CHAPTER 17
Brain Image Analysis and Atlas Construction

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17.1 Challenges in brain image analysis

The tremendous pace of development in brain imaging technologies has revolutionized our ability to investigate brain structure and function. Techniques are now available to capture features of anatomy and function at both molecular and whole-brain scales, mapping neuronal dynamics and gene expression as well as growth and degenerative processes that span multiyear time scales. The number of brain imaging investigations is also increasing exponentially [1]. A major goal of these studies is to analyze how the dynamically changing brain varies across age, gender, disease, across multiple imaging modalities, and in large human populations. To tackle these questions, many laboratories are using sophisticated algorithms for brain image analysis. Engineering approaches drawn from computer vision, image analysis, computer graphics, and artificial intelligence research fields are required to manipulate, analyze, and communicate brain data. Novel image analysis algorithms continue to uncover new patterns of altered structure and function in individuals and clinical populations, and mathematical strategies are being developed to relate these patterns to clinical, demographic, and genetic parameters.

17.1.1 Image analysis and brain atlases

In this chapter, we review current challenges in brain image analysis, focusing on the main algorithms, their technical foundations, and their scientific and clinical applications. The approaches include methods for automated registration and segmentation, anatomical parameterization and modeling, tissue classification and shape analysis, and pathology detection in individuals or groups. Algorithms are also described for generating *digital brain atlases*. Atlases are fundamental to brain image analysis, as they offer a powerful framework to synthesize the results of disparate imaging studies [2–5]. Built from one or more representations of the brain, atlases are annotated representations of anatomy in a 3D coordinate system. They serve as standardized templates on which other brain maps can be overlaid, for subsequent comparison and integration. To align new imaging data with an atlas, a variety of registration algorithms may be employed (see also Chapter 8 for other applications). Once registered, brain maps can be pooled across subjects and combined mathematically and statistically. As such, atlases provide a standardized 3D coordinate system to express observations from different individuals and a framework for interlaboratory communication.

17.1.2 Adaptable brain templates

Imaging algorithms are also significantly improving the flexibility of digital brain templates. *Deformable brain atlases* are adaptable brain templates that can be individualized to reflect the anatomy of new subjects. This allows the automated labeling of structures in new patients' scans [6–12]. High-dimensional image registration, or warping algorithms [8,13–23] (see [3] for a review), apply local dilations and contractions to a labeled digital atlas, elastically deforming it to fit a new subject's anatomy. These algorithms can transfer 3D maps of functional and vascular territories onto the scan of any subject, as well as information on tissue types, cytoarchitecture, and histologic and neurochemical content [24]. These algorithms are discussed in detail, later in the chapter.

17.1.3 Mapping structural differences

As a valuable by-product, 3D warping algorithms also *quantify* local and global shape changes. The complex profiles of dilation and contraction required to warp an atlas onto a new subject's brain provide an index of the anatomical shape differences between that subject's brain and the atlas [18, 19, 25–27]. Differences in regional shape can be assessed by the displacement required to locally deform one brain volume into another and can be further examined by applying vector and tensor field operators to the transformation field [28–32]. As a result, deformable atlases not only adapt to individual anatomy, but they offer a powerful strategy to analyze developmental, age-related, or pathologic variations.

17.1.4 Probabilistic atlases

As imaging studies expand into ever-larger patient populations, *population-based* atlases are required to identify statistical trends. These include group patterns of tissue distribution, anatomical asymmetry, and disease-specific features, which are often obscured in an individual due to the complexity of normal anatomy [33–36]. *Probabilistic atlases* identify these patterns by storing detailed quantitative information on cross-subject variations in brain structure and function [37]. Information stored in the atlas can then be used to identify anomalies and label structures in new patients. Based on well-characterized subject groups, these atlases contain thousands of structure models, as well as composite maps, and average templates, and allow visualization of structural variability, asymmetry, and group-specific differences (Fig. 17.1).

17.1.5 Encoding cortical variability

Because cortical anatomy is so variable across subjects, it presents unique challenges in brain image analysis. Specialized algorithms are needed to correct for wide variations in gyral patterns and to identify alterations in cortical anatomy in groups or individuals. Using mathematical equations derived from continuum mechanics and random field theory, probabilistic atlases can be used to detect cortical features not apparent in individual patients' scans. These include subtle changes in brain asymmetry during late brain development and early changes in gray matter distribution in degenerative disease [25, 26, 31–34, 38–42]. From an algorithmic standpoint, information on anatomic and functional variability can also guide algorithms for knowledge-based image analysis, including automated image labeling [14, 43–45] and functional image analysis [46].