

SHAPE OPTIMIZING DFFEOMORPHISMS FOR COMPUTATIONAL BIOLOGY

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Keywords: Normalization, Morphometry, Atlases, Brain

This project will contribute a new collaboration for implementing rigorous spatiotemporal medical image analysis in a large scale computing environment. The system will dramatically enhance the neuroimaging community's quantitative understanding of normal and pathological aging and correlated variables.

Medical images capture the changes that occur in an individual over time and samples the range of anatomical and functional differences visible in a population lifespan. Our goal is to associate these differences with causes, for example, innate population variability, injury, pathology, or the effects of genotype on phenotype. The recently proposed *Diffeomorphometry* (DM) system quantifies and relates these variables to an optimal spatiotemporal coordinate system. This novel technique allows the atlas to *evolve in time* along with the population to statistically capture effects of age, disease or other factors. This common, evolving map space gives a wealth of prior knowledge, allowing one to build probabilities describing ranges and types of variation in shape and function. These aggregate population attributes may then be studied and visualized, used in research, as well as teaching and diagnosis.

Our DM method is designed with the axioms of *symmetry* (the algorithms must be symmetric) and *specificity* (the analysis should be optimal in the study space) in mind and with the ability to automatically generate database-specific atlases. The rigorous and symmetric definition of change given by DM captures differences in neuroanatomy with superlative accuracy, reproducibility and high level of detail. Consequently, a DM study maximizes the information extracted from a neuroimaging cohort, especially when correlated with, for instance, genetic or behavioral variables. Furthermore, DM satisfies pressing research needs in neuroimaging: *DM derives optimal atlases from arbitrarily sized databases and gives large deformation optimization of anatomical correspondence, through landmark and statistical guidance*. The resources in the UCLA Center for Computational Biology (CCB) will allow these methods to be applied on the large datasets they were designed for and at an unprecedented resolution and scale.

The project has three distinctive aims: collaboration, methodology and clinical evaluation/application.:

- Instantiate a collaboration between UPenn and UCLA, where data and algorithms are shared and disseminated via the Center for Computational Biology
- Develop Diffeomorphometry into a cutting-edge, large-scale, publicly available computational tool
- Evaluate and refine the developed methodology, as well as compare with CCB brain mapping tools, on neuroimaging studies of structure-function associations under neurodegenerative conditions

This work is supported by the USPHS under grant EB006266.

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