EMERGENCE OF NEURONAL DYNAMICS FROM BRAIN STRUCTURE IN MULTI-MODAL RESTING-STATE BRAIN IMAGING

A Dissertation

Presented to the Faculty of the Weill Cornell

Graduate School of Medical Sciences

in Partial Fulfillment of the Requirements for the Degree of

Doctor of Philosophy

by

Xihe Xie

April 2021

EMERGENCE OF NEURONAL DYNAMICS FROM BRAIN STRUCTURE IN MULTI-MODAL RESTING-STATE BRAIN IMAGING

Xihe Xie, Ph.D.

Cornell University 2021

The direct link between human neurobiology and observed brain dynamics drives fundamental research efforts in neurosience. How does functional brain patterns arise from the underlying anatomy? Alongside technological advances, multimodal brain imaging enlarged the coverage of observable brain characteristics, and data-driven network theoretics emerged as a valuable framework for understanding large datasets and building biophysically based models of brain structure and function. This dissertation explores structure function models of different complexity and spatiotemporal scale, utilizing tools from signal processing, dynamical systems, optimization, and stochastic processes.

With diffusion imaging derived white matter streamlines, we built whole brain networks describing the underlying anatomical connections of the brain. The combination of connection strengths and inter-region delays provided anatomical networks that were rich in information. We showcase linear, low dimensional and highly interpretable network models of brain function that fully utilizes the brain's anatomical connectivity. Moreover, we found these models to capture the spatial patterns of brain activity in addition to observed functional patterns of the brain. We also examine a non-linear neural mass model of neuronal mean-field oscillations, in order to determine how parameterization and model complexity dictate model performance.

This document is dedicated to all Cornell graduate students.

ACKNOWLEDGEMENTS

The author wishes to acknowledge the generous contribution of several individuals and organizations that have made this dissertation posssible. Foremost is Dr. Ashish Raj, who's role as advisor has provided me with countless opportunities to explore the interdisciplinary field of neuroscience. The Neuroscience Department at Weill Cornell Graduate School has provided a welcoming community, funding, and outstanding opportunities for teaching and organizing around specific topics of interest. The University of California San Francisco has welcomed me with open arms as a visiting graduate. UCSF's Open Science Group, the Brainhack community, and Neurohackademy kept me energized and shared valuable knowledge in scientific knowledge, publishing, ethics, and data practices. The ReproNim team, INCF, and the ReproNim Fellowship trainers and trainees. Finally, many scientists and friends have given selflessly their expertise and support, including:

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1
INTRODUCTION

Elucidating how structure shapes observable function is at the heart of a wide spectrum of scientific disciplines. Often, functional units have easily discernible structures governing their roles in a biological system. For example, the 3D molecular structure of a protein forming an ion channel receptor for transport across membranes. As the system becomes more complex, it becomes increasingly difficult to explain emergent function in relation to its underlying structure. Currently, the most complex physical system in the known universe is the central nervous system; the dense synaptic connections and staggering axonal projcets in the brains of even simple organisms underly the myriad of fascinating behaviors in nature.

The relationship between the brain's structure and function is of particular interest in neuroscience, as morphological variants of the nervous system have repeatedly been shown to be associated with behavioral changes due to the brain's organizations [1, 2].

CHAPTER 2

ALICE IN WONDERLAND

2.1 The Black Kitten

One thing was certain, that the WHITE kitten had had nothing to do with it:—it was the black kitten's fault entirely [**?**]. For the white kitten had been having its face washed by the old cat for the last quarter of an hour (and bearing it pretty well, considering); so you see that it COULDN'T have had any hand in the mischief.

The way Dinah washed her children's faces was this: first she held the poor thing down by its ear with one paw, and then with the other paw she rubbed its face all over, the wrong way, beginning at the nose: and just now, as I said, she was hard at work on the white kitten, which was lying quite still and trying to purr—no doubt feeling that it was all meant for its good.

But the black kitten had been finished with earlier in the afternoon, and so, while Alice was sitting curled up in a corner of the great arm-chair, half talking to herself and half asleep, the kitten had been having a grand game of romps with the ball of worsted Alice had been trying to wind up, and had been rolling it up and down till it had all come undone again; and there it was, spread over the hearth-rug, all knots and tangles, with the kitten running after its own tail in the middle.

2.2 The Reproach

'Oh, you wicked little thing!' cried Alice, catching up the kitten, and giving it a little kiss to make it understand that it was in disgrace. 'Really, Dinah ought to have taught you better manners! You OUGHT, Dinah, you know you ought!' she added, looking reproachfully at the old cat, and speaking in as cross a voice as she could manage—and then she scrambled back into the arm-chair, taking the kitten and the worsted with her, and began winding up the ball again. But she didn't get on very fast, as she was talking all the time, sometimes to the kitten, and sometimes to herself. Kitty sat very demurely on her knee, pretending to watch the progress of the winding, and now and then putting out one paw and gently touching the ball, as if it would be glad to help, if it might.

'Do you know what to-morrow is, Kitty?' Alice began. 'You'd have guessed if you'd been up in the window with me—only Dinah was making you tidy, so you couldn't. I was watching the boys getting in stick for the bonfire—and it wants plenty of sticks, Kitty! Only it got so cold, and it snowed so, they had to leave off. Never mind, Kitty, we'll go and see the bonfire to-morrow.' Here Alice wound two or three turns of the worsted round the kitten's neck, just to see how it would look: this led to a scramble, in which the ball rolled down upon the floor, and yards and yards of it got unwound again.

'Do you know, I was so angry, Kitty,' Alice went on as soon as they were comfortably settled again, 'when I saw all the mischief you had been doing, I was very nearly opening the window, and putting you out into the snow! And you'd have deserved it, you little mischievous darling! What have you got to say for yourself? Now don't interrupt me!' she went on, holding up one finger.

'I'm going to tell you all your faults. Number one: you squeaked twice while Dinah was washing your face this morning. Now you can't deny it, Kitty: I heard you! What that you say?' (pretending that the kitten was speaking.) 'Her paw went into your eye? Well, that's YOUR fault, for keeping your eyes open—if you'd shut them tight up, it wouldn't have happened. Now don't make any more excuses, but listen! Number two: you pulled Snowdrop away by the tail just as I had put down the saucer of milk before her! What, you were thirsty, were you?

CHAPTER 3

CHAPTER 4

CHAPTER 4

APPENDIX A

CHAPTER 1 OF APPENDIX

Appendix chapter 1 text goes here

BIBLIOGRAPHY

[1] David J. Sharp, Christian F. Beckmann, Richard Greenwood, Kirsi M. Kinnunen, Valerie Bonnelle, Xavier De Boissezon, Jane H. Powell, Serena J. Counsell, Maneesh C. Patel, and Robert Leech. Default mode network functional and structural connectivity after traumatic brain injury. *Brain: A Journal of Neurology*, 134(Pt 8):2233–2247, August 2011.

[2] Xilin Shen, Emily S. Finn, Dustin Scheinost, Monica D. Rosenberg, Marvin M. Chun, Xenophon Papademetris, and R. Todd Constable. Using connectome-based predictive modeling to predict individual behavior from brain connectivity. *Nature Protocols*, 12(3):506–518, March 2017.