# BIRS Workshop on Mathematical Methods for Medical Image Analysis (MMMIA)

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## 1 Workshop Objectives

The main objective of the workshop was to bring together top-tier international researchers in the field of medical image computing for brainstorming sessions culminating with definition of current research challenges in the area and potential solutions. The workshop's specific goals included:

- Fostering exchange of information, sharing of insights, and seeding of new collaborations between participants in areas of mutual interest.
- Establishing connections between Canadian researchers and well-established internationally-renowned research groups world-wide.
- Improving communication between related disciplines in this multidisciplinary area including Mathematics, Computer Science, Engineering, Medicine, and Physics.
- Enabling in-depth scientific discussions through exciting talks and lively panel discussions on important problems in medical image computing and state of the art analysis techniques that are currently under active research.

## 2 Workshop Overview

This workshop was a five-day scientific retreat held at the Banff International Research Station for Mathematical Innovation and Discovery (BIRS). The workshop attracted many of the best known international researchers in the area of medical image analysis who represented top universities and industries.

The workshop provided a forum for in-depth discussions and stimulating interactions among high caliber researchers working on development and application of mathematical methods for solving problems in medical imaging. The workshop helped foster multidisciplinary research in medical image computing by bringing together mathematicians, computer scientists, engineers, physicists and clinicians.

## 3 Overview of the Field

Biomedical imaging is revolutionizing medicine in our modern society and the impact of novel computational multi-dimensional data analysis methods on enhancing healthcare is enormous. Applications in clinical and biomedical settings are far reaching, e.g., in computer aided-diagnosis, image-guided intervention, therapy evaluation, monitoring and quantification of disease progression etc. The current research focus of the medical image analysis community is on topics related to image reconstruction, denoising, registration, segmentation, geometric and statistical modeling, and visualization of complex visual medical datasets. The development of algorithms for solving such problems in medical image datasets (such as scalar, vector, and tensor fields) involves various mathematical tools including transforms, spectral analysis, PDEs, nonlinear multivariate statistics, solutions to inverse problems, and optimization methods.

## 4 Recent Developments and Open Problems

Over the past two decades, medical imaging has become one of the main pillars of modern healthcare. The increasingly rich spectrum of available structural and functional imaging technologies provides exquisite medical data that offer tremendous opportunities for non-invasive visualization and quantitative analysis of anatomy and physiology. Applications, some of which are clinical realities, vary from basic computer-assisted diagnostics to elaborate image-guided interventions. Exploiting the enormous amounts of information embedded in such medical image data is, however, a very complicated task. In fact, the lack of efficient, accurate, and robust computational analysis techniques poses huge challenges that seriously hinder optimal extraction and use of image information in practice. Manual analysis is mostly not feasible, even impossible in certain cases, as it is prohibitively time-consuming (i.e., expensive), very tedious, can be quite inaccurate, and prone to serious inter- and intra-user variability. This renders automated techniques indispensable for achieving the high accuracy, reproducibility, robustness and efficiency rates needed for real-world medical research and practice. Despite continuous efforts, success in automating medical image analysis tasks has so far been modest and of limited applicability due to numerous complicating factors associated with real medical image data. These factors include extensive variability (normal and pathological) in anatomical and functional image information, serious imaging artifacts and data noise, patient-related artifacts, e.g., motion, and most importantly, the substantial underlying complexity of biological structures and processes.

## 5 Participants

Thirty seven participants attended the workshop representing a large number of internationally renowned research labs specializing in medical image computing at top universities, e.g., Harvard, John's Hopkins, Yale, Imperial College, and at giant industries, e.g., Siemens and Philips. Below is a complete list of participants along with their affiliation.

- Abolmaesumi, Purang: Queens University, Kingston, ON, Canada
- Abugharbieh, Rafeef: The University of British Columbia, Vancouver, BC, Canada
- Archip, Neculai: Harvard Medical School, Boston, MA, USA
- Atkins, Stella: Simon Fraser University, Burnaby, BC, Canada
- Beg, Mirza Faisal: Simon Fraser University, Burnaby, BC, Canada
- Boykov, Yuri: University of Western Ontario, London, ON, Canada
- Celler, Anna: Vancouver Coastal Health Research Institute, Vancouver, BC, Canada
- Christensen, Gary: University of Iowa, Iowa City, IA, USA
- Cootes, Tim: University of Manchester, Manchester, UK
- Ellis, Randy: Queen's University, Kingston, ON, Canada
- Flores-Mangas, Fernando: University of Toronto, Toronto, ON, Canada
- Hamarneh, Ghassan: Medical Image Analysis Lab, Simon Fraser University, Burnaby, BC, Canada
- Huang, Albert: The University of British Columbia, Vancouver, BC, Canada
- Larsen, Rasmus: Technical University of Denmark, Lyngby, Denmark
- Lee, Tim: BC Cancer Agency, Vancouver, BC, Canada
- Lenglet, Christophe: Siemens Corporate Research Inc., Princeton, NJ, USA

- Lorenz, Cristian: Philips-Germany, Germany
- McIntosh, Chris: Simon Fraser University, Burnaby, BC, Canada
- McKeown, Martin: The University of British Columbia, Vancouver, BC, Canada
- Miller, Michael: John Hopkins University, Baltimore, MD, USA
- Möller, Torsten: Simon Fraser University, Burnaby, BC, Canada
- Ng, Bernard: The University of British Columbia, Vancouver, BC, Canada
- Pizer, Stephen: University of North Carolina, Chapel Hill, NC, USA
- Rohling, Robert: The University of British Columbia, Vancouver, BC, Canada
- Rueckert, Daniel: Imperial College, London, UK
- Salcudean, Tim: The University of British Columbia, Vancouver, BC, Canada
- Siddiqi, Kaleem : McGill University, Montreal, QC, Canada
- Sonka, Milan: University of Iowa, Iowa City, IA, USA
- Sossi, Vesna: The University of British Columbia, Vancouver, BC, Canada
- Staib, Lawrence: Yale University, New Haven, CT, USA
- Styner, Martin: University of North Carolina, Chapel Hill, NC, USA
- Tam, Roger: The University of British Columbia, Vancouver, BC, Canada
- Ward, Aaron: Simon Fraser University, Burnaby, BC, Canada
- Warfield, Simon: Children's Hospital, Boston, MA, USA
- Westin, Carl-Fredrik: Harvard Medical School, Boston, MA, USA
- Whitaker, Ross T.: The University of Utah, Salt Lake City, UT, USA
- Worsley, Keith: McGill University, Montreal, QC, Canada

# 6 Sessions and Presentations

Eight scientific sessions were held over five days. Each session included 3-4 short presentations by distinguished participants which were followed by a lengthy panel discussion by a subset group of specialists. A total of 29 presentations and 8 panel discussions were held.

# 7 Presentation Highlights

## 7.1 Session 1: Mathematical Methods (Worsley, Miller, Boykov, Staib)

- Worsley, Keith (McGill University): Detecting Sparse Connectivity: MS Lesions, Cortical Thickness, and the 'Bubbles' Task in an fMRI Experiment

We are interested in the general problem of detecting sparse connectivity, or high correlation, between pairs of pixels or voxels in two sets of images. To do this, we set a threshold on the correlations that controls the false positive rate, which we approximate by the expected Euler characteristic of the excursion set. The first example is a data set on 425 multiple sclerosis patients. Lesion density was measured at each voxel in white matter, and cortical thickness was measured at each point on the cortical surface. The hypothesis is that increased lesion density interrupts neuronal activity, provoking cortical thinning in those grey matter regions connected through the affected white matter regions. The second example is an fMRI experiment using the 'bubbles' task. In this experiment, the subject is asked to discriminate between images that are revealed only through a random set of small windows or 'bubbles'. We are interested in which parts of the image are used in successful discrimination, and which parts of the brain are involved in this task.

- Miller, Michael (John Hopkins University): Computational Functional Anatomy

Computational Anatomy is the study of the shape and structure of manifolds in human anatomy. This talk reviews results from CA along these lines, including (i) embedding of shapes into a metric structure via flows of diffeomorphisms (ii) conservation laws for geodesics describing metric connection of shapes (iii) statistics on families of shapes encoded via these metrics. The emerging focus in Computational Functional Anatomy is the inclusion of the study of function in the curved coordinates of anatomical manifolds. Methods for performing inference in this setting are examined coupled to morphometric studies.

- Boykov, Yuri (University of Western Ontario): Global Optimization of Geometric Surface Functionals

Optimization of geometric surface functionals is a very common approach to formulating image analysis problems. Combinatorial algorithms (e.g. graph cuts) allow global optimization of a wide class of geometric functionals common in N-D image analysis that were previously addressed mainly via local variational techniques (e.g. level-sets) or other gradient descent methods. In this talk we describe geometric functionals that can be addressed via graph cuts and show applications.

- Staib, Lawrence (Yale University): Models for Biomedical Image Analysis

Biomedical image analysis methods may be enhanced by the incorporation of models, which may come in many forms. Difficulties in the ability to accurately and reproducibly recover quantitative information arise from issues related to image quality and the variability of normal and abnormal anatomy and physiology. Models can provide a crucial constraint on the analysis by providing information related to the manifestation of the relevant anatomy or physiology in the images. Models for shape are particularly useful. Some problems are well suited to the constraints that global geometric information provides, where the shapes of the organs or structures are very consistent and are well characterized by a specific shape model. Other problems involve structures whose shapes are highly variable or have no consistent shape at all and thus require more generic shape information. Biomechanical models, either for regularization or for true modeling, can also be powerful. We describe model-based approaches to a variety of problems illustrating the varying uses of models for image analysis.

## 7.2 Session 2: Image Registration (Christensen, Rueckert, Celler)

- Christensen, Gary (University of Iowa): Non-rigid Image Registration Evaluation Project (NIREP)

Non-rigid image registration is an essential tool for morphologic comparisons in the presence of intra- and inter-individual anatomic variations. Many non-rigid image registration methods have been developed, but are especially difficult to evaluate since point-wise inter-image correspondence is usually unknown, i.e., there is no "Gold Standard" to evaluate performance. The Non-rigid Image Registration Evaluation Project (NIREP) has been started to develop, establish, maintain, and endorse a standardized set of relevant benchmarks and measures for performance evaluation of non-rigid image registration algorithms. This talk will describe the initial work of the NIREP which includes constructing an initial neuroanatomical evaluation database, reports on the initial evaluation measures and gives baseline registration performance. Registration comparisons will be presented as images to correlate algorithm performance spatially with the underlying anatomy and are presented in tabular and graphical formats to compare trends over the population. Finally, this talk will discuss standards for reporting registration results based on the recommendations of the Standards for Reporting of Diagnostic Accuracy (STARD) Initiative and the registration evaluation framework developed by Pierre Jannin et al.

- Rueckert, Daniel (Imperial College): Quantification of Brain Development during Early Childhood Using Medical Image Computing

The majority of brain growth occurs during the first two years of life, much occurring in-utero prior to birth at 40 weeks gestational age, and a full understanding of human brain development must include this early period of rapid development. The characterization of early brain development is particularly important in infants who are born prematurely. Preterm birth affects around 5% of births in industrialised countries and its consequences contribute to significant individual, medical and social problems. The principle morbidity among survivors is neurological, resulting from the profound effect of preterm birth on the developing brain: half of all infants born at less than 25 weeks have neurodevelopmental impairment at 30 months of age, and in less immature infants, neuropsychiatric problems are common in the teenage years. The anatomical correlates of functional disorders are, however, poorly characterized. Using state-of-the-art MR imaging it is nowadays possible to study the brain development and maturation process in infants born prematurely from as young as 25 weeks onwards. Recent advances in MR imaging also enable the acquisition of high-resolution fetal images. This allows us to study the brain development in-utero as well as ex-utero. In this talk we describe the computational challenges in the analysis of these images. In particular we describe how non-rigid registration can be used in cross-sectional and longitudinal studies to quantify brain development and growth between the last trimester of pregnancy and early childhood.

## 7.3 Session 3: Visualization and Clinical Applications (Sonka, Archip, Lee, Möller)

- Sonka, Milan (University of Iowa): Multi-Surface Segmentation of 3D Retinal OCT

3D spectral OCT has become a new imaging modality available in clinical care starting in the fall of 2007. Retinal segmentation and quantitative analysis - both dealing with the total retina and individual retinal layers - is a challenging new direction of ophthalmologic research and clinical care. A novel n-surface segmentation approach will be presented that is applicable to retinal layer segmentation of the macular and peripapillary 3D OCT scans. Validation results and in vivo segmentation examples will be provided.

- Archip, Neculai (Harvard Medical School): Medical Image Analysis for Image Guided Therapy

Image guided therapy is combining advances in imaging and therapeutic technology to develop minimally invasive surgical and interventional techniques. Innovations in imaging and image analysis have enabled key improvements in a) preoperative planning, b) intraoperative targeting, navigation and control, and c) postoperative assessment. We describe recent algorithmic advances that have enabled enhanced surgical navigation, by multi-modality fusion of pre-operative high resolution imaging with low quality intra-procedural images. One of the challenges of developing such algorithms is to meet the hard real-time constraints of intra-operative surgical decision making. In this context, several clinical applications requiring advanced quantitative image analysis will be demonstrated. It will include image guided neurosurgery, where pre-operative DT-MRI, T1w MRI and fMRI are fused with intra-operative MR imaging for enhanced visualization of tumor margin and white matter tractography during brain tumor resection. We will also present new approaches for improved lesion targeting during abdominal intervention procedures (such as liver biopsy and radio frequency ablation), by combining pre-procedural MRI and PET scans, with intra-procedural CT images.

- Lee, Tim (BC Cancer Agency): Analysing Pigmented Skin Lesion Images

The incidence of cutaneous malignant melanoma has been increasing rapidly throughout the world in the last four decades in the countries with the large light-skin population. Statistics have shown that early detection of malignant melanoma plays an important role in the treatment of the disease. Therefore, there are increasing activities in research for computer-aided diagnostic systems to help health professionals in diagnosing the disease and to reduce their workload. Dermatologists and researchers often use white light imaging to diagnose skin lesions, monitor high risk patients, and study the etiology of the disease. In this presentation, I will review some of the development, issues and challenges of automating the macro and micro imaging of skin lesions using white light imaging.

- Möller, Torsten (Simon Fraser University): Graphics and Visualization Approaches to Medical Imaging

In this talk I will summarize some of our research on the visualization of functional medical imaging. Further, I will look into the application of graphics algorithms to tomography algorithms and their mapping to Graphics Programming Units (GPUs).

## 7.4 Session 4: Image-Guided Intervention (Ellis, Rohling, Abolmaesumi)

- Ellis, Randy (Queen's University): From Scans to Sutures: Computer-Assisted Orthopedic Surgery in the Twenty-First Century

Computer-assisted surgery is the process of using medical images, such as CT scans, X-ray fluoroscopy, or 3D ultrasound, to improve patient care. A typical surgical procedure begins by acquiring and processing a CT scan with specially developed image-analysis software. A surgeon then performs a "virtual surgery" on the patient to develop a preoperative plan. In the operating room the medical image is registered to the patientś anatomy by finding an optimal rigid-body transformation. This transformation allows an object or motion in one coordinate frame to be represented in the other frame, and thus a surgeon can visualize the location of an instrument deep within concealed anatomy while avoiding structures at risk. The operating surgeon can also use computer-tracked fluoroscopy or ultrasound for 3D guidance. For the past decade, our interdisciplinary research group has been investigating fundamental problems in orthopedic surgery of bones and joints. This talk will be an overview of the problems and solutions that have been tested in a set of pilot clinical trials in which we have treated more than 350 patients for early or advanced arthritis, poorly healed bone fractures, and treatment of deep bone tumors.

- Rohling, Robert (University of British Columbia): Automated Interpretation of Ultrasound Images

The field of ultrasound imaging continues to grow and evolve with each new generation of technology. In recent years, there has been a substantial improvement in image quality due to new image formation and image processing techniques. There has also been a drive towards the development of smaller and lower cost systems. As access to ultrasound is made easier, ultrasound is expanding beyond its traditional place in obstetrics and is found increasingly frequently in other domains such as anesthesiology and emergency medicine. Newer imaging methods such as elastography and high-frequency imaging have also advanced and made their way into clinical use. One of the outcomes of these driving forces is that ultrasound is no longer an imaging method used only be experienced sonographers and radiologists. In many cases, ultrasound is now being used by users who are relatively unskilled in ultrasound interpretation. Ultrasound is also used in larger systems, such as image-guidance systems for interventions. In both cases, automatic ultrasound processing and data extraction is beneficial. For inexperienced operators, automatic processing can provide an aid in interpretation for a specific task. For image-guidance systems, automatic processing can be used for target/tool tracking and validation of a procedure. This talk will cover some examples of automatic processing algorithms and applications. It will also discuss the advent of commercial open-architecture ultrasound systems and the impact they have on the field.

- Abolmaesumi, Purang (Queens University): Ultrasound-Guided Computer-Assisted Orthopaedic Surgery

In recent years, computer-assisted surgery has evolved and developed due to the need to integrate the information derived from different sensory inputs in the operating room and also the necessity to track the surgical operation quantitatively during and after the surgery. The current research in this area envelops all phases of a surgical procedure: preoperative planning, intra-operative registration and guidance, and post-operative follow-ups. A few of the main medical imaging modalities used to plan and perform these operations include ultrasound, X-ray, CT and MRI. This talk will cover the research currently being conducted at the Medical Image Analysis Laboratory at Queen's University regarding the application of medical imaging modalities in both the preoperative planning and intra-operative registration phases of computer-assisted orthopaedic surgery. With regards to the former, the goal is to reconstruct anatomical models of patients from medical images with little computational cost. Regarding the latter, the aim is to register in real time, the patient's anatomy to the pre-operative 3D models extracted from the ultrasound, CT and MRI images. These reconstruction and registration techniques have been incorporated in the design of new user interfaces that will improve intra-operative guidance of surgical tools.

## 7.5 Session 5: Diffusion Tensor Imaging (Siddiqi, Westin, Styner, Whitaker, Lenglet)

- Siddiqi, Kaleem (McGill University): On the Differential Geometry of White Matter Fibre Tracts: Generalized Helicoids and Diffusion MRI

Recovering the differential geometry of white matter fibre tracts from Diffusion MRI is largely an open problem. We develop a characterization of such structures by considering the local behaviour of the associated 3D frame field, leading to the associated tangential, normal and bi-normal curvature functions. Using results from the theory of generalized minimal surfaces we adopt a generalized helicoid model as an osculating object and develop the connection between its parameters and these curvature functions. These developments allow for the construction of parametrized 3D vector fields (sampled osculating objects) to locally approximate these patterns. We apply these results to the analysis of diffusion MRI data via a type of 3D streamline flow. Experimental results on human brain data demonstrate the advantages of incorporating the full differential geometry.

- Westin, Carl-Fredrik (Harvard Medical School): Geodesic-Loxodromes for Diffusion Tensor Interpolation

In algorithms for processing images of diffusion tensors, two common ingredients are interpolating two tensor values, and measuring the distance between them. We propose a new class of interpolation paths for tensors, termed geodesic-loxodromes, which explicitly preserve clinically important tensor attributes, such as mean diffusivity or fractional anisotropy, while using basic differential geometry to interpolate tensor orientations. This contrasts with previous Riemannian and Log-Euclidean interpolation methods that preserve the tensor determinant. From path integrals of the tangents of geodesic-loxodromes, we create a novel measure of over-all difference between two tensors, as well measures for shape difference and orientation difference.

- Styner, Martin (University of North Carolina, Chapel Hill): Automated Fiber-Based DTI in the Developing Brain of Human and Non-Human Primates

Diffusion tensor imaging (DTI) has become increasingly important as a means of investigating the structure and properties of neural white matter, with many applications in our own research of the developing brain in humans and macaque monkeys. Several analysis frameworks have been proposed, such as region based, voxel-based as well as fiber tract based analysis frameworks. I will present our current work in this field using both fiber tract and region based analysis, as well as our developments championing an automated analysis of atlas based, parameterized DTI fiber tracts for the quantitative analysis of the diffusion properties. Additionally the use of DTI based connectivity information is the basis for a novel, population based cortical correspondence computation.

- Whitaker, Ross T. (University of Utah): Volumetric Connectivity: Formulation and Computational Solutions

Diffusion tensor imaging (DTI) offers an opportunity to study, in vivo, the white matter connections between different functionally or structurally relevant regions in the cortex. In this work, we describe a methodology for defining volumetric, white-mater regions from DTI that are associated with the connections between predefined brain regions. The method relies on a Hamilton-Jacobi formulation of white-matter paths and produces a volumetric mask of DTI measurements that contain the optimal path as well as near-optimal paths that provide evidence of a particular connection. This talk will discuss the Hamilton-Jacobi formulation, the mathematical properties of volumetric connectivity, and methods for using these masks to analyze white-matter structure using nonparametric regression. We will also discuss the numerical methods associated with the Hamilton-Jacobi solver, a new algorithm for efficiently solving these equations, and a GPU implementation, which allows user to interactively define and visualize white-matter regions.

- Lenglet, Christophe (Siemens Corporate Research Inc.): DTI Tractography - Applications and Shortcomings

I will introduce a front propagation technique for DTI tractography. I will then illustrate the algorithm through results obtained on the human motor and visual systems. This will be used as a starting point to discuss some open questions for the tractography problem.

## 7.6 Session 6: Knowledge-Based Image Analysis (Lorenz, Warfield, Atkins)

- Lorenz, Cristian (Philips-Germany): Using Domain Knowledge in Medical Imaging

Today, it is not sufficient for a medical imaging device company, to just deliver medical images of good quality. The imaging process itself and further processing such as image segmentation, quantification, computer assisted diagnosis and therapy planning needs to be efficient and highly automated. Currently, mainly knowledge about the human anatomy and about clinical workflow is used to achieve this goal, however, physiological and pathology models will become increasingly important in the future. The talk will try to show current approaches and challenges for the future from the perspective of industrial research.

- Warfield, Simon (Children's Hospital Boston): Algorithms for Quantitative Assessment of Pediatric Brain MRI

In the last trimester before birth, the developing human brain undergoes tremendous changes as it grows. Premature birth during this period is associated with an increased risk of adverse outcomes, with up to 50% of very low birth weight infants going on to develop cognitive and motor deficits. The analysis of magnetic resonance images has a crucial role to play in characterizing normal brain development, and in understanding the impact of early brain injury upon the path of later brain maturation. However, there are a number of unique challenges in quantitatively assessing early brain MRI due to the limited contrast between different types of tissue, the rapid progression of brain maturation, and the logistical challenges of imaging newborn infants. Particular challenges include overcoming the effects of image acquisition artifacts, imaging system noise, and patient-specific normal and pathological variability. Advances in image acquisition and medical image computing algorithms now enable sophisticated characterization of early brain development. We will present recent work in developing and evaluating image analysis algorithms to improve our capacity to characterize early brain maturation and early brain injury and to assess potential therapeutic interventions.

- Atkins, Stella (Simon Fraser University): Role of Eye Gaze Tracking in Medical Applications: A Window into the Mind

I will introduce the basic science involved in eye gaze tracking and the hardware we use, and describe two medical applications: in radiology workstation design, and in surgery.

## 7.7 Session 7: Statistical Shape Analysis (Pizer, Cootes, Larsen)

- Pizer, Stephen (University of North Carolina, Chapel Hill): Robust Estimation of Probability Distributions on One or More Anatomic Objects

Both segmentation and statistical shape analysis of one or more anatomic objects can benefit from estimation of a probability distribution on the geometry of the entity. This geometry will include positional information and sometimes orientational information as well, such as boundary or medial sheet normals. Frequently, training samples are very expensive, so the robustness of the probability distribution estimation as a function of the number of training samples is an important issue. The overall topic of this talk is how to achieve this robustness and how to measure the robustness of estimation. The talk will include: * Definition of application-independent measures of this robustness, measured in both feature space and in the ambient space in which the images are formed. * Discussion of how to use these measures to compare probability distribution estimations on models with different primitives (in particular, b-rep PDMs vs. m-reps). * Means of achieving robust probability distribution estimation by multiscale estimations using successive residues from larger spatial scales together with successive re-alignment with decreasing spatial scale. Application to the segmentation of objects in the male pelvis from CT will be used to illustrate the approach and its results.

- Cootes, Tim (University of Manchester): Automatic Construction of Statistical Shape Models Using Group-wise Non-Rigid Registration

Statistical models of shape and appearance have been shown to be powerful tools for image interpretation, as they can explicitly deal with the natural variation in structures of interest. Such models can be built from suitably labelled training sets. Given a model of appearance we can match it to a new image using the efficient optimisation algorithms, which seek to minimise the difference between a synthesized model image and the target image. To construct such models we require a set of points defining a dense correspondence between every image and every other. This can be very time-consuming to achieve manually, and is potentially error prone. There is considerable demand for algorithms to automatically construct such models from training data, with minimal human intervention. Building on work on registering 2D boundaries and 3D surfaces, we have developed methods for registering unlabelled images so as to construct compact models. This talk will describe the approach, and demonstrate its application to a variety of 2D and 3D datasets.

- Larsen, Rasmus (Technical University of Denmark): Sparse Statistical Models for Relating Anatomical Differences to Clinical Outcome

Natural phenomena can often be explained by a set of few underlying parameters. This property has been used in many years in statistics, e.g. in factor rotation for easier interpretation [1]. In recent years sparsity has been used as design criterion to overcome the problem of the dimensionality of measurements vastly exceeding the number of observations available. Mathematically sparsity is envoked by putting a L0 penalty on the parameters. However, this is computationally intractable. Fortunately, in many situation the L1 penalty - for which computationally feasible solution are available - can work as a proxy for the L0 penalty as is used for instance in LASSO and LARS regression [2,3]. In this presentation we will show how sparse statistical regression and subspace methods can be use to explore hyper-dimensional image data such as shape differences and deformation fields and relate these variables to clinical outcome. The examples will include relating corpus callosum shape as well as whole brain deformations to clinical and cognitive parameters and analysing cranio-facial growth patterns.

## 7.8 Session 8: Functional Imaging and Energy Minimization Methods (Sossi, Salcudean, Ng (Ph.D. student of Rafeef Abugharbieh), McIntosh, Ward (Ph.D. students of Ghassan Harmarneh))

- Sossi, Vesna (University of British Columbia): PET Data Analysis

This talk will review methods of extracting quantitative, biologically relevant parameters from dynamic PET images.

- Salcudean, Tim (University of British Columbia): Imaging Issues in Prostate Brachytherapy

We will outline some of the image processing problems and our approaches for prostate brachytherapy, including boundary segmentation, localization of sources and elasticity modelling based on ultrasound elastography.

- Ng, Bernard (University of British Columbia, Ph.D. student of Rafeef Abugharbieh): Spatial Encoding of Brain Activation in fMRI

Patients with neurological diseases are often found with altered brain activity, and functional magnetic resonance imaging (fMRI) provides a non-invasive means to examine such changes. By far, the most widely used method to analyze fMRI data is statistical parametric mapping (SPM), which involves warping the brain of each subject to a common atlas to draw group inferences. However, due to inter-subject variability in brain shapes and sizes, especially for diseased patients, mis-registrations can easily occur. To avoid warping, the alternative approach is to specify regions of interest (ROIs) for each subject and examine statistical properties of regional brain activation. Conventionally, only magnitude-based features are considered under this ROI-based approach to mitigate the effects of inter-subject variability in brain shapes, brain sizes, and subjectÕs orientation in the scanner. However, the information encoded by the spatial distribution of activated voxels within an ROI is in fact an important attribute of brain activity. Thus, we exploit this spatial information in our analysis by using invariant spatial features. We also extended this spatial analysis to the temporal domain, which provided a spatio-temporal characterization of brain activity. Applying these methods to real clinical data detected brain activity changes that were undetected with traditional means, thus demonstrating the importance of incorporating spatial information in fMRI analysis.

- McIntosh, Chris (Simon Fraser University, Ph.D. student of Ghassan Hamarneh): Learning Optimal Parameters for Medical Image Segmentation

Energy functional minimization is an increasingly popular technique for image segmentation. However, it is far too commonly applied with hand-tuned parameters and initializations that have only been validated for a few images. Fixing these parameters over a set of images assumes the same parameters are ideal for each image. We highlight the effects of varying the parameters and initialization on segmentation accuracy and propose a framework for attaining improved results using image adaptive parameters and initializations. We provide an analytical definition of optimal weights for functional terms through an examination of segmentation in the context of image manifolds, where nearby images on the manifold require similar parameters and similar initializations. Our results validate that fixed parameters are insufficient in addressing the variability in real clinical data, that similar images require similar parameters, and demonstrate how these parameters correlate with the image manifold. We present significantly improved segmentations for a set of 470 clinical examples.

- Ward, Aaron (Simon Fraser University, Ph.D. student of Ghassan Hamarneh): Learning Optimal Landmark Shape and Appearance Features for Point Correspondence Establishment

We propose a highly automated approach to the point correspondence problem for anatomical shapes in medical images. Manual landmarking is performed on a small subset of the shapes in the study, and a machine learning approach is used to elucidate the characteristic shape and appearance features at each landmark. A classifier trained using these features defines a cost function that drives key landmarks to anatomically meaningful locations after MDL-based correspondence establishment. Results are shown for artificial examples as well as real data.

# 8 Scientific Progress Made

The workshop focused on investigating and discussing the latest in mathematical methods for solving problems in medical image analysis including segmentation, registration, shape and functional modeling in a multitude of imaging modalities including structural and functional data. Experts in the field exchanged ideas and insights on how to best address the various problems identified especially in image segmentation, registration, feature extraction and object modeling. The challenges in the field were identified and potential approaches for addressing them were debated.

# 9 Outcome of the Meeting

The workshop was prominently and internationally recognized as a major event in the field of medical image computing. In fact, it was by chance was held very close to the dates of the premier conference on Medical Image Computing and Computer Assisted Intervention (MICCAI 07 which was held in Brisbane Australia) and many distinguished scholars chose to attend the Banff workshop over MICCAI. Some participants also flew all the way from Australia to Banff to participate despite the gruesome travel requirements.

A number of professional connections and scientific collaborations were facilitated by the workshop. Many researchers met for the first time and a number strengthened ties already established. The organizers received very positive feedback from the participants their appreciation of the scientific atmosphere and the ample opportunities for discussing various challenges in the field of medical image computing. To date, the organizers still receive many inquires whether there will be a sequel event to the first workshop which we hope to be able to hold sometime in the near future.

## 10 Summary of Challenges

Participants largely agreed that the challenges facing the area of medical image computing mainly include:

- High dimensionality of image and shape data and low number of training samples.
- Lack of samples and models of pathological cases to train methods.
- Sensitivity of developed methods to parameter setting.
- Designing energy functionals whose minima are correct solutions of medical image and shape analysis problems.
- Encoding expert and high level knowledge in methods.
- Optimizing energy functionals (local minima problems in iterative optimization, discrete subset of search space or simplified functionals in global optimizers).
- Fusion of data from multiple modalities.
- Fusion of data from multiple scales.
- Building Biomechanical and physiological models of anatomy and function.
- Building shape and appearance models of normal and pathological states.
- Need for mechanisms for intuitive interaction methods for highly automated analysis methods.
- Scarcity of viable options for validation of developed methods.
- Need to standardized metrics to compare algorithms.

## 11 Workshop Homepage

The workshop home page provides full details including complete presentation slides. The page can be viewed at: http://bisicl.ece.ubc.ca/mmmia2007