Map No 39)

09:00 09:25 Registration + Tea/Coffee
09:25 09:30 Prof Andy Cossins: "Introduction / Welcome"

SESSION 1 --- Chair: Prof Andy Cossins, Director of Biocomplexity Institute / Director of LINSET

T1	09:30	10:10	Prof Arvid Lundervold: "Mathematics in biomedical imaging – examples from cell imaging, brain imaging and kidney imaging"
T2	10:10	10:30	Prof Asoke Nandi: "Machine learning and image processing for breast cancer diagnosis"
T3	10:30	10:50	Prof Peter Giblin: "Singularity theory and geometry in computer vision"
T4	10:50	11:10	Prof Ke Chen /Mr C Brito /N Chumchob /N Badshah: "Variational models for automatic image segmentation and registration"
	11:10	11:40	Refreshments

SESSION 2 --- Chair: Prof Peter Giblin, Dept of Mathematical Sciences

T5	11:40	12:20	Prof Alan Nahum: "Radiobiologically optimised radiotherapy"
T6	12:20	12:40	Prof Neil Roberts /Dr Laura Parkes: "Non-invasive Measurement of Brain Structure, Function, Integrity, Connectivity and Metabolism"
T7	12:40	13:00	Dr Colin Baker: "State of the art radiotherapy and the need for advanced imaging capabilities"
	13:00	13:50	Lunch [*Free/online registration before 23 Nov required*]

SESSION 3 --- Chair: Prof Ke Chen, Dept of Mathematical Sciences

T8	13:50	14:30	Prof Chris Moore: "Image Processing in Measurement Guided radiation Therapy"
T9	14:30	14:50	Dr Hane M Aung /Dr Y Goulermas: “An image analysis and measurement system for video-fluoroscopic (vf) evaluation of swallowing dysfunctions”
T10	14:50	15:10	Dr Ren Cooper / Dr A Boston / Dr H Boston / Prof Paul Nolan: "Gamma-Ray imaging with segmented HPGe detectors"
	15:10	15:40	Refreshments

SESSION 4 --- Chair: Dr Colin Baker, Division of Medical Imaging and Radiotherapy, School of Health Sciences

T11	15:40	16:20	Dr John Kleijne: "Fluorescence in Vivo imaging of disease biology"
T12	16:20	16:40	Dr Steve Barrett / Prof Peter Weightman : "Spin-offs from image analysis for scanning microscopy"
T13	16:40	17:00	Dr Bernard Diaz / Dr Derek Gould: "CRUEL imaging - problems and techniques from the UK CRAIVE project for Interventional Radiology"
T14	17:00	17:20	Dr David Spiller / Dr P Gould / Prof M White: "Higher throughput multi-parameter time lapse imaging and analysis of living cells"

CONTENT OF ABSTRACTS

T1. Prof Arvid Lundervold

"Why we need mathematics in biomedical imaging --- examples from cell imaging, brain imaging and kidney imaging"

Abstract:
Medical and biological imaging technology have become increasingly sophisticated in terms of spatial resolution, temporal resolution, and the ability to acquire multichannel or multispectral images from a given organ or tissue sample, both in vivo and in vitro. The amount of imaging data from a medical examination or a biological experiment can be several tenths or even hundreds of megabytes, where relevant tissue or cellular information is usually distributed in both time and space. Frequently, the clinician or biologist will not only inspect and describe these images qualitatively, but ask quantitative questions to the data that are related to "size", "shape", "change", or "motion", as well as physiological or molecular parameters that can be estimated from the data, such as "flow", "perfusion", and "diffusion".

We will present problems and data from cell imaging (automated detection of tunneling nanotubes in 3D images), brain imaging (tissue segmentation, hippocampal morphometry, and diffusion tensor imaging), and dynamic contrast enhanced MR imaging of the kidney (motion correction and voxel-based time course analysis). All examples represent current research problems at various laboratories and research groups at the University of Bergen, i.e. the Molecular Imaging Center (http://www.uib.no/med/mic)
in the fMRI group (http://fmri.uib.no) of the Department of Biomedicine, and the Image Processing group (http://math.uib.no/BBG) of the Department of Mathematics, where these problems are attacked partly in collaboration with other investigators abroad.

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T2. Prof Asoke K Nandi

"Machine learning and image processing for breast cancer diagnosis"

Abstract:
In my research group many researchers have worked in different aspects of this problem. I would like to review some of these works, including the achievements. This represents work of about four people. I hope to give a view of future work.

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T3. Prof Peter J Giblin

"Singularity theory and geometry in computer vision"

Abstract:
I shall describe briefly the areas of computer vision in which I have been involved over the past 20 years, applying methods of differential geometry and singularity theory. These include: motion from apparent contours (silhouettes), skeletons (medial axes) and views of illuminated surfaces.

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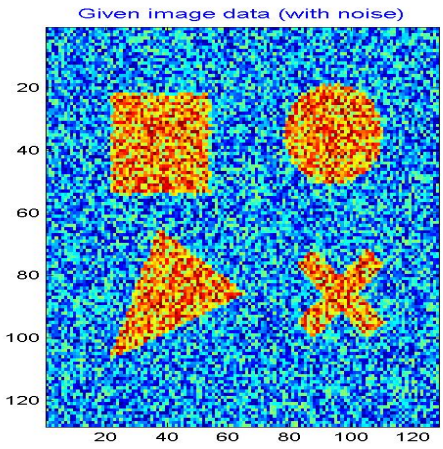
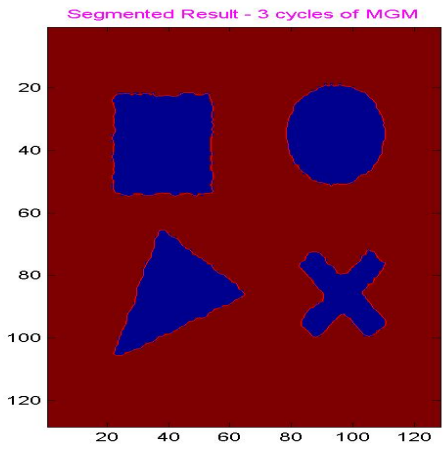
T4. Prof Ke Chen

"Variational Models for Automatic Image Segmentation and Registration"

Variational image models provide a recent set of nonlinear image processing tools for many image sciences applications, traditionally tackled by linear models and techniques. Such models typically minimize a suitably chosen energy functional that is connected to the geometry of the underlying (desired) image - mathematically sharp features of an image are provided by functions with a low differentiability such as from the space of bounded variations. Overall, variational image models provide a rich source of nonlinear PDEs and nonlinear optimisation problems for mathematicians in various disciplines.

In this talk, we first highlight some simulation results that can be achieved with some of these models. We then review some modeling and computational algorithms' details for 2 of such models, namely, an Image Segmentation model and an Image Registration model. Our main expertise is in the development of fast multilevel / multigrid algorithms, without which the variational models can be prohibitively expensive to implement.





Finally we conclude with some recent (and preliminary) work done in our group for multimodality co-registration models and an outline of future work.

[*] *The included figure shows a noisy input image z (left) that has been by segmented by 3 cycles of our MG method solving the T F Chan-L Vese (2001) model, which combines the Mumford-Shah functional minimization with the level set approach. Our numerical method is as least 20 times faster than the existing method if the image size is large.*

General references:

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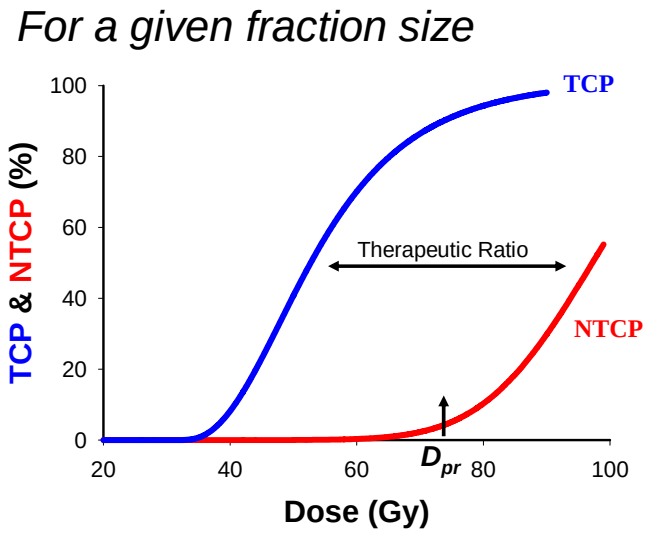
T5. Prof Alan E. Nahum

"Radiobiologically Optimised Radiotherapy"

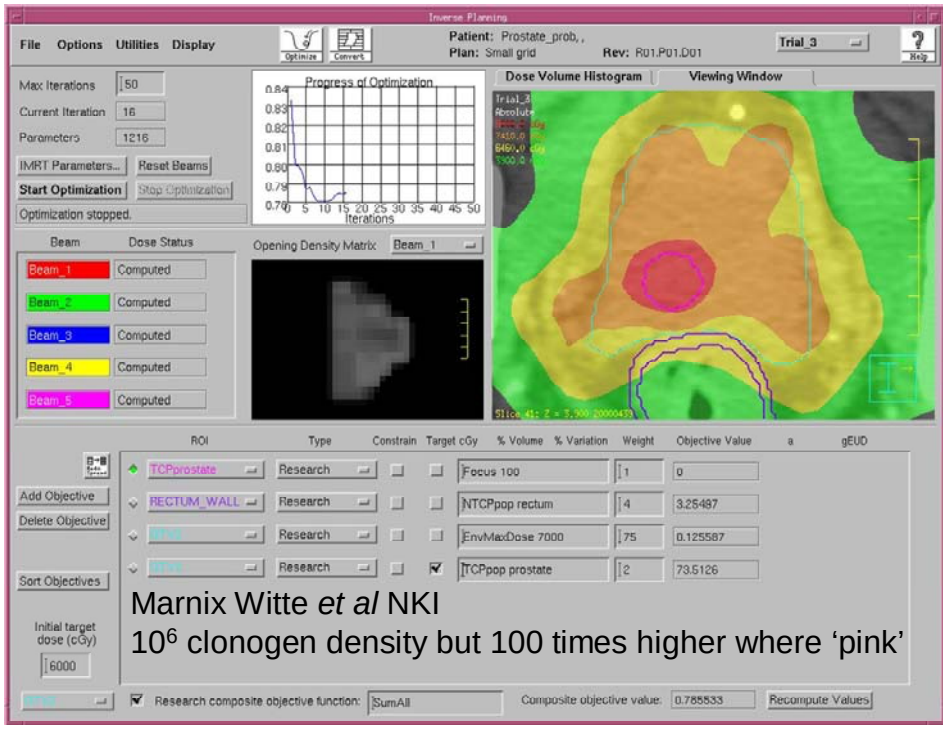
Advances in technology and in computing have given us computer-controlled linear accelerators equipped with multileaf collimators and wonderful 3D graphics workstations to perform treatment planning; additionally we have conceptual advances such as stereotaxy (cranial and extra-cranial) intensity modulation (IMRT) and helical tomotherapy. Functional imaging modalities such as PET and MRI/S promise information on the 'biology' of the patient's tumour and organs at risk. However, if we don't know how to convert 'physics', i.e. dose distributions, into clinical outcome then these technological advances will have much less impact on radiotherapy outcome than they ought to have.

Radiobiology has traditionally concerned itself with determining surviving fraction vs. (uniform) dose curves for human tumour cell lines. However, in the 3D era we need models which connect dose *distributions* (and fractionation regimens) in tumours and normal tissues (generally in the form of dose-volume histograms) with the probabilities of tumour (local) control – TCP - and of complications – NTCP. Such models now exist and their active use in treatment planning ushers in the era of *Conformal Radiobiology*.



How can we use TCP and NTCP models in optimising radiotherapy outcome? The most basic or 'Level-I' optimisation is to take an existing 'standard' treatment plan with its standard total dose and fraction size, compute the NTCP and then adjust the total dose until an accepted complication risk is obtained: *isotoxic customised dose prescription.* This will yield immediate benefits in, for example, lung-tumour radiotherapy. 'Level-II' optimisation uses the TCP and NTCP functions 'upfront' in the optimisation process to determine the beam weights and even angles, or, in the case of IMRT, to perform 'inverse

planning'. A typical criteria might be 'Maximise the TCP for NTCP = 2.5%'. In this Level-II mode no constraints need be set regarding uniform dose in the target volume – the TCP model will take of this.



We need to start experimenting now with radiobiologically based optimisation, without waiting until the TCP and NTCP models are 'perfect'. The clinician may still use conventional tools such as single-CT slice isodoses and DVHs to approve a radiobiologically optimised plan but she/he is going to find a marked improvement in the quality of such a plan.

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T6. Prof Neil Roberts and Dr Laura Parkes

"Non-invasive Measurement of Brain Structure, Function, Integrity, Connectivity and Metabolism in Health and Disease"

The research programme at MARIARC is focussed in Neuroscience. In particular, a team of Physicists, Mathematicians, Computer Scientists and Radiographers have over the past two decades been collaborating with Psychologists, Biologists and Clinicians developing methods for quantifying the composition, organisation and functioning of tissues and compartments in the living human body in health and disease. In order to pursue this research programme we have exploited the versatility of Magnetic Resonance Imaging (MRI) techniques and more recently have added the complementary modalites of Magnetoencephalography (MEG) and Electroencephalography (EEG) and the screening technique of functional trans-cranial doppler (fTCD) ultrasound.

A variety of approaches have been used to enable measurement of parameters of interest for a wide range basic science and clinical science applications and in clinical practice. For example, with regard to brain structure and tissue characterisation (using stereology, voxel based morphometry (VBM) and MR relaxometry) through longstanding collaborations with the Department of Psychology and the Walton Centre for Neurology and Neurosurgery (WCNN) we have measured hippocampal volume and tissue integrity in investigations of the neural bases of memory in healthy subjects and for the pre-surgical investigation of patients with clinical evidence of temporal lobe epilepsy. We have also used this combination of stochastic geometry and statistical probability, and image segmentation and image registration algorithms, to study the neural bases of expert musical ability in symphony orchestra musicians, to identify the region of the frontal lobes supporting fluid intelligence and to test Crow's hypothesis that schizophrenia "is the price we pay for language".

With regard to brain metabolism we have applied Magnetic Resonance Spectroscopy (MRS) in collaboration with the Department of Geriatric Medicine to measure the variation in brain water content and tissue chemistry associated with healthy ageing, and in collaboration with the Department of Musculoskeletal Science to study the performance of healthy and diseased muscle during exercise.

Studies of brain function make use of the high spatial resolution provided by functional Magnetic Resonance Imaging (fMRI) and the inherently high temporal resolution of MEG and EEG. In the case of fMRI the majority of studies have been based on the Blood Oxygen Level Dependent (BOLD) contrast mechanism and more recently we are employing the inherently more quantitative technique of Arterial Spin Labelling (ASL). Mathematical modelling of the physiological response allows measurement of the change in cerebral blood flow and oxygen metabolism which may be important indicators of cerebrovascular disease. We are developing new analysis methods, moving from single-

voxel approaches to the classification of multi-voxel activation patterns across the brain. The data present challenges due to very large dimensionalities but very small numbers of samples per class. This novel approach considers the brain as a connected system rather than the traditional view of a collection of isolated functional areas. We have a programme of translational research using functional imaging to improve diagnosis, management and treatment of neurological disorders, such as chronic pain, autism, depression, psychosis, multiple sclerosis, stroke and epilepsy.

In the health sciences and the humanities we are investigating whether we can use brain imaging to predict instrumental preference, and studying the neural correlates of Shakespeare's functional shift with Philip Davis of the School of English, the brain's response to touch (e.g. massage) in collaboration with Unilever Research and the brain changes associated with skill acquisition in collaboration with The Learning Partnership, The University of Lancaster and the Royal Northern College of Music.

Finally, in a group of inter-related studies we are investigating the significance for cognitive ability and performance of structural brain asymmetry and functional lateralisation, the validity of Crow's prediction that these are influenced by a gene on the sex chromosomes, their relationship to language and handedness, and the point at which they entered the evolutionary record (i.e. primates, modern humans, Neanderthals) and its potential significance, backed by support from the European Union programme 'What it means to be human'. Also, in collaboration with the Department of Biological Science we are investigating the neural bases of self-referential processing, attraction and mate choice and testing Dunbar's hypothesis that brain size and cognitive capacity is related to social group size.

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T7. Dr Colin Baker

"State of the art radiotherapy and the need for advanced imaging capabilities"

Abstract

Recent years have seen significant advances in the technology available for cancer treatment with external beams of ionising radiation, both in terms of treatment delivery and in the availability of a variety of imaging modalities.

Advanced technology provides opportunities for refining patient treatment in several areas:

- Improved tumour localisation through image registration and fusion
- Tracking of inter- and intra-fraction tumour motion, leading to adaptive radiotherapy and beam gating
- Functional imaging of tumour and normal tissue, having the potential for concurrent dose boosting and/or normal tissue sparing.

An outline of the above areas of state of the art radiotherapy will be presented and the potential for further development discussed.

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T8. Prof Chris J Moore

"Image Processing in Measurement Guided radiation Therapy"

Abstract

This presentation will consider measurement guided radiation therapy (MGRT). At the Christie Hospital MGRT grew from the multidisciplinary, collaborative foundations laid in European Framework-IV projects INFOCUS (BMH4-CT95-0567 Burton, Moore et al) and ARROW (BMH-98-3660 Moore, Burton et al). The primary aim remains to move towards seeing and measuring a treatment as it is given, dynamically in 3D, in order to provide the 4D evidence for patient setup, tumour targeting and treatment adaptation, and improve our understanding of the impact of changing patterns of motion and deforming anatomical shape on treatments.

At the Christie Hospital, a prototype Synergy X-ray image guided radiation therapy (IGRT) machine from Elekta has been made clinically useful by both pre- and post reconstructive X-ray image processing [1]. A priority has been (and remains) to increase cone beam CT (CBCT) image quality to that seen in the corresponding pre-treatment CT planning scan, which is used as a positioning reference standard and for dosimetric computation. For bone based patient positioning/setup, it was shown that only a fraction of the X-ray image profiles theoretically needed for full CBCT volume reconstruction was needed for use with automated 3D matching to planning CT scans [2]. However, for tumour targeting and treatment re-planning/adaptation, improved soft-tissue visibility is essential. To this end prior knowledge of the low frequency changes to grey scale content in the planning CT scans themselves has recently been used to correct CBCT image volumes (patent pending Moore & Marchant).

Radiotherapy structure delineation has remained largely subjective, until recently failed to capitalise on prior knowledge, and is ill suited to the avalanche of relatively poor quality CBCT emerging from the treatment room. In project SCULPTER (GR/S41340/01 Moore) the evidence needed for constructing a 3D target or organ was reduced to a sparse cloud of clinically defensible points. Compactly supported radial basis functions allowed points to interact, analogous to varying the elasticity of the surface, and variable 3D detail was provided by changing the number of spherical harmonic coefficients included in an advanced statistical shape model, developed from archived expert data [3,4]. This clinician led approach now has to be married with a plausible segmentation/refinement approach that functions with suboptimal CBCT image quality.

Optical body sensing has been researched and a simple method of assessing the impact of measured surface changes, in terms of expected organ deformations, on conformal treatments demonstrated for rectal cancer [5] and, most recently, developed for breast IMRT using CBCT IGRT [6]. In early 2007 work began on EPSRC project MEGURATH (Moore, Burton & Shark EP/D078415/1, EP/D077540/1 & EP/D077702/1). The aim is to develop real-time, wrap round, optical body sensing, synchronised with CBCT scanning to link surface and volumetric tissue deformations and make it possible to test the hypothesis

that deformable mapping [7] of the pre-treatment planning CT scan into the measured surfaces can significantly reduce the need for X-ray IGRT.

References:

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T9. Dr Hane M Aung

"An Image Analysis and Measurement System for Video-Fluoroscopic (Vf) Evaluation of Swallowing Dysfunctions"

The clinical procedure known as the Modified Barium Swallow is one of the principal investigation techniques in assessing swallowing dysfunctions or Dysphagia. Commonly the X-Ray sequence of this procedure is captured onto video, a process known as Video-Fluoroscopy (VF), and used in the clinical domain as a standard assessment technique. Spatial-temporal measurements such as the time taken for the liquid (bolus) to transit out of the oral cavity (Oral Transit Time) are vital quantitative measures in investigating Dysphagia. However the current frame by frame inspection methods to determine these quantities have a high level of subjectivity and a low level of repeatability.

A novel semi-automated user steered framework that extracts the measures is presented. The framework is based on live wire delineation of anatomical landmarks and visualization of intensity change at the landmarks over time. The live wire technique creates weighted sum multi-objective cost functions based on edge, gradient magnitude and directional information of the image with a minimum located by the user. A greedy local search algorithm traces a path from the hovering point of the mouse cursor to the minimum. The spatial-temporal measures can be determined from the change in intensity at the location of the delineation over the whole sequence.

An inherent problem arises from movement of the patient in the video. Therefore there is need to adjust the location and shape of the delineated landmark. Areas based methods to register consecutive frames are currently being investigated to address this issue. Furthermore this method must also account for occlusion of the landmark by the passing bolus in some frames.

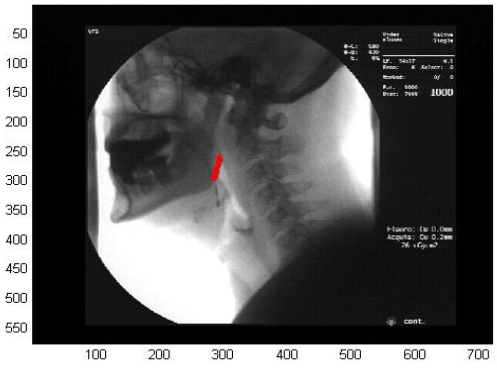

Fig.1 *Ramus of Mandible* landmark selected with user steered live wire.

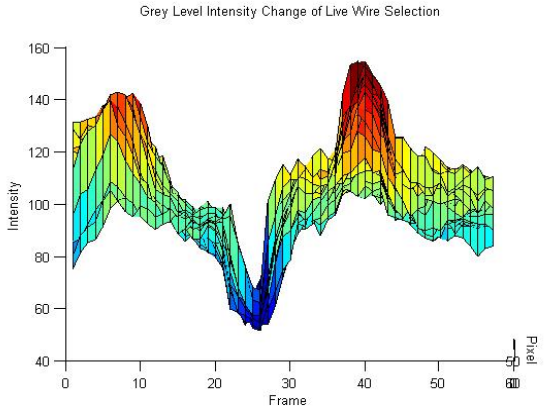

Fig.2 Intensity change per frame at the selected landmark, low intensity indicates bolus passing.

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T10. Dr Reynold Cooper

"Gamma-Ray Imaging with Segmented HPGe Detectors"

Applications of gamma-ray imaging ranging from medicine to defence and homeland security have long relied on the use of scintillation detectors. Scintillation detectors, while providing high stopping power offer poor energy resolution and limited position sensitivity, often prohibiting the development of new devices and techniques.
In contrast, the unrivalled energy resolution provided by Hyperpure Germanium (HPGe) has made them the detector of choice for gamma-ray spectroscopy studies for over 20 years. Recent advances in the manufacturing of HPGe detectors have led to the development of devices with segmented electrode structures. This, coupled with the development and application of digital Pulse Shape Analysis (PSA) algorithms, has enabled segmented HPGe detectors to achieve spatial resolutions of around $1mm^3$, while the use of gamma-ray tracking (GRT) techniques will allow the accurate reconstruction of the path of a scattered gamma-ray through the detection medium.
The application of this technology to Positron Emission Tomography (PET) is being investigated by the SmartPET project through the development and evaluation of a small animal PET system based on the use of planar HPGe detectors. The SmartPET system has been used to image a range of point-like and distributed sources, employing both analytic (Filtered Back Projection – FBP) and statistical (Maximum Likelihood Expectation Maximisation – MLEM) reconstruction techniques. These results show that the system is capable of achieving reconstructed spatial resolution limited by the physical constraints of positron physics while providing the opportunity to include greater fractions of events in the reconstruction data set.
In addition, these advances in 3D position sensitive HPGe detector technology have allowed the development of Compton imagers which exploit the well defined kinematics of Compton scattering to provide high efficiency imaging. Through the use of Compton "cone beam" reconstruction the Compton camera is finding application in homeland security and may also provide a high efficiency alternative to the conventional gamma camera employed in clinical Single Photon Emission Computed Tomography (SPECT) imaging.

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T11. Dr John Kleijne

"Fluorescence *In Vivo* Imaging of Disease Biology"

Over the past decade, breakthrough advances in genomics and proteomics have driven a fundamental evolution in our understanding of the molecular basis of disease. VisEn Medical provides technologies that translate this new knowledge into real-time molecular mapping of disease states in vivo in research, drug development and into the clinic. Quantitative in vivo fluorescence imaging transcends the boundaries of traditional optical imaging of biological structures and physiology by providing information at the molecular level about disease states and therapeutic response.

VisEn Medical's proprietary in vivo fluorescence imaging probes and Fluorescence Molecular Tomography (FMT) system represent a powerful tool for research and drug development in the imaging of biological processes and pharmaceutical activity in living animals. VisEn's FMT system enables true quantification and tomographic slicing of fluorochrome concentration and distribution at any depth in small animal research models. Traditional mouse models of cancer rely primarily on ex vivo measurements of disease morphology and histologic analysis for the assessment of tumor burden. These measurements of disease may be distant from the actual biological targets of interest and can be time consuming, expensive, and impractical for measuring local disease biology in context. Further, these metrics do not enable measurements in living animals and merely focus on changes in shape or size within the affected tissue. In contrast, by using VisEn's near infrared (NIR) in vivo imaging probes in combination with VisEn's FMT system, the biological processes that change with disease progression and therapeutic response, rather than alterations in morphology, can be visualized non-invasively over time.

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T12. Dr Steve Barrett

"Spin-Offs from Image Analysis for Scanning Microscopy -- Generating Custom Solutions For One-Off (?) Problems"

Image SXM is a version of the public domain program NIH Image that has been extended to handle image processing and image analysis of scanning microscope images [1]. Although intended as a set of software tools to help users of scanning microscopy systems to load and display their image data, it has also been used as a platform on which to build solutions for specific imaging problems within microscopy more generally.

Examples include: identifying shapes, complete and incomplete, within an image [2]; finding and straightening chromosomes to simplify karyotype mapping [3]; enhancing and identifying the features in an image having particular rotational symmetry [4]; quantifying the degree of entanglement of linear objects such as carbon nanotubes [1]; quantifying the extent of particulate matter in images of cells [5]; identification of parasites in images of cells [5].

The nature of the problems may be categorised as image processing (how can the image be processed to reveal the information required?) or image analysis (what properties of the objects in the image can be used to quantify the desired parameter?) or recognition (how can this object be distinguished from the other objects?). Each problem being considered may benefit from the solution of an earlier problem, or even a generic solution, but in many cases the particular set of circumstances that define a specific problem requires that the solution is 'custom-made'. The philosophy behind the exploration and development of algorithms that lead to useful solutions will be discussed for the examples given above.

1 http://www.ImageSXM.org.uk

2 Software for scanning microscopy, S D Barrett, Proc. Roy. Microsc. Soc. 37 (2002) 167-174

3 A software tool to straighten curved chromosome images, S D Barrett and C R de Carvalho, Chromosome Res. 11 (2003) 83-88

4 Imaging quasicrystal surfaces using scanning tunnelling microscopy, R McGrath, L Leung, S D Barrett and J Ledieu, Proc. Roy. Microsc. Soc. 40 (2005) 215-220

5 In collaboration with the School of Tropical Medicine (algorithms still under development)

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T13. Dr Bernard Diaz

"CRUEL Imaging"

Abstract

The CRAIVE Research Unit Liverpool (CRUEL) is the local wing of a multi-group collaboration looking at simulation and other issues associated with Interventional Radiology.

The problem is how to train clinicians to perform all the tasks associated with these "pin-hole" interventions. Among the problems is that the clinician uses multi-modal imagery, typically Fluoroscopy and CT but also US, NMR, and MRI to do this work.

The presentation will outline the work done in CRAIVE, and in Liverpool by CRUEL, and will cover some of the imaging issues that have to be resolved. One of these, initial work on vascular segmentation that is used when comparing beginner and expert renal catheterisation, will be described in some detail, including coverage of the level set method, and the use of the ITK toolkit.

The talk concludes with an outline of some novel approaches to the issues based on quaternion tesseral addressing and outlines how this impacts on the image processing that has to be done.

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T14. Dr David G Spiller

"Higher throughput multi-parameter time lapse imaging and analysis of living cells"

Multiple signalling pathways control cell fate through regulation of transcription. The dynamic configuration of signalling networks enables cells to respond appropriately to biological signals & stresses. The number of central signalling nodes that regulate key processes in the mammalian cell remains relatively small. Loss or abnormal functioning of key proteins (e.g. p53 or NF-κB) can result in aberrant cell function leading to diseases such as inflammation and cancer. The efficacy of the cellular information processing steps that filter multiple signal information is critical for the organism to avoid disease.

Some of the most important tools for the elucidation of intracellular signalling in living cells have been proteins from luminescent organisms. These proteins have now been mutagenised to form a wide range of colours and have led to a revolution in quantitative non-invasive measurement of cellular processes. We have developed multi-parameter imaging approaches to study signalling, gene expression and cell fate in single living mammalian cells. Signalling by the transcription factor Nuclear Factor kappa B (NF-κB) involves its release from Inhibitor kappa B (IκB) in the cytosol, followed by translocation into the nucleus. NF-κB regulation of IκBα transcription represents a delayed negative feedback loop that drives oscillations in NF-κB translocation. Single cell time-lapse imaging and computational modeling of NF-κB (RelA) localization showed asynchronous oscillations following cell stimulation that decreased in frequency with increased IκBα transcription (1). Transcription of target genes depended on oscillation persistence, involving cycles of RelA phosphorylation and dephosphorylation. The functional consequences of NF-κB signalling may depend on number, period and amplitude of oscillations and may depend on the kinetics of formation of different NF-kB complexes in the nucleus (2).
The discovery of these complex dynamic characteristics of the important NF-κB signalling pathway underlines the importance of timelapse imaging in single cells. The discovery that the other important cellular stress pathway, p53, is also oscillatory, raises the possibility that other signalling networks may oscillate with different frequencies, which may be important in signal pathway cross-talk. We are developing transfected cell arrays to investigate these processes with a higher throughput. This involves integrated development of genomics, imaging, automated image analysis and database technology.

(1) Nelson, D.E., Ihekwaba, A.E.C., Elliott, M., Johnson, J.R., Gibney, C.A., Foreman, B.E., Nelson, G., See, V., Horton, C.A., Spiller, D.G., Edwards, S.W., McDowell, H.P., Unitt, J.F., Sullivan, E., Grimley, R, Benson, N, Broomhead, D, Kell, DB & White,M.R.H. (2004) Science 306: 704-8.

(2) Nelson, D.E., Sée, V., Nelson, G. and White M.R.H. Oscillations in transcription factor dynamics: a new way to control gene expression.(2004) Biochem. Soc Trans. 30: 1090-192.

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