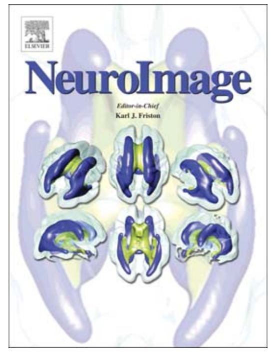
Accepted Manuscript



Preface: Special Issue on Mathematics in Brain Imaging

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PII:	S1053-8119(08)01161-0
DOI:	doi: 10.1016/j.neuroimage.2008.10.033
Reference:	YNIMG 5785
To appear in:	*NeuroImage*
Received date:	15 October 2008
Accepted date:	15 October 2008

Please cite this article as: Thompson, Paul M., Miller, Michael I., Poldrack, Russell A., Nichols, Thomas E., Taylor, Jonathan E., Worsley, Keith J., Ratnanather, J. Tilak, Preface: Special Issue on Mathematics in Brain Imaging, *NeuroImage* (2008), doi: 10.1016/j.neuroimage.2008.10.033

Preface: Special Issue on Mathematics in Brain Imaging

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Submitted and accepted at *NeuroImage*: October 15, 2008

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This special issue of *NeuroImage*, entitled “Mathematics in Brain Imaging,” consists of 18 invited papers from some of the finest research groups in brain imaging today. These articles cover in depth many of the mathematical techniques used in structural and functional neuroimaging studies, including diffusion tensor imaging. They highlight a diverse array of mathematical and statistical approaches: state-of-the-art algorithms for computational anatomy and algorithms for meta-analysis of functional images, and methods to relate imaging information to genetics. Also described are cutting-edge methods for image registration and segmentation—indispensable steps in all brain image analyses. New types of mathematics are applied to tackle key challenges in brain imaging, including sophisticated modeling of cortical anatomy and function, statistics of anatomical variation in development and disease, creation of anatomical templates and atlases to represent populations, and automatic labeling of brain structures. We hope that the contents of this issue will pique the interest of mathematicians and brain imagers alike—in short, anyone interested in the mathematical developments in the field.

This issue grew out of a workshop held at the UCLA Institute for Pure and Applied Mathematics, from July 14-25 2008, which was organized by the guest editors of this Special Issue. At the request of *NeuroImage's* founding editor-in-chief, Dr. Arthur Toga, and with the approval of the current editor-in-chief, the workshop organizers selected a representative set of participants to contribute reviews of their work on mathematics in brain mapping. To guarantee the highest technical accuracy, all contributions were rigorously peer-reviewed by at least one of the other contributors and one of the guest editors. In many cases, additional reviews were sought from mathematicians working outside brain mapping, with expertise in the specific mathematics covered in the papers.

Several papers report innovations in the automated analysis of images from clinical populations, revealing disease effects on anatomy with remarkable precision and statistical power. Morra et al. (this issue) report their development of a new hippocampal segmentation method, which they apply to scans of 490 elderly subjects scanned twice, one year apart, identifying genetic factors that affect rates of atrophy in Alzheimer’s disease and those at risk. Miller et al. present an entire mathematical framework for representing, understanding, and analyzing anatomy and function using mathematical ideas from differential geometry, differential equations, and statistics on diffeomorphisms to infer differences in clinical populations. Younes et al. further pursue the underlying mathematical theory of this framework, showing how evolution equations such as the Euler-Poincaré differential equation may be used to model anatomical shape and shape change. Qiu and Miller study a related topic - they use large-deformation diffeomorphic metric maps

(LDDMM) to recover shape and geometry changes in time-series of images, quantifying differences between anatomical shapes, with applications to the study of neurodegenerative diseases. Taking up the challenge of making registration algorithms produce diffeomorphic mappings (one-to-one invertible mappings that are twice differentiable, as are their inverses), Vercauteren et al. adapt a popular, and highly efficient nonlinear registration method – the Demons algorithm – and improve it to ensure diffeomorphc maps are produced. On a similar theme, Baloch and Davatzikos observe that in structural imaging studies, nonlinear registration is not completely accurate in registering anatomy across subjects. They propose an ingenious method to use the residuals to analyze anatomical characteristics not captured by the registration transformations. Turning to the cortex, Hurdal and Stephenson cover a popular technique for cortical modeling, known as conformal mapping, showing how to construct conformal maps from cortical and cerebellar surface models, and how these models provide insight into the functional organization of the cortex. Also analyzing surface models of anatomy, Yushkevich et al. propose a new surface-based representation of anatomy called the continuous medial representation, or "*cm-rep*", which offers an elegant and natural parameterization of subcortical structure shapes for population studies.

Several contributions report developments in diffusion tensor imaging (DTI). DTI is an imaging modality sensitive to fiber integrity and connectivity in the brain, and is rich in mathematical concepts to represent diffusion signals, fiber pathways, and statistics on these geometrical constructs. Lenglet et al. provide a comprehensive mathematical overview of concepts that arise in the mathematical analysis of DTI, reviewing methods for analyzing fiber tracts, tract clustering and computing DTI statistics. Niethammer et al. propose a method for fiber bundle segmentation in DTI, using a statistical model of diffusion orientation. Goodlett et al. develop a method for group analysis of DTI-derived fiber statistics, using unbiased atlas building to develop a coordinate system for populations of diffusion images.

Following up on the idea that diffusion tensor signals lie on a differentiable manifold with a non-Euclidean metric, Fletcher et al. formulate the notion of a geometric median for statistical data lying on a manifold, and show illustrative applications of this concept in DTI, shape analysis, and computational anatomy. Extending the modeling of DTI still further, Barmpoutis et al. develop a sophisticated framework to model DTI using 4^{th} order tensors (ternary quartics), preserving more of the information in the diffusion signal than is retained by the standard diffusion tensor model.

Imaging genomics is a rapidly growing area of great scientific interest, in which genetic influences on features in images can be examined. Calhoun et al. provide a stimulating review of independent component analysis (ICA) for group analysis of fMRI data, and also show its power as a method to perform joint inference in imaging, genetics, and event-related potential (ERP) data.

Woolrich et al. provide an elegant and detailed overview of Bayesian analysis in the popular neuroimage analysis software package, FSL. Lindquist et al. tackle the important issue of modeling the hemodynamic response function in fMRI, comparing several techniques that vary in their assumptions, model complexity, and interpretation; their studies highlight the substantial differences among models in terms of power, and bias. Pereira et al. review the intriguing area of machine learning, which is increasingly popular as an exciting new method to recover information from neuroimaging data.

Wager et al. focus on the topic of meta-analysis in fMRI. They propose the multilevel kernel density analysis (MKDA) framework, which has been used in recent studies to evaluate the consistency and specificity of regional activation, identify distributed functional networks from patterns of co-activation, and test hypotheses about functional pathways.

We express our thanks to all reviewers for their timely and in-depth reviews of these papers. We are extremely grateful to the members of the UCLA Institute of Pure and Applied Mathematics – including its new director, Dr. Russel Caflisch, and its outgoing director, Dr. Mark Green, who initiated and funded the workshop on Mathematics in Brain Imaging, which provided the basis for this Special Issue. We also appreciate the significant funding for the workshop from the Center for Imaging Science at Johns Hopkins University (PI: Michael Miller) and Grants P41 RR013642 and U54 RR021813 (PI: Arthur Toga). Finally, we thank all of the authors for their contributions, which reveal the remarkable impact mathematics is making on brain imaging today and its exceptional promise in taking the field forward into new dimensions not previously imagined.

The primary costs of producing this Special Issue were supported by the National Institutes of Health through the NIH Roadmap for Medical Research, grant U54 RR021813 entitled Center for Computational Biology (CCB), and Resource Grant P41 RR013642 funded by NCRR (PI: Arthur Toga, UCLA Laboratory of Neuro Imaging).