Handbook of Neuroimaging Data Analysis

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In the introduction to *Handbook of Neuroimaging Data Analysis*, Dr. John Aston writes, "understanding the brain has become arguably one of the most complex, important and challenging issues in science, and imaging has become an invaluable tool in this endeavor." The development of imaging methods has provided applied researchers with a set of minimally invasive techniques to study the brain *in vivo*, and heavily influences contemporary medical and psychological research. Since neuroimaging's origin, the field has always been rich with statistical and computational challenges. From image reconstruction, to multi-image alignment, to modeling and analysis, a complete synthesis of neuroimage data depends on a series of computational techniques. Moreover, raw neuroimage data can exhibit complex spatio-temporal correlation structure, and applied work is often replete with difficult-to-remember acronyms, a host of possible data formats, and at times unintuitive measurements of quantities like "white matter integrity," or "cortical volume." For reasons like these, the activation energy required for quantitative researchers to enter into the world of neuroimaging can be quite high. In *Handbook of Neuroimaging Data Analysis* (hereafter, *Handbook*), editors (and contributors) Ombao, Lindquist, Thompson, and Aston work to reduce this barrier by providing readers with a single volume introduction to quantitative neuroimaging analysis.

Reflecting the relative popularity of magnetic resonance imaging (MRI) based applied research, the majority of *Handbook* is dedicated to summarizing developments in statistical analysis of different MRI data types. Much more could be (and has been) written about, for example, image coregistration algorithms, or the mathematics behind solutions to other preprocessing problems. Writing as a biostatistician, most datasets we encounter will have already been heavily preprocessed by collaborators or the data collection team. After an initial introductory chapter, the text is divided into two main sections: the first an overview of the many different data types that neuroimaging entails, and the second a comprehensive survey of areas of active research into statistical methods to work with each modality. In my review to follow, I will generally summarize *Handbook*'s content by section and topic first. Individual chapters may be listed out of order.

As noted, Chapters two through seven orient readers to specific data types, including positron emission tomography (PET, Chapter 2); MRI (structural MRI–Chapters 3 and 5, diffusion weighted MRI–Chapter 4, and functional MRI–Chapter 6); and electroencephalography (EEG, Chapter 7). Functional near-infrared spectroscopy and magnetoencephalography are notably absent from the survey of imaging modalities, though in practice analyses of these data may have much in common with analysis of functional MRI and EEG. For PET, MRI, and EEG, however, this section of the text very successfully synthesizes the broad domain-specific knowledge of each data type into introductory chapters intended for quantitative researchers.

In particular, though aimed specifically at structural MRI with a clinical flavor, Chapter 5 is written as a part-tutorial to basic features of image preprocessing like magnetic field inhomogeneity correction and affine transformation. The chapter also includes brief code snippets to introduce image manipulation with the R programming language and preprocessing with existing software. This chapter would make an excellent introduction to the basics of MR image analysis in general, and is explained clearly enough to be accessible to a beginning graduate student or advanced undergraduate. Chapter 4 also provides a quite thorough overview of diffusion MRI including tractography. Here, the authors detail what the data represent mathematically while retaining a high-level feel and noting several important open questions for research, like how to estimate uncertainty in tractographic maps. Similarly, the authors of Chapter 6 summarize the myriad techniques related to functional MRI analysis. Authors Lindquist and Wager review task-related activity localization and discuss notions of "functional connectivity" as a way for researchers to study systems of functionally correlated brain regions. Finally, Chapter 7 introduces EEG data and the many challenges it may present including artifact removal and modeling of stationary and nonstationary time series.

The final section of *Handbook* functions as a thorough overview of modern statistical research into methods for modeling MRI and EEG data. Methods for EEG are covered at the end in a two chapter (Chapters 20 and 21) *tour de force* surveying time and frequency domain analysis, dynamic linear and vector autoregressive modeling, frequency coherence analysis, and change point detection. Most other topics in this section are covered in relation to MR imaging. For example, Chapter 8 introduces the MR image reconstruction process that underlies absolutely all research with the resultant images. Chapter 10 contains an interesting review of MRI and EEG preprocessing pipelines and a variety of criteria that have been employed in the literature to evaluate the reliability and reproducibility of the output of these pipelines.

For structural MRI, Chapter 9 reviews advanced techniques for direct modeling of structural features or morphology. Chapter 18 meanwhile discusses general methods for modeling longitudinal series of images as outcomes. Outcome images of course need not be structural in nature, but much of the discussion in Chapter 18 is expressed in terms of intuitive, easily visualizable cortical thickness data. Matters of functional MR image analysis are presented starting with estimation of the hemodynamic response function in Chapter 11, and continuing through contemporary approaches to classical group-level modeling in Chapter 12. Chapter 14 begins a series of chapters devoted to functional connectivity methods with an explanation of the many different connectivity metrics used in the literature. The overall discussion of connectivity is deepened by a review of notions of effective connectivity for estimating causal relationships in Chapter 16, and formalized by Ginestet, Kramer, and Kolaczyk in their chapter on graph theory (Chapter 17). Rounding out the set of chapters on functional connectivity, Bowman, Simpson, and Drake present cutting-edge work on joint modeling of functional connectivity and anatomical tractographic imaging (Chapter 19). Other general topics are discussed as well: methods for control of family-wise or false-discovery error rates—always a concern with high dimensional data—are reviewed in Chapter 13. Last but not least, in Chapter 15, Eloyan, Zipunnikov, Yang, and Caffo have written a particularly clear introduction to matrix decomposition methods and their application to neuroimaging data. This chapter is augmented by a review of literature on computation of independent component analysis (ICA) or blind source separation in high dimensions. ICA in particular is a cornerstone technique for much applied functional connectivity work, and so many researchers may find this section useful.

Overall, *Handbook* functions more as a reference than a text, but very much succeeds in that regard. A researcher looking to embark on, say, research in structural MRI methodology would be very well served by successively reading through Chapters 5, 3, and 10 for an introduction to the data and general familiarity with image preprocessing. Following that or similar sequence, Chapters 18 and 9 might provide a survey of more advanced modeling of structural data types, and importantly supply our researcher with an armful of vetted references for further study. I certainly noted quite a few useful references while reading through *Handbook*, and will be returning to reread chapters for years to come.