**Distribution Agreement**

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

Alexander John Poplawsky Date

Direct Detection of Neural Magnetic Fields with Fast-Temporal Resolution Magnetic Resonance Spectroscopy

By

Alexander John Poplawsky

Doctor of Philosophy

Graduate Division of Biological and Biomedical Science

Neuroscience

Xiaoping Hu, Ph.D.

Advisor

Raymond Dingledine, Ph.D.

Committee Member

George Andrew James, Ph.D.

Committee Member

Shella Keilholz, Ph.D.

Committee Member

Krishnankutty Sathian, M.D., Ph.D.

Committee Member

Accepted:

Lisa A. Tedesco, Ph.D.

Dean of the James T. Laney School of Graduate Studies

Date

Direct Detection of Neural Magnetic Fields with Fast-Temporal Resolution Magnetic Resonance Spectroscopy

By

Alexander John Poplawsky

B.S., University of Pittsburgh, 2004

Advisor: Xiaoping Hu, Ph.D.

An abstract of

A dissertation submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in the Graduate Division of Biological and Biomedical Science

Neuroscience

2011

**ABSTRACT**

Direct Detection of Neural Magnetic Fields with Fast-Temporal Resolution Magnetic Resonance Spectroscopy

By Alexander John Poplawsky

Functional magnetic resonance imaging (fMRI) indirectly detects brain activation by measuring the hemodynamic response to increased energy demand. The detection of neural magnetic fields (NMFs) with MRI seeks to improve the temporal and spatial accuracy of fMRI by directly measuring the electrical responses of the brain. *In vivo* studies of the human brain provide conflicting results for the true detection of NMFs and are hypothesized to be contaminated by signal changes originating from the blood. Our experiments are the first to measure axonal NMFs by examining the free-induction decay (FID) at a sub-millisecond temporal resolution. Two *in vitro* preparations were chosen to eliminate confounding signal changes attributed to the vasculature and simultaneous field potential recording was used to time-lock neural activity to the onset of the FID. In the first study, we experimentally measured an FID phase change associated with a single evoked action potential from the earthworm giant axon system. A maximum phase change of [-1.2 ± 0.3] x 10-5 radians was observed in the background-subtracted FID. In addition, the experimental phase time course correlated well with a theoretical phase time course in both amplitude and temporal characteristics. In this way, this study provides the first evidence for the direct detection of a magnetic field from an evoked action potential using magnetic resonance technology. In the second study, we determined that the signal changes associated with evoked CA1 neurons of the rat hippocampal slice were 25 to 100 times below our detection limits. Theoretical simulations and experimental measurements support that our methods are sensitive to axonal components of the evoked NMF and insensitive to dendritic components. In this way, our technique measures signal changes originating from the white matter, unlike current fMRI techniques that measure signal changes originating from the gray matter.

Direct Detection of Neural Magnetic Fields with Fast-Temporal Resolution Magnetic Resonance Spectroscopy

By

Alexander John Poplawsky

B.S., University of Pittsburgh, 2004

Advisor: Xiaoping Hu, Ph.D.

A dissertation submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in the Graduate Division of Biological and Biomedical Science

Neuroscience

2011

**ACKNOWLEDGMENTS**

Graduate school would have been much more difficulty, if not impossible, without the many people who surrounded and supported me. To them, I would like to dedicate this manuscript as it belongs to them as much as it belongs to me.

First, I would like to thank my advisor, Xiaoping Hu, who gave me the freedom and courage to pursue such a difficult, but rewarding, project. At times, I would become frustrated with the amount of time invested in developing our new technique, only to find negative results at the end. Thank you for your support during those times and trusting that there was something great around the corner.

Next, to my committee member (and unofficial advisor), Ray Dingledine. Thank you for opening your doors and accepting me as one of your own lab members. Not only did your guidance provide the key element of “simultaneous electrophysiology” to our experiments, but you opened my mind to a new way of thinking about this project. Without you and Geidy Serrano, the earthworm experiment would have never had legs.

To my other committee members, Andy James, Shella Keilholz and Krish Sathian. Your advice always cleared my vision and your encouragement allowed me to keep a confident attitude toward my goals.

To all the others at the BITC, Ray’s lab and the Neuroscience class of 2005, thank you for your friendship and good times. Without you, I would have prematurely gone crazy in my mid- to late-twenties instead of my golden years. You are all the best and I thank you for being there with me.

Finally, I would have never arrived here at Emory or completed this voyage without my family. Mom and Dad, thank you for giving me your good genes. I see and hear both of you every day and I am forever grateful to have both of you as my inspiration. Jon, we have been brothers and best friends for as long as we were together. Your excitement for life is infectious and has me always looking up to you. Lastly, to my lovely wife, Megan. You have brought so much color and fun to my life with your endless passion and your goofy humor. But mostly, you were my motivation for getting the hell out of here. I don’t know who I would be without you.

**TABLE OF CONTENTS**

**CHAPTER 1: General Introduction**

* 1. Introduction 2
  2. Magnetic Resonance Spectroscopy (MRS) Physics and

Theory of Neural Magnetic Field (NMF) Detection 3

* 1. Magnetoencephalography 5
  2. Phantom Models 6
  3. Computer Modeling 7
  4. Human Studies 9
  5. *In Vitro* Studies 11
  6. Summary 12

**CHAPTER 2: The Direct Detection of a Single Evoked Action Potential with Magnetic Resonance Spectroscopy in *Lumbricus Terrestris***

2-1 Abstract 15

2-2 Introduction 16

2-3 Materials and Methods 21

2-3.1 Earthworm Nerve Cord Preparation 21

2-3.2 Chamber Allowing Simultaneous Field Potential

Recordings and MRS 21

2-3.3 Data Acquisition – Electrophysiology 22

2-3.4 Data Acquisition – MRS 23

2-3.5 Data Analysis – Electrophysiology 24

2-3.6 Data Analysis – MRS 24

2-3.7 Correction of Action Potential Timing Based on

Conduction Velocity 25

2-3.8 Modeled Magnetic Resonance (MR) Magnitude and

Phase Change 26

2-4 Results 31

2-4.1 Measuring an Evoked Action Potential with

Simultaneous Electrophysiology and MRS 31

2-4.2 Theoretical MR Magnitude and Phase Change 31

2-4.3 Correlation of Theory and Experiment 32

2-2.4 Individual Worm Analysis 32

2-5 Discussion 39

2-5.1 Technical Considerations 39

2-5.2 Phase Difference 41

2-5.3 Volume Conductor Model 42

2-5.4 Symmetrical vs. Asymmetrical Distribution of the NMF 43

2-5.5 Physiology of the Phase Change 44

2-5.6 Lorentz Effect Imaging 46

2-5.7 Extrapolation to *In Vivo* Studies and Application 47

2-6 Conclusion 48

**CHAPTER 3: Examining the Direct Detection of Evoked Potentials in the CA1 Region of the Rat Hippocampus with Magnetic Resonance Spectroscopy**

3-1 Abstract 50

3-2 Introduction 51

3-3 Materials and Methods 54

3-3.1 Rat Brain Isolation and Preparation 54

3-3.2 Hippocampal Slice Preparation 55

3-3.3 Electrodes and Electrophysiological Equipment 56

3-3.4 Field Recordings of Spontaneous CA1 Activity 56

3-3.5 Field Recordings of Evoked CA1 Activity 57

3-3.6 Manufacture of Radio-Frequency (RF) Microcoils and

Circuit Boards 58

3-3.7 Chamber Allowing Simultaneous Field Potential

Recordings and MRS 60

3-3.8 Tuning, Matching and Quality Factor of the Microcoil 62

3-3.9 Calculating B0 Phase Difference Maps 62

3-3.10 Calculating the Microcoil Signal-to-Noise Ratio (SNR)

and Signal Decay Time (T2\*) 63

3-3.11 Determining the Microcoil Excitation Power 64

3-3.12 Simultaneous Field Recording Acquisition 65

3-3.13 Simultaneous MRS Acquisition 67

3-3.14 Data Analysis – Simultaneous Electrophysiology 68

3-3.15 Data Analysis – Simultaneous MRS 68

3-3.16 Modeled MR Magnitude and Phase Change 68

3-4 Results 76

3-4.1 Preliminary Field Potential Recordings 76

3-4.2 Phase Difference Maps 76

3-4.3 Free-Induction Decay (FID) SNR and T2\* 77

3-4.4 Microcoil Excitation Power 78

3-4.5 Simultaneous Field Potential Recordings and MRS

in the Hippocampal Slice 78

3-5 Discussion 87

3-5.1 Silicon vs. Glass Microcoil Substrate 87

3-5.2 Determination of the Excitation Power 89

3-5.3 Simultaneous Field Potential Recordings and MRS

Following Evoked Activity in CA1 91

3-5.4 Simulated Effects of Evoked CA1 Hippocampal Neuron

Activity on the MR Signal 93

3-5.5 Comparing the Simultaneous Hippocampal Experiment

to the Simulation in CA1 Pyramidal Neurons 96

3-5.6 Inability to Detect Hippocampal NMFs and

Future Directions 97

3-6 Conclusion 100

**CHAPTER 4: Conclusions and Future Directions**

4-1 Conclusions 102

4-2 Future Directions 104

**REFERENCES** 108

**List of Figures**

**CHAPTER 1: General Introduction**

Figure 1-1 Summary of *In Vivo* Studies 13

**CHAPTER 2: The Direct Detection of a Single Evoked Action Potential with Magnetic Resonance Spectroscopy in *Lumbricus Terrestris***

Figure 2-1 Earthworm Nerve Cord Cross-Section 20

Figure 2-2 Chamber Allowing Simultaneous Field Potential

Recordings and MRS 29

Figure 2-3 MRS Timing Diagram 30

Figure 2-4 Experimental Field Potential Recordings and FIDs 34

Figure 2-5 Theoretical Magnitude and Phase Changes in the FID 36

Figure 2-6 Comparing Theory and Experiment 37

Figure 2-7 Statistical Analysis of Individual Worm Subtractions 38

**CHAPTER 3: Examining the Direct Detection Of Evoked Potentials in the CA1 Region of the Rat Hippocampus with Magnetic Resonance Spectroscopy**

Figure 3-1 Surface RF Microcoil 70

Figure 3-2 Coil Circuit Board and Connections to the RF

Transmission Line and MRS Preamplifier 71

Figure 3-3 Chamber Allowing Simultaneous Field Potential

Recordings and MRS for the Hippocampal Slice 72

Figure 3-4 Photograph of the simultaneous hippocampal field

recording and MRS experiment 74

Figure 3-5 Timing of the Simultaneous Field Potential Recordings

and MRS Experiment 75

Figure 3-6 Spontaneous and Evoked Hippocampal Field Recordings 80

Figure 3-7 Phase Difference Maps 82

Figure 3-8 FIDs from Glass and Silicon Microcoils 83

Figure 3-9 Determining the Microcoil Excitation Power 84

Figure 3-10 Spectral Densities of Theory and Experiment 85

Figure 3-11 Comparing Theory and Experiment 86