The Neuroinformatics Studio: Digitally Exploring The Human Cerebral Cortex

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Abstract

This document outlines the major topics of the UCLA Neuroinformatics Studio course, Digitally Exploring the Human Cerebral Cortex, *as offered in Spring 2003. The Studio will introduce you to the computational study of the human cerebral cortex. Topics include cortical architecture, cortical development, neurogenetics, microanatomy, functional activation, topological mapping, and cortical plasticity. In the studio, you will explore each of these topics interactively using advanced computational methods.*

Introduction

The Neuroinformatics Studio (Psychology 186D) provides UCLA undergraduates with an introduction to the emerging field of neuroinformatics, the application of the methods of informatics to the problems of neuroscience. Specifically, the structure, organization, and functions of the primate (and human) cerebral cortex will be examined. The UCLA Neuroinformatics Studio is—to the best of our knowledge—the first such course offered anywhere in the world, but it certainly will not be the last.

We have adopted a studio setting to introduce neuroinformatics. The concept of an instructional studio originated in the arts and architecture, where students spend most of their class time working on projects under the guidance of a faculty member. Recently, this teaching format has been extended to physics and mathematics with great success (Wilson, J.M., Studio Courses: How Information Technology is Changing the Way We Teach, On Campus and Off, *Proceedings of the IEEE*, January 2000). We think the studio format is appropriate for neuroinformatics as well.

The UCLA Neuroinformatics Studio will be a seamless blend of three standard UCLA teaching formats: the lecture, the discussion section, and the laboratory. But unlike the traditional procedure of separately scheduling these three components, in the studio we will move between them as the situation dictates. Most sessions will begin with a minilecture, then move into the laboratory format with the possibility of returning to the lecture mode when needed. Discussion will be continuous and spontaneous. Laboratory exercises and problems are intermixed to provide the opportunity to actively explore issues as they are raised in class. Thus, fluidity, flexibility, and—above all—active learning are the hallmarks of a scientific studio.

Neuroinformatics

First, we survey briefly current developments in the field of neuroinformatics and suggest some differences between contemporary neuroinformatics and previous approaches to understanding the human brain and its function. We then outline the major topics to be examined in the studio.

Beatty, J. (2002). Whats new about neuroinformatics? In Valafar, F., editor, *Proceedings of the 2002 International Conference on Mathematical and Engineering Techniques in Medicine and Biological Science*, pages 3–7. Computer Science Research, Education, and Applications Press.

Shepherd, G. M., Mirsky, J. S., Healy, M. D., Singer, M. S., Skoufos, E., Hines, M. S., Nadkarni, P. M., and Miller, P. L. (1998). The human brain project: Neuroinformatics tools for integrating, searching, and modelling mulidisciplinary neuroscience data. *Trends in Neuroscience*, 21:460–468.

Van Essen, D.C. (2002). Windows on the brain. The emerging role of atlases and databases in neuroscience. *Current Opinion in Neurobiology*, 12:574–579.

Cortical Anatomy

The human cerebral cortex forms the surface of the two cerebral hemispheres. It is a thin sheet of neurons, which are responsible for a wide range of complex computations.

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Here, we introduce the anatomy of the cortical sheet from the perspective of classical neuroanatomy and consider some aspects of its formation.

Brodal, A. (1981). The cerebral cortex. In *Neurological Anatomy in Relation to Clinical Medicine*. New York: Oxford University Press.

Although the intrinsic geometry of the cerebral cortex is that of a simple, thin, 2–dimensional sheet of neural tissue, within the human skull that sheet is irregularly folded into a complex 3–dimensional structure. There is considerable advantage to recovering the 2–dimensional, or flatmap, representation of the cortex when undertaking its analysis.

Today, flatmap analysis of the 3–dimensional cortical complexity is greatly simplified by the use of advanced neuroimaging software and normalized probablistic cortical databases. Here, we introduce these software tools to explore both human cortical neuroanatomical landmarks and cytoarchitectural areas.

Software and Databases: The Caret flatmap system, the AFNI MRI viewer, and the LONI probabilistic human brain atlas.

Van Essen, D. C., Drury, H. A., Joshi, S., and Miller, M. (1998). Functional and structural mapping of human cerebral cortex: Solutions are in the surfaces. *Proceedings of the National Academy of Sciences of the United States*, 95:788–795. (*For reference use.*)

Van Essen, D. C., Drury, H. A., Harwell, J., and Hanlon, D. (2002). Caret-AFNI quick start: User's guide and tutorial. Technical report, Washington University School of Medicine, Saint Louis, Missouri.

Van Essen, D.C., Dickson, J., Harwell, J., Hanlon, D., Anderson, C.H. and Drury, H.A. (2001). An Integrated Software System for Surface-based Analyses of Cerebral Cortex. *Journal of American Medical Informatics Association*, 41: 1359-1378. (*For reference use.*)

Beatty, J. (2003). Using Caret and AFNI in the Neuroinformatics Studio: An Introduction to Flatmaps. *A Neuroinformatics Studio Document*, Los Angeles: UCLA.

Cortical Development

The human cerebral cortex, like that of other species, develops from cells located at the ventricular surface. We first examine this curious developmental process, which helps us to understand both the cellular architecture of the cortex and how changes in cortical size can be of use to a species.

Rakic, P. (1995). A small step for the cell, a giant leap for mankind: A hypothesis of neocortical expansion during evolution. *Trends in Neuroscience*, 18:383–388.

Van Essen, D. C. (1997). A tension-based theory of morphogenesis and compact wiring in the central nervous system. *Nature*, 385:313–318.

Northcutt, R. G., and Kaas, J. H. (1995). The emergence and evolution of mammalian neocortex. *Trends in Neuroscience*, 18:373–379.

Neurogenetics

A great deal has been learned about the genome in the past decade—so much so that genetics, molecular biology, and bioinformatics are in a position to provide real help to a neuroscientist interested in understanding higher brain function and its genetic basis.

Unlike the simple Mendalian properties governed by single genes, multiple genes on one or more chromosomes together determine a complex anatomical structure, function, or behavior. Here, we attempt to discover the genes that regulate cortical development and size in the mouse, a species that is very amenable to genetic characterization.

We will use a very powerful anatomical measurement tool, NIH ImageJ, to determine an index of cortical size in different strains of recombinant inbred mice of the genetic family, BXD. Then we will do a genome-wide search for markers on the mouse genome that correlate with cortical size using WebCTL. The correlated markers will define a quantitative trait loci (QTL) for cortical size. Finally, we will search for known genes in the vicinity of the QTLs using the UCSC Genome Browser for mice.

Software and Databases: NIH ImageJ, WebQTL, the UCSC Genome Browser, and the Mouse Brain Library.

Airey, D. C., Lu, L., and Williams, R. W. (2001). Genetic control of the mouse cerebellum: Identification of quantitative trait loci modulating size and architecture. *Journal of Neuroscience*, 21:5099–6109.

Glazier, A. M., Nadeau, J. H., and Aitman, T. J. (2002). Finding genes that underlie complex traits. *Science*, 298:2345–2349.

Kent, W. J., Sugnet, C. W., Furey, T. S., Roskin, K. M., Pringle, T. H., Zahler, A. M., and Haussler, D. (2002). The Human Genome Browser at UCSC. *Genome Research*, 12:996–1006. (*For reference use.*)

Korstanje, R., and Paigen, B. (2002). From QTL to gene: The harvest begins. *Nature Genetics*, 31:235–236.

Williams, R. W. (2000). Mapping genes that modulate mouse brain development: A quantitative genetic approach. In Goffinet, A. F. and Rakic, P., editors, *Mouse Brain Development*, pages 21–49, New York. Springer-Verlag. (*For reference use.*)

Laughlin, R. (2003). A protocol for measuring cortical size in the mouse. *A UCLA Neuroinformatics Studio Document*, Los Angeles. UCLA.

Microanatomy and Cell Physiology

Cortical neurons are highly stereotyped cells, with a few common cell morphologies dominating the cortical landscape. Here, we introduce several cortical neurons as objects of realistic neural simulations based on measured data. These simulations provide a mechanism for learning about the biophysical properties of cortical neurons specifically as well as neurons more generally.

Software and Databases: Neuron and NeuronDB.

Green, C. (2003). Using Neuron in the Neuroinformatics Studio: Introduction to Neural Simulation. *A Neuroinformatics Studio Document*, Los Angeles: UCLA.

Häusser, M. (2000). The Hodgkin-Huxley theory of the action potential. *Nature Neuroscience Supplement*, 3:1165.

Hines, M. L. and Carnevale, N. T. (2001). Neuron: A tool for neuroscientists. *The Neuroscientist*, 7:123–133.

Lisman, J. E. (1997). Bursts as a unit of neural information: Making unreliable synapses reliable. *Trends in Neuroscience*, 20:3843.

Cortical Connections

Given the striking microanatomical similarities between all regions of the primate cerebral cortex, what is it that provides each area with its distinctive physiological and functional properties? One possibility is that the functional specificity of each area is determined by its connections.

Software and Databases: SPSS and CoCoMac.

Passingham, R. E., Stephan, K. E., and Kötter, R. (2002). The anatomical basis of functional localization in the cortex. *Nature Reviews: Neuroscience*, 3: 606-616.

Kozloski, J., Hamzei-Sichani, F., and Yuste, R. (2001). Stereotyped position of local synaptic targets in neocortex. *Science*, 29:868–872.

Cortical Activation and Cognition

Neurons of the cerebral cortex, like other nerve cells, increase their metabolic activity when they process information. Functional brain imaging technology exploits this relation to map patterns of cortical activation during periods of controlled cognitive processing. We introduce these methods, along with procedures for integrating such measurements with existing quantitative brain atlases using AFNI and Caret. We then look at experiments in which functional imaging methods have been used to identify perceptual and language systems of the normal human cerebral cortex.

Software and Databases: Caret, AFNI, and the fMRIDC database.

Haxby, J. V., Grady, C. L., Horowitz, A., Ungerleider, L. G., Mishkin, M., Carson, R. E., Herscovitch, P., Shapiro, M. B., and Rapaport, S. I. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proceedings of the National Academy of Sciences of the United States*, 88:1621–1625.

Mellet, E., Tzourio, N., Crivello, F., Joliot, M., Denis, M., and Mazoyer, B. (1996). Functional anatomy of spatial mental imagery generated from visual instructions. *Journal of Neuroscience*, 16:6504–6512.

Cortical Maps and Cortical Plasticity

One striking characteristic of the cortex is that many cortical areas are characterized by unique internal patterns of topographic organization. Topological mapping and its development are explored here by simulations.

It is interesting to note that topographic patterns characteristic of a particular sensory area emerge spontaneously when sensory input to that area is surgically redirected to another cortical region. This and observations of topographic reorganization following partial sensory denervation have led to the neuronal empiricism hypothesis, which suggests that all cerebral cortex might contain a common computational algorithm that extracts statistical regularities—or knowledge—from the input that it receives.

Software: MATLAB and SOM-PAK.

Blasdel, G. G. and Salama, G. (1986). Voltage sensitive dyes reveal a modular organization in monkey striate cortex. *Nature*, 321:579–585.

Chapman, B., and Bonhoeffer, T. (1998). Overrepresentation of horizontal and vertical orientation preferences in developing ferret area 17. *Proceedings of the National Academy of Science, USA*, 95:2609–2614.

Kohonen, T. and Hari, R. (1999). Where the abstract feature maps of the brain might come from. *Trends in Neuroscience*, 22:135–139.

Kohonen, T. (1998). The self-organizing map. *Neurocomputing*, 21:1–6.

Pons, T. P., Garraghty, P. E., Ommaya, A. K., Kaas, J. H., Taub, E., and Mishkin, M. (1991). Massive cortical reorganization after sensory deafferentation in adult macaques. *Science*, 252:1857–1860.

Roe, A. W., Pallas, S. L., Hahm, J. O., and Sur, M. (1990). A map of visual space induced in primary auditory cortex. *Science*, 250:818–820.

Sharma, J., Angelucci, A., and Sur, M. (2000). Induction of visual orientation modules in auditory cortex. *Nature*, 404:841–847.

Chapman, B. and Bonhoeffer, T. (1998). Overrepresentation of horizontal and vertical orientation preferences in developing ferret area 17. *Proceedings of the National Academy of Sciences of the United States*, 95:2609–2614.

Individual Project Reports

If time permits, individual students or groups of students will carry out a project based upon a previous demonstration or experiment in the studio. Students will report their results to the class.

Evaluation

Evaluation will be based upon a) short examinations or written assignments following each major topic, b) class participation, and 3) individual projects, if time permits.