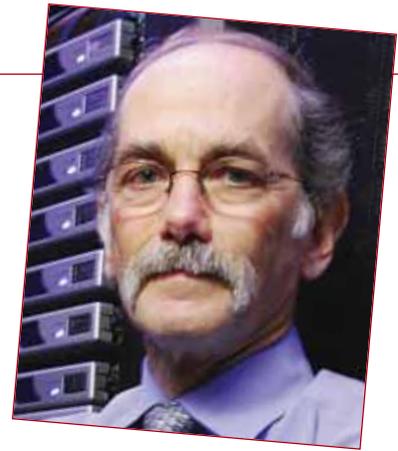


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A Vision of Computational Anatomy



Today, the knowledge, experience and memory of clinicians or scientists function as the exclusive resource for distinguishing normal from abnormal brain images; identifying signatures or biomarkers of disease in vast collections of images; and determining whether a particular surgical trajectory will help or damage a patient's brain. These experts decide, infer, interpret and estimate mostly qualitatively and often in reliance upon a personal knowledge base.

In my vision of the future, things will be quite different. We will use database information to reference and compare new or novel cases; to search for and compute biomarkers; and to determine the safest surgical course. How far are we from making this happen? Not as far as you'd think.

WHERE WE ARE NOW: HONING IN ON LOCATIONS AND INTEGRATING DATA

We are in the middle of one of the most significant scientific transformations in the study and treatment of the brain since the development of CT scans. Computational strategies that combine, compare, measure and visualize data-based images can provide enormous quantitative power to our understanding of brain structure and function in health and disease. Furthermore, we are now able to integrate disparate information from different modalities and at different scales, much as the brain itself apparently operates. And we can test relationships between data that comes from different cohorts, using different methods, to study different aspects of the brain, on different subjects, from different laboratories.

Comparing and contrasting brain image data requires a complete description of 'where' things are happening in the brain. Sometimes the best approach is to point to things in different ways. Just as a house can be described by its address, GPS coordinates, neighbors, appearance, or proximity to an intersection, we can describe brain locations in a variety of ways. For example, we can locate an activation site by area (e.g., Brodmann area 46); by coordinate system (Talairach and Tournoux coordinate (x,y,z)); by brain region (e.g., the pars opercularis of the inferior frontal gyrus); or by proximity to a blood vessel or layer of the cortex. None of these individually is very precise but, collectively, these descriptions make it easier to identify and compare regions where an activation occurred. This is now being done by a number of computational labs, and refinements will one day make these approaches avail-

able for a broad range of investigative and clinical applications.

In addition to mapping locations in the brain, computational anatomists must deal with differences among individuals in a probabilistic way, retaining information regarding variability and other group statistics. Ongoing efforts are creating better canonical atlases to represent subpopulations—of, say, healthy 20-somethings or Alzheimer's patients—while retaining well-resolved anatomical features that are vital to assist automated algorithms for aligning data to them. These atlases can even have a time-varying component allowing subjects of different ages to be brought into the atlas using an age-appropriate transformation. Rather than average images together voxel-by-voxel to produce a blurred template, as was done in many "first generation" statistical atlases, many groups are developing practical methods to create well-resolved canonical atlas images that represent the statistical mean anatomy for a population, using deformation averaging and Lie group methods on deformation tensors or geodesics on groups of diffeomorphic flows. These approaches are complex, but are advantageous as they are close (in a strictly defined mathematical sense) to the brains being normalized to them and are likely to improve spatial accuracy and reduce sources of bias when comparing datasets in a canonical coordinate system.

WHERE WE NEED TO GO

We are now within striking distance of creating robust methods for atlasing the brain and for integrating data to build more diverse and specific atlases of subpopulations. But designing appropriate reference systems for brain data presents considerable ongoing challenges, since these systems must capture how brain structure and function vary in large populations, across age, gender, and different disease states as well as across imaging modalities, time and even across species. And to get to the point where computational anatomy has utility in both investigative and clinical scenarios, we need to put it all together in an intuitive way. Only then will it be adopted by the people who could take full advantage of it by letting it guide their judgments.

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