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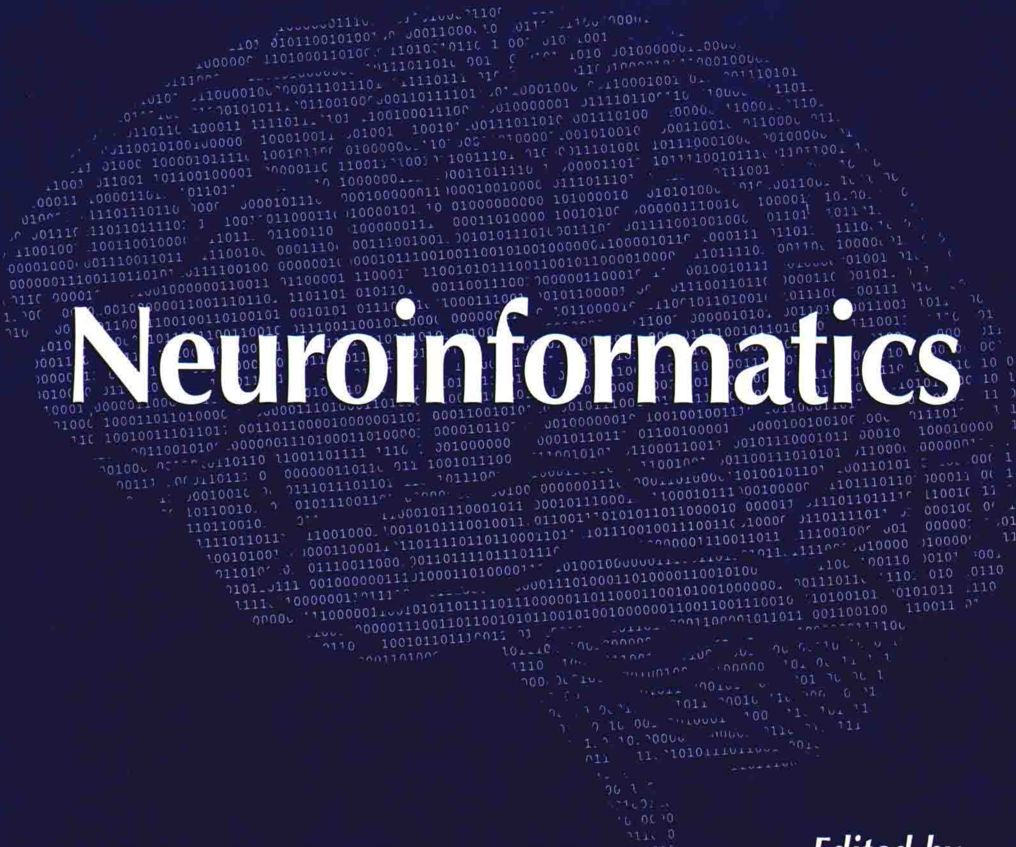

Neuroinformatics

Edited by

Chiquito Joaquim Crasto

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METHODS IN MOLECULAR BIOLOGY™

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For Cherie

Preface

> If the human brain were so simple that we could understand it, we would be so simple that we couldn't
>
> Emerson M. Pugh

The inception of the Human Brain Project (HBP) in the early 1990s gave birth to a new field of study—Neuroinformatics. Neuroinformatics sought to bring together computational scientists and neuroscientists to further understand the complex processes that govern the nervous system. Although the field of Neuroinformatics has provided myriad results, most will agree that we have merely begun to scratch the surface of what remains to be discovered.

I decided to give the areas of research that received support from the HBP funding agencies preferred representation in this volume. My work in the development of "NeuroText" to mine relevant neuroscience information from the biomedical literature came under the auspices of the HBP, as did the development of the SenseLab project at the Yale University School of Medicine, where I worked.

The four sections of this volume focus on: (1) concepts used in the development of databases and the dissemination of neuroscience knowledge; (2) presenting new developments and facets of imaging research as applied to the neuroscience; (3) developing computational methodologies to simulate neuronal processes through modeling, simulation, and the use of neural networks; and (4) applying neuroinformatics to neurogenentics and the understanding of neurological disorders.

As a domain of research and discovery, neuroinformatics is limitless. Just as the evolution of neuroinformatics will result in new avenues of discovery, this volume, one hopes, will find an extended readership. Experimental neuroscience workers should find this volume important as an introduction to how information science can be applied to their fields of study. The sections in every chapter in this volume are formatted (with bullet points and/or enumeration) for a point-by-point explication of the topics discussed. The writing style is simple enough to be appreciated by undergraduate and graduate students.

Several techniques and methodologies presented in this work, while developed for neuroscience, are easily extensible to other biomedical domains of research.

Over the last few years, neuroinformatics has grown to be a vital part of neuroscience. It mirrors the importance that information technology has had on almost every aspects of modern life. This volume, I hope, will be informative and yet make the reader want to know more about this complex system we call the nervous system—as much as it does neuroinformatics researchers.

Chiquito Joaquim Crasto

Foreword

Neuroinformatics heralds a new era for neuroscience research. As evidenced by the chapters ahead, the growing field of Neuroinformatics has met the first set of challenges in assuring its longevity and success: the creation of a web-based infrastructure for neuroscience data sharing, integration, and analysis. Once populated, these databases will provide the entire research community with impossibly rich sets of data for reanalysis, integration, and computational analysis. For the first time, neuroscientists will be able to rapidly integrate, analyze, and optimally synthesize vast neuroscience data from diverse heterogeneous modalities under investigation, greatly enhancing our collective and individual understanding of brain function and, ultimately, the human nervous system.

Clearly, the next significant litmus test for Neuroinformatics will be how quickly, and how completely, the neuroscience community populates these databases. As Neuroinformatics continues to build momentum as a field of research and a critical path to unraveling one of science's greatest mysteries, monographs such as *Neuroinformatics* will play a critical role in providing this community with the tools and impetus to share their research and papers with their colleagues around the globe by offering insights, information, and, importantly, compelling examples of success on which we can all build.

Background

Neuroinformatics combines neuroscience and informatics research to develop and apply innovative tools and approaches essential for facilitating a major advancement in understanding the structure and function of the brain. Neuroinformatics research is uniquely placed at the intersections of biomedical, behavioral sciences, biology, physical, mathematical sciences, computer science, and engineering. The synergy from combining these disciplines will enable the acceleration of scientific and technological progress, resulting in major medical, social, and economic benefits *(1)*.

The end goal of Neuroinformatics is to understand the human nervous system, one of the greatest challenges of the twenty-first century. The accumulation of data on nervous system development and function across the life span of many species has been impressively rapid. There has been an explosive growth in both the number of neuroscientists and the rate of data collection; the latter has occurred primarily through the development of various high-throughput technologies, the completion of the mapping of the human genome, and the new capabilities of discovery approaches using computational analysis. However, current insights into the integration and functional significance of the data are not optimal. Neuroinformatics should enhance our understanding of the detailed and fine grain heterogeneous data available, as well as facilitate the efforts of discovery neuroscience through the sharing of data and the use of computational models *(2,3)*.

The field of Neuroinformatics was created in 1993 through the efforts of a number of US funding agencies: National Institutes of Health, National Science Foundation, National Aeronautics and Space Administration, and the Department of Energy. The genesis of Neuroinformatics was a study by the National Academy of Science (NAS) commissioned by these same Federal agencies to evaluate: (1) the need and desirability of the field of Neuroscience research to share data and (2) the capability of the information technology (IT) field to handle the diversity, complexity, and quantity of data currently available and to become available in the future. This question was timely given the start of the Human Genome project, whose goal is to share broadly all genome data. The NAS 2-year study found that a neuroinformatics program is critical to understand brain development and function and to understand, treat, and prevent nervous system disorders *(4)*.

For Neuroinformatics to succeed, the field of neuroscience, in cooperation with other research fields, would need to develop an interoperable infrastructure and analytical capabilities for shared data. This would include interoperable web-based neuroscience data and knowledge bases, analytical and modeling tools, and computational models.

Upon launch, the initial US program was called the Human Brain Project. As it expanded globally, the moniker morphed into Neuroinformatics.

Neuroinformatics is timely, appearing nearly a decade and a half after the Human Brain Project launched. As the neuroscience community is beginning to harvest the results of this inaugural phase, Neuroinformatics progenitors and advocates are already looking to re-evaluate progress, challenges, and new directions for the field given rapid developments in IT and neuroscience. This publication should help refocus and enhance some of the research in this area, as it informs new and current practitioners of Neuroinformatics.

Neuroinformatics is conceptually divided into four sections:

Neuroscience Knowledge Management has outstanding chapters dealing with the critical issues germane to computer science as applied to neuroscience, namely managing knowledge, databases interoperability, database architectures, data representation, and model specification, and neuroscience ontologies. A significant challenge in knowledge management is extracting text from the scientific literature. NeuroText is a new automated program with these capabilities that Crasto et al. describe with examples of its utility, extracting information relevant to the SenseLab databases at Yale. Interoperability is one of the greater challenges in the field of Neuroscience. Marenco et al. take on this difficult problem, providing a substantive overview of ongoing efforts, and have constructive suggestions on approaches to overcoming this pivotal issue. Nadkarni and Marenco review the important principles of database architectures and introduce and explore the value of the entity-attribute-value model. Crook and Howell do an excellent job showing the benefits of XML data representation and how it is used in Neuroinformatics. Bowden et al integrate some of the major issues in knowledge management, using real-life examples influencing interoperability, controlled vocabularies, and data heterogeneity, and show how to manage this problem using a neuroanatomical nomenclature: NeuroNames.

Computational Neuronal Modeling and Simulations presents in-depth expert summaries on specific computational models and simulations as well as approaches to data mining. Bower and Beeman, the creators of Genesis, provide expert descriptions of this simulator along with information on its routine use and abilities to create new simulations. Lytton and Stewart discuss the use of their new data-mining tool as an adjunct to the simulator Neuron, bringing both novice and expert to new levels of understanding in computational neuroscience. The chapter by Prinz provides an excellent demonstration and discussion on unraveling the components of neural networks into their component parts.

Imaging focuses on informatics representation and approaches to the structural complexity of the brain using a variety of both traditional and non-invasive imaging methods. The challenge here is accurate representation of the data in either 2D or 3D space. Ultimately, the data are best represented in four dimensions, a true, additional challenge. Two of the premier groups working in this area present two different approaches, each valuable in its own right, for the creation of data-rich probabilistic atlases. Toga and his team present the Minimum Deformation Atlases as used to capture the variations of brain structure because of genetic manipulation. Nissanov and his colleagues approach the issue by extracting and placing data onto a normalized atlas and providing a query system to extract the integrated data sets. Both chapters provide the reader with a detailed explanation of these two different approaches, along with their advantages and limitations—certainly a must read for work in this area.

The two chapters dealing with fMRI, while technically robust, are also invaluable for working with and creating databases of functional brain data. Liu presents an excellent detailed approach to creating an fMRI database, which in this case is for mapping the olfactory brain areas. Fissell, on the contrary, presents in her chapter a complete and efficient analysis of structural or functional MRI data that are applicable to most research. Kötter presents a highly detailed review of his receptor database, a critical tool for reviewing and understanding the distribution of brain receptor systems.

Neuroinformatics in Genetics and Neurodegenerative Diseases will be of great interest to individuals interested in genomic approaches to understanding the nervous system and its disorders. The reader will benefit greatly from the integrated material. These chapters demonstrate the value of using components of Neuroinformatics as a way to understand the complex disorders of Dementia, Schizophrenia, and Alzheimer's disease and demonstrate how to use informatics in a systems approach to unravel the intricate interactions between networks of genes. Rosen et al. on trait analysis, Duch on dementia and other neurological disorders, Middleton et al. on Schizophrenia, and Kinoshita and Clark on Alzheimer's disease all present excellent cases of Neuroinformatics, successfully leading to the discovery of neuroscience. The four examples provide the reader with a gestalt of how this all comes together to provide a better understanding of brain function and malfunction.

Future Trends and Challenges

Has the field of Neuroinformatics developed sufficiently to sustain itself and to be a placeholder for other areas of Biology and Biomedical Research? Is it a rational approach? This monograph and others do an excellent job of reviewing and demonstrating the advantages and success of the developing field of Neuroinformatics *(5,6)*.

There is plentiful evidence elsewhere as well that the field is firmly established and flourishing. First, there are new field-specific journals providing a platform for cutting-edge research, such as *Neuroinformatics* and the *Journal of Integrative Neuroscience*. That these publications have quickly developed, following is a true testament to broad interest in the field, particularly given the great abundance of journals already covering neuroscience.

There are indications from the National Institutes of Health as well that the field is considered critical and sustainable. The original NIH program to stimulate and support initial research on Neuroinformatics, which received significant funding over the past 15 years, has concluded; scientists seeking support for new Neuroinformatics research programs can now do so through traditional NIH research mechanisms, through specific disease-oriented research institutes. And NIH continues to invest in support infrastructure to develop the field. In October 2006, NIH announced a new Road Map program, a 5-year, $3.8 million grant to the NIH Blueprint for Neuroscience Research to build an Internet-based clearinghouse to promote the adoption, distribution, and evolution of neuro-imaging tools, vocabularies, and databases.

Neuroinformatics is receiving support and attention from other US institutions as well. The Society for Neuroscience (SfN) has recently established a Neuroinformatics committee composed of international neuroscientists. Their goal is to monitor both the informatics needs of the community and the centralized gateway for neuroscience databases and to advise the SfN leadership on opportunities to enhance data sharing. Complete information on the functions of this committee is available on their Web site ***(7)***. In Seattle, Washington, the Allen Institute for Brain Science is freely sharing through the Web an enormous quantity of mouse brain anatomical genomic expression data, at the cellular structural level ***(8,9)***.

Globally, there is also long-term commitment to Neuroinformatics. Many countries involved in neuroscience research have initiated Neuroinformatics funding programs and have jointly created the International Neuroinformatics Coordinating Facility (INCF) ***(10)***. The INCF's responsibility is to coordinate the Neuroinformatics activities of its member countries, thereby creating an integrated global capability for neuroscientists.

The milestones and accomplishments cited above, along with the publication of this new monograph, confirm that Neuroinformatics is a thriving field of research with a bright future ahead. Individuals interested in keeping up with the latest issues in Neuroinformatics and/or learning about and joining this field of research will greatly benefit from the outstanding and timely material and concepts drawn together by these Neuroinformatics experts and presented in *Neuroinformatics*.

Stephen H. Koslow

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