Guest Editorial
Special Issue on Computational Neuroanatomy

THIS Special Issue of the *IEEE Transactions of Medical Imaging*, devoted to the topic of Computational Neuroanatomy, presents a selection of the finest work in this growing field. It provides an update on recent developments to all those working in medical imaging, and will excite those developing new mathematical algorithms or interested in applying computational anatomical tools in clinical projects.

Computational neuroanatomy has emerged over the last decade as an important field of applied science, spurred on by advances in differential geometry and statistics, and fueled by powerful imaging methods that assess the living human brain. This new field is greatly advancing medical research, with applications to basic biological science and clinical practice. One line of work develops models of changing anatomy over time; this work is expanding into large-scale studies of human development and disease, as well as clinical trials involving hundreds to thousands of subjects. Detailed anatomical models, atlases, and templates for surgical planning and teaching are also being developed and widely used. Brain mapping studies that report structure-function correlations in the brain, and their associations with behavior or disease processes, are similarly supported by underlying automated image registration programs that align subject studies within a documented structural space. Image segmentation programs are also being rapidly refined. Drawing upon new ideas from machine learning, Bayesian statistics and partial differential equations, several papers in this Special Issue report novel algorithms to extract detailed models and maps of specific structures, in both conventional magnetic resonance imaging (MRI) and diffusion tensor MRI. As these studies expand to populations of hundreds and even thousands of subjects, automated segmentation algorithms are vital to identify structures in the brain automatically, for subsequent volumetric measurement, shape analysis and longitudinal assessment.

The 16 papers presented here run the gamut of new developments in brain image registration and segmentation. They present new work on deformable geometry and surface-based anatomical modeling, with illustrative applications to morphometry and structure-function correlations. Several papers focus on the analysis of anatomical shape, with applications to disease classification and computer-aided diagnosis. Several also report new types of statistical analyses of structural brain images, with the goal of comparing groups or clinical populations and detecting differences with optimal accuracy and power.

Some of the most mathematically fundamental work in the Special Issue is in the field of image registration, including nonlinear and cross-modality approaches. Gholipour *et al.* provide a timely and incisive review of the registration approaches now applied to localize brain function, including a survey and classification of the image registration techniques related to this problem. Schwarz *et al.* analyze neuropsychiatric disease using deformation-based morphometry—an approach in which the nonlinear registration fields that align anatomical images to a standard template are analyzed to detect systematic structural differences. Wang *et al.* provide a richly detailed mathematical approach to examine the shape of the human hippocampus, based on large-deformation diffeomorphic metric mappings. A complementary paper by Lord *et al.* maps hippocampal asymmetry, in an epilepsy application where the quantification of asymmetry is ideal for characterizing the primarily unilateral disease process.

Several key papers address the still challenging problem of automatically segmenting brain structures from MRI. Han *et al.* address the important issue of cross-scanner variability. They advocate an improved approach for structure segmentation, which introduces an intensity renormalization procedure to adjust the prior atlas intensity model to new input data. With a similar goal, Bazin *et al.* present a new framework for multiple object segmentation in medical images that respects the topological properties and relationships of structures given by a template. Toews *et al.* propose a more complex statistical "parts-based" model for segmentation, which explicitly addresses the case where one-to-one correspondence does not exist between all subjects in a population due to anatomical differences, as model parts are not required to appear in all subjects. Xia *et al.* take a complementary but more inductive approach, proposing a highly accurate algorithm to segment the caudate nucleus from MRI scans of the brain. In this approach, they first extract the adjacent lateral ventricles, and then automatically localize the caudate guided by anatomical knowledge of the structure.

As the primary target of most functional brain mapping studies, the cerebral cortex has always presented unique challenges for image analysis. In a new approach to model the remarkably complex geometry and folding patterns of the cortex, Segonne *et al.* extract 3-D cortical models from brain MRI, creating surfaces with provably spherical topology by automatically correcting the topology of segmentations derived earlier in the processing stream. Kao *et al.* propose a new framework to identify and model the major cortical sulci—notoriously variable landmarks in the cortical surface—which they extract with a sequence of steps based on depth maps, spline curve modeling, and connectivity constraints. Tu *et al.* report a related system for detecting the major cortical sulci in the brain, by learning a discriminative model using the probabilistic boosting tree algorithm. This work is an example of the fruitful cross-fertilization of novel machine learning approaches applied to the unique challenges arising in brain imaging. Duchesnay *et al.* pursue this approach further with a cortical folding analysis system that successfully distinguishes (with 98% accuracy) between the left and right hemispheres on the basis of the shape of automatically extracted sulci (size, depth, etc.). All these results push the state-of-the-art in the

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field of cortical analysis, and highlight the attractiveness of multivariate recognition models combined with appropriate descriptor selection for cortical feature extraction and modeling.

Chung *et al.* provide an interesting paper outlining a novel weighted Fourier series representation for cortical surfaces. Its basic properties are compared with the traditional spherical harmonic representation, and applied to quantify the amount of gray matter in a group of high functioning autistic subjects. Related work by Yu *et al.* applies a spherical wavelet transformation to extract cortical shape features. In an application that will be of significant interest to neuroscientists, they study the development of cortical folding in newborn children using a Gompertz model in the wavelet domain, allowing them to characterize the order of development of large-scale and finer folding patterns independently. Nain *et al.* also use a spherical wavelet representation to extract parametric surfaces from brain images, using multiscale prior coefficients as parameters in their optimization procedure. This paper highlights the ongoing benefits of combining mathematical methods from shape analysis, functional analysis, and segmentation, to improve the accuracy and detail in automatically extracted models.

Finally, one paper in the Special Issue tackles the higher order notion of spatially correlated anatomical variation of brain substructure. Rather than treating each structure as an independent target of study, Makrogiannis *et al.* argue that important morphological characteristics are frequently not captured by deformation transformations mapping the anatomy to a common template. With this in mind, they develop a new "lossless" representation of anatomy that leads to higher classification rates in group comparisons or normal and atrophied anatomy.

In summary, we hope that this Special Issue on Computational Neuroanatomy contributes a valuable record of the state of the field in 2007. It should serve as an update for practitioners but will also arouse the interest of those working in areas of medical imaging far removed from this field.

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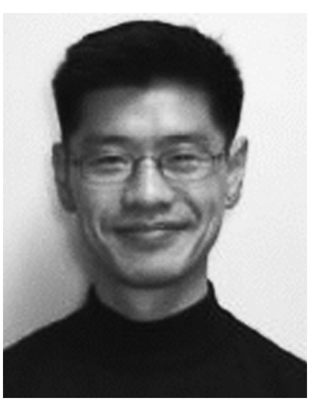

James C. Gee is Associate Professor of Radiologic Science and Computer and Information Science, Director of the Penn Image Computing, and Science Laboratory (PICSL), and Program Co-Director of the HHMI-NIBIB Integrated Graduate Training Program in Biomedical Imaging and Informational Sciences, all at the University of Pennsylvania, Philadelphia. Well known for its contributions to biomedical image analysis and, in particular, the emerging field of computational anatomy, PICSL[1]s work focuses on the development of methods for quantifying the ways in which anatomy can vary in nature, over time, or as a consequence of disease or intervention. Some recent developments include approaches for symmetric image registration and shape averaging in the diffeomorphic space, and statistical shape characterization with the medial representation.

Paul M. Thompson received the M.A. degree in mathematics and latin and greek languages from Oxford University, Oxford, U.K., in and the Ph.D. degree in neuroscience from the University of California at Los Angeles (UCLA), in .

He is Associate Professor of Neurology at UCLA. His research group of 13 mathematicians and neuroscientists develops new methods to analyze brain images. His 250 peer-reviewed publications describe collaborative projects analyzing brain growth in childhood, and mapping the spreading waves of tissue loss in Alzheimer's disease and schizophrenia. His team's work has helped understand how the brain is damaged by HIV/AIDS and chronic methamphetamine use (Top 100 Discoveries of 2004, *Discover* magazine). After research as a Fulbright Scholar and Howard Hughes Investigator at UCLA, he is Associate Editor for six medical imaging journals, including the IEEE TRANSACTIONS ON MEDICAL IMAGING, and is mentor for Ph.D. degree students in biomedical engineering, neuroscience, biomedical physics, and statistics.