From *SIAM News*, Volume 40, Number 2, March 2007

Geometry, Partial Differential Equations, and the Brain

By Guillermo Sapiro

Brain research in general, and brain imaging in particular, pose abundant mathematical and computational challenges, many of which can be addressed with tools from geometry and geometric partial differential equations. With the potential for applications ranging from the understanding of normal development to the study of diseases like Alzheimer's, brain imaging analysis is a vivid example of mathematics at work.

Let's start with the example of one of the earliest and still most challenging tasks in brain imaging: the labeling of different tissues in data obtained by magnetic resonance imaging. The initial goal is to classify, from 3D volumetric data, gray matter, white matter, and cerebrospinal fluid. The challenges arise from the relative noisiness of the data and the very highly convoluted and deeply folded nature of gray matter. The low resolution of MRI is also a bottleneck: The resolution of most MRI data is 1–2 mm, while gray matter, on average, varies in thickness between 2 and 4 mm. (High-strength magnetic fields, such as those employed at the Center for Magnetic Resonance at the University of Minnesota, are starting to produce better resolution.)

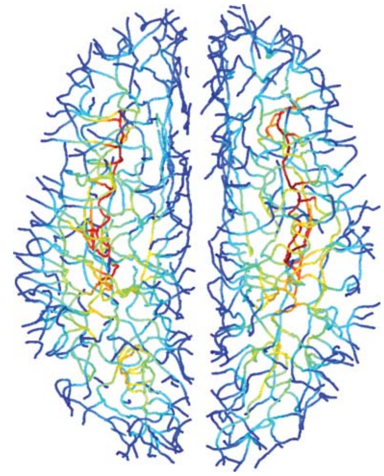

Figure 1. *Automatically computed network of sulcal fundi (color-coded according to the geodesic depth of the curves.*

Combining techniques from Bayesian theory, computational topology, and geometric PDEs, P. Teo, B. Wandell, and I have developed a labeling technique that exploits anatomical knowledge of the cortex and provides topologically correct results in very reasonable computational times, while computing critical connectivity information as well. The software package we developed is currently in use by numerous brain research groups. Wandell's group, for instance, has used it in studies of learning disabilities, plasticity and development, color, and general mappings of the visual field (see http://white.stanford.edu/wandell.html).

Segmentation of the cortex is often an important step in computing anatomical deformations; examples can be found at http://www.loni.ucla.edu/~thompson/thompson.html and in work on computational anatomy under way at Washington University, Brown University, Johns Hopkins University, and Georgia Institute of Technology, to name just a few. Such computations are based on geometric PDEs and require boundary conditions. The boundary conditions are often provided by sulcal fundi, 3D curves that lie in the depths of the cortex and that are also of intrinsic importance to brain research.

We recently developed a geometric algorithm that automatically extracts sulcal fundi from MRI data and represents them as spline curves lying on the extracted mesh representing the cortical surface. Given the cortical surface, perhaps extracted by the labeling technique described above, we begin by using fast Hamilton–Jacobi solvers to compute a geometric depth measure for each triangle on the cortical surface mesh; based on this information, we extract sulcal regions by checking for connected regions exceeding a specified depth threshold. Using a moving least-squares technique, we then identify endpoints for each region; we delineate the fundus by thinning the connected region while keeping the endpoints fixed. The curves thus defined are regularized with weighted splines on the surface mesh (that is, a geometric PDE is solved on the surface), to yield high-quality representations of the sulcal fundi.

This framework, which has been extensively validated, exemplifies the need for strong interdisciplinary teams in brain imaging. Among the developers are C.Y. Kao (a mathematician who spent two years at the Institute for Mathematics and its Applications and the VA Hospital in Minnesota), M. Hofer (a geometer), myself (from electrical and computer engineering), and J. Stern, K. Rehm, and D. Rottenberg, all from the VA Hopital.

Figure 1 shows an automatically computed network of sulcal fundi, color-coded according to the curves' geodesic depth. Further study of this complicated network is an exciting open research area that calls for a lot of applied mathematics.

Geometry and geometric PDEs have been used for many other tasks in brain imaging, including enhanced signal detection in functional MRI via adaptive anisotropic spatial regularization with metrics adapted to the fMRI signal; again, progress in this area depends on interdisciplinary collaboration (the members of the team responsible for this work—from engineering, MRI, and brain research—include A. Sole, S.C. Ngan, X. Hu, A. Lopez, and myself). The usefulness of such tools, which form part of the ITK initiative (the National Library of Medicine Insight Segmentation and Registration Toolkit; www.itk.org), is not limited to the cortex or gray matter; they have also found applications in the white matter, and in particular in the new modality of diffusion tensor imaging. Groups at INRIA, Brigham and Women's Hospital, in Boston, and the University of Florida, to name just a few, have developed extraordinary geometric and PDE-based tools for DTI data, and especially for studying connectivity in the brain. An example is the use of tools from Riemannian geometry and the geometry of manifolds of probability distributions, as developed at INRIA–Sophia Antipolis.

Brain imaging encourages innovative use of mathematics and at the same time opens novel mathematical questions. This has been reflected in numerous research projects, not only in geometry and PDEs, but also in such areas as statistics (as in work of J. Taylor and collaborators). In an instance of the intersection of current work in brain imaging with the most modern mathematics, F. Memoli (Stanford), P. Thompson (UCLA), and I recently began to investigate the use of locally minimizing Lipschitz extensions and infinite Laplacians for brain warping; our inspiration has been theoretical and computational results from G. Aronsson, V. Caselles, J.M. Morel, L.C. Evans, R. Jensen, A. Oberman, and many others. An example is shown in Figure 2, in which shading encodes the amount of geodesic deformation, that is, the local geodesic Lipschitz constant, as obtained while warping between two left hemispheres. Relatively little deformation (dark areas) is required to match features on the flat interhemispheric surface. This is consistent with the lower variability of the gyral pattern in the cingulate and medial frontal cortices. By contrast, significant expansion is required to match the posterior occipital cortices, especially at the poles, which are the target of many functional imaging studies of vision.

The examples mentioned here, a small subset of those available, are offered to give readers a sense of the importance of geometry and PDEs in brain research. Many interdisciplinary groups are actively working in the area, and the future for such collaborations is both promising and challenging. Advances in analysis and development are needed to keep pace with fascinating rapid advances in acquisition technology (in MRI as well as in such areas as cryo-microscopy; see http://electron.nci.nih.gov/).

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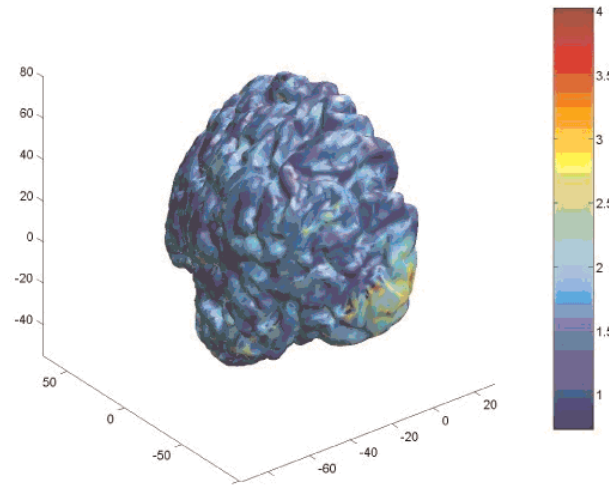

Figure 2. *Geodesic deformation, with dark blue indicating relatively small amounts of deformation.*