SRINIVAS, SUNDAR. Micromagnetic Neurostimulation for Implantable Systems. (Under the direction of Dr. Gianluca Lazzi).

Recent neuroengineering research has demonstrated that human functions and senses in patients that are affected by neurodegenerative diseases can be partially restored by means of electrical neurostimulators. One such example is the artificial retina, where patients affected by degenerative retina diseases can regain partial vision by means of a retinal prosthetic device. However, electrode arrays currently used to replace endogenous electrical activation present several drawbacks, such as the exposure of metal contacts to conductive tissue, the potential need for excessive charge density to achieve stimulation with contact electrode arrays when electrode size is small, and the lack of tolerance with respect to imperfect contact between the electrode contacts and the neural tissue.

This dissertation investigates a new class of microcoils and microcoil arrays as neural microstimulators for the use in neuroprostheses. Being coils generating time-varying magnetic fields, the mechanisms of neural stimulation are based on eddy currents and their gradients of the magnetically induced electric fields. Thus coils do not need direct contact with the tissue and they can therefore be completely insulated thus removing the possibility of material reactions with conductive neural or surrounding tissue. Further, coils can potentially offer a larger number of options to control the shape of the induced magnetic fields (and therefore eddy currents) compared to traditional stimulators, and their operation will not be affected by contact capacitances.

This dissertation proposes a novel concept of eliciting neural responses by using a class of very small coils carrying time varying currents. Methods to increase the induced electric fields and other electromagnetic quantities such as using ferrite cores, ferrite slabs, figure of eight coils etc. are investigated. Preliminary theoretical analysis is done for coils encircling a long ferrite core. A novel Finite Difference scheme for the solution of the diffusion equation involving magnetic vector potential for static and quasi-static conditions has been developed and used to calculate
magnetic fields and induced currents for geometries involving discontinuities in permeabilities. To drive the developed coils, a new bootstrap circuit is utilized. Finally, experimental results depicting the neural response of rat sciatic nerves to our proposed configuration will be presented. This work demonstrates that small coils can be used to induce neural responses and, therefore, are a promising alternative to existing electrical neurostimulators.
“MagStim”: Micromagnetic Neurostimulation for Implantable Systems

by
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Doctor of Philosophy

Physics

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DEDICATION

To Dr. Gianluca Lazzi, My Supervisor and Well Wisher

Thank You Sir for everything.
BIOGRAPHY

Sundar Srinivas did his Bachelor of Technology from the Indian Institute of Technology, Bombay in Engineering Physics. He joined the Dept. of Physics at the North Carolina State University to pursue Doctoral Degree with emphasis on magnetism in biomedical applications. Hopefully with God’s grace we can prove magnetism as an exact dual, if not better, to electricity in biomedical applications. This research is a quest to see if Faraday’s duality of electricity and magnetism holds even in Biological Applications.
ACKNOWLEDGMENTS

I would like to thank Lord Shiva for his kindness. Few people are bestowed with his grace because of which I always met good people around the world. I am a nonentity without the love, trust and generosity of all these people.

It would be a futile attempt to express in words my gratitude to Mr. D. Venkat Rao, Mrs. D. Veena Rao, Ms. A. Neelima, my parents and my sister for the pain they had to go through for my studies.

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My stay in Raleigh had been of utmost happiness and fun thanks to my friends. Seniors and brother like friends: Abhijit & Kinjel Raval, Amit and Neha Acharya, Swamy and Satya Pati, Mohanraj Prabhugoud, Kannan, Raoul Jetley, Narendra Roy, Ravi Jenkal, Kunal Kandekar, Rahul Srinivas, Vivek Shankam, saw me through the first phases of my life in Raleigh. Again
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Music has been an integral part of my life and I found some of the best friends of my life through music. I would like to express my warmth to my fellow musicians and friends: Yatin ‘Ticket’ Tawde, Gaurav ‘gogo’ Mehta and Mrudula Mehta, Vinit ‘Uncle’ Singh, Anuj and Ramya Kapadia, Harini Ramaprasad, Dave Hoff, Sandeep Hathangady. Special thanks to “Ticket Tawde”, however oxymoronic it might seem, to drive me everywhere for practices. Whatever his timing sense in traffic was, he was a real mentor to me in gaining sense of tempo in music which I lack in my guitar skills. Uncle and I could play guitar for hours without even preparing!

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CHAPTER 1

Introduction

1.1 Motivation

Functional Electrical Stimulation (FES) refers to the technique in which externally delivered electric currents are used to elicit neural responses in tissues possibly to provide a partial remedy to paralysis induced by brain injury, spinal cord injury, or any other neurological disorder. Medically, a device that elicits a neural response by inducing a current externally is called a Neurostimulator. In the past decade, remarkable progress has been made toward the realization of implantable neurostimulators. One such example is a retinal prosthesis to restore partial vision to the blind, which is called the “Artificial Retina Project” [1]-[13]. In this example, like all actively pursued neurostimulators, the lost functionality (whether senses or movement) is partially restored by direct current stimulation, usually achieved through a high-density electroneural array.

The example of the artificial retina excellently illustrates the degree of sophistication of current electroneural stimulators, as it comprises all subsystem modules found in most implantable devices, with additional complexities associated to the impervious medium that houses the implant (the eye humor), high stimulation rates, and additional components (camera, battery-pack, etc) that increase the level of sophistication of the device compared to other neurostimulators. The idea builds on the successful realization of the cochlear implant [8], where a few electrodes can offer to patients with impaired hearing an audible perception of varying degree of quality. In blind patients affected by retinal degeneration caused by the deterioration of photoreceptor cells, such as in the case of Retinitis Pigmentosa (RP) or Age-Related Macular Degeneration (AMD), ganglion and bipolar retinal cells survive at a high rate. The idea behind the retina prosthesis system is to replace the functionality of the lost or damaged photoreceptors by providing the electrical signal that should have been generated by this important neural layer as a response to light stimuli [1]-[3]. There are many
technological challenges associated with the development of retinal prosthesis systems, and a few research groups in the US and abroad are actively pursuing devices with varying resolutions and characteristics. In the US, leading teams are those led by the Doheny Retina Institute at USC [2] and MIT/Harvard[4]-[6]. The team at Doheny Retina Institute has implanted seven patients with an epiretinal electrode array with 16 electrodes (4 x 4) and currently has 240 electrode devices in clinical trials. MIT/Harvard [4]-[6] advocates a subretinal array implant to mimic more closely the actual function of the missing photoreceptors (which are the last layer in the retina).

The retinal prosthesis system pursued by DOE Artificial Retina team which comprises of the group of Prof. Gianluca Lazzi, is conceptually illustrated in Figure 1. It is composed of two units: the extraocular unit acquires video images that are encoded and transmitted to the intraocular unit composed of a power and signal transceiver and processing chip, a stimulation-current driver, and a stimulating electrode array mounted on the retina. Figure 2 shows the stimulating electrode array.

The image obtained through the stimulating electrode array is a pixellated bitmap image, with resolution limited by the number of electrodes. Current implanted devices have 16 electrodes in a matrix of 4 x 4; however, 60 and 240 electrode designs are under development. Each electrode forces current through the retina, with the intent of inducing enough current and potential gradients in the ganglion and bipolar cell layers to elicit vision – essentially inducing a phosphene.
These concepts of retinal prostheses are in general applicable to stimulation of neurons in other parts of human body.

While effective, there are a number of drawbacks with electrical neurostimulators, including:
a) The stimulating electrodes are in direct contact with neural tissue, and are therefore exposed to highly corrosive substances (water, salt, sugar) that could harm their integrity over long periods of time; b) Contact capacitances are relatively large; c) Current spreads in a somewhat arbitrary pattern in the tissue, without much control, thus likely not to be optimal; d) Excitation is a strong function of how well the surgeon positioned the array on the tissue – a slight lift of the electrode array may leave enough space between electrode and tissue to render impossible the electrical stimulation altogether.

By contrast, magnetic stimulation appears to be very attractive for the following reasons:

1. Since the human body has unitary relative magnetic permeability, it is very well penetrable to low frequency magnetic field

2. Coils to generate magnetic fields need not to be in direct contact with the tissue to be stimulated, thus removing the problem of achieving “zero spacing” between stimulating electrode and retina.
3. Magnetic fields can be shaped effectively by changing the shape and properties of the coils (simple coils, ferrite filled coils, figure-eight coils, “slinky” coils, etc.). We can therefore utilize an important degree of freedom in the design of the array.

4. Unlike forced conduction currents, neural cells are penetrable to magnetic fields, thus eddy currents are induced both inside and outside the cell membrane, potentially reducing the threshold of the potential gradient needed for stimulation.

5. Encoding the visual stimuli in the complex-layered retinal structure hides opportunities yet to be explored: recent evidence suggests that there could be sufficient spatio-temporal signal correlation in the retina itself so that higher frequencies compared to those traditionally used for neural stimulation could prove useful and perhaps critical in “mimicking” more closely the natural behavior of the retina when used in an array.

As shown in the next sections, this would prove an asset for magnetic stimulation, which is achieved through capacitance discharge. Its effectiveness and “ringing effects” increase with the shortening of the stimulating pulse.

1.2 Brief Introduction to Neural Magnetic Stimulation

In this section we briefly describe how traditional Transcranial Magnetic Stimulation (TMS, stimulation of brain using magnetic fields) is performed. Then we shall introduce our novel concepts exploring the possibility of using neural magnetic stimulation for implantable devices.

English Physicist Michael Faraday in 1831 discovered the phenomenon of Electromagnetic Induction where electric fields are introduced in space due to the presence of time-varying currents. The solution to this problem involves solving the diffusion equation for Magnetic vector potential, which will be discussed in detail in chapters 3-6. D’Arsonval in 1896 [14] reported that the brain could be magnetically stimulated by a coil carrying a high time-varying current. In 1985 Barker et. al. [15] demonstrated that momentary depolarization of the nervous system using pulsed currents induced by time varying magnetic fields.
Since then magnetic stimulation has been extensively studied and applied for various purposes. Some of these include testing of motor function, vision, language, and studying the pathophysiology of brain disorders, therapy, particularly in psychiatry. It is especially useful as a monitoring tool for anaesthetized patients undergoing spinal surgery. The unique features of TMS are particularly useful in evaluating spinal cord injury and recovery. [16]

Neural magnetic stimulation has been achieved by low frequency magnetic fields or a RLC discharge. The operation of TMS relies on the principle of a pulsed discharge circuit, which is depicted Figure 3. A capacitor is charged to a certain voltage through the switch and then is discharged through the inductor. This involves the basic principles of a LCR discharge circuit. A rapidly varying current flows in the inductor coil due to this discharge. This coil is placed in proximity of the neural tissue to be stimulated as shown in Figure 3. This induces electric fields and corresponding eddy currents in the conducting media (brain, heart or retina as show here). These fields are believed to elicit neural responses depending on the strength and pulse width of pulse generated by the discharged circuit.

It should be noted that all applications mentioned in the description of the existing TMS methodology above are studied and applied, non-invasively, from outside of the human body. As an example the magnetic stimulation of the human nerve trunk is shown in Figure 4. We see that a coil is placed at a certain distance from the actual nerve to be stimulated (which is below the skin layer deeper). Typical coils used for existing magnetic stimulators have diameters in the range of few centimeters and use very high charging voltages (~ 1kV). While this is suitable for transcranial magnetic stimulation, the research work presented in this dissertation focuses on downsizing these values so that the principle of magnetic stimulation can be used in implantable devices. To the best of our knowledge, there is no existing work which has demonstrated the potential use of microcoils for implantable devices. Tables 1 and 2 summarize the various mechanical and electromagnetic quantities used in TMS from available literature.
**Figure 3.** Magnetic stimulator circuit with stimulating coil placed in front of the neural tissue to be stimulated

**Figure 4.** Stimulating coil above the human arm intended to induce responses in human radial nerve [17]
Table 1. Review of existing literature summarizing the coil and magnetic stimulator circuit parameters

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<td>figure 8 coils wire radius 1.25 mm</td>
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### Table 2. Review of existing literature summarizing electromagnetic quantities involved in TMS

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<th>Ref</th>
<th>I peak (kA)</th>
<th>dI/dt peak (A/µs)</th>
<th>B peak (T)</th>
<th>E peak (V/m)</th>
<th>dE/dy peak (V/m^2)</th>
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<td>7967</td>
<td>A/m³</td>
<td>1146</td>
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**Table 2 Continued**

- round slinky-1
- round slinky-2
- round slinky-3
- round slinky-4
- round slinky-5
- rectangular slinky-2

- round slinky-2
- round slinky-2
- round slinky-2
- round slinky-2
- round slinky-2

- L = 90 µH
- L = 265 µH
- L = 1010 µH

- array_scalp
- array_brain

- current flowing in opposite directions

- same directions diff. directions
Table 2 Continued

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An explanation of the terminology used in above tables is provided below:
m.r.- mean radius
o.r. -outer radius
i.r. -inner radius
l -length
N - number of turns
L -inductance
R -resistance
C -capacitance
\(V_0\) - charging voltage
*max dB/dt = 31 kT/s

We notice the large values of source voltages (~1kV) and currents in the coils (kA range). Also the dimensions of these coils do not permit their use in implantable devices. Since all magnetic stimulation data given in Tables 1 and 2 involve outer body stimulation the distance from the actual nerve to the coil is relatively large. As the B fields fall off dramatically in the z (axial) direction with increasing distance and decreasing radius of the coil, these coils need to be relatively large and must be fed with such voltages in order to induce enough E fields in the tissue. It should be noted that the mechanism of nerve stimulation using time varying magnetic fields is not yet understood: - some neural tissues react to much lower induced current densities compared to others. Table 3 gives a survey of selected existing literature that report threshold induced currents for eliciting a neural response.
Table 3. Review of existing literature summarizing threshold values of induced current densities, pulse widths/frequency which involve neural responses

<table>
<thead>
<tr>
<th>No.</th>
<th>Amplitude (Am²)</th>
<th>Rise time (µs)</th>
<th>Total decay time (µs)</th>
<th>Frequency (Hz)</th>
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<td>Nollet et. al. [16]</td>
<td>10-200</td>
<td>100</td>
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<tr>
<td>Barker et. al. [36]</td>
<td>~60-200</td>
<td>~800</td>
<td>~800</td>
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<tr>
<td>McRobbie [27]</td>
<td>10</td>
<td>350</td>
<td>~1000</td>
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<tr>
<td>Havel [38]</td>
<td>~400</td>
<td></td>
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<td>Walsh [39]</td>
<td>150</td>
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<td>Yamaguchi [18]</td>
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<td>Roth [24]</td>
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<td>20000</td>
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<td>Peters, C.R. [40]</td>
<td>0.0001</td>
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<td>3-25</td>
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<td>Beecroft [41]</td>
<td>0.050-0.700</td>
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<td>250-5000</td>
</tr>
<tr>
<td>Miyoshi [42]</td>
<td>0.010-0.050 (depending on distance)</td>
<td></td>
<td></td>
<td>DC</td>
</tr>
<tr>
<td>Kowalski [29]</td>
<td>2.500</td>
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<td>Repacholi [43]</td>
<td>0.010</td>
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<td>Kaune [44]</td>
<td>1.000</td>
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As shown in Table 3, there is a significant variation in the stimulating thresholds depending on the nerve being considered, the frequency (if oscillatory fields are used) or the pulse width (if pulse discharge is used). Whether the Electric Field (and hence the induced current
densities) or the spatial gradient of the Electric Field in the direction parallel to the nerve is the most significant parameter to induce neurostimulation is a much debated question. A detailed discussion regarding this subject with relevant references shall be presented in chapter 5.

### 1.3 Outline of our Novel Concept of Using Magnetic Stimulation with an eye on implantable devices

The focus of this dissertation is on exploring the use of very small magnetic coils, which we termed “micromagnetic coils,” in eliciting neural response, thus establishing whether we can ultimately develop implantable devices using such small coils instead of electrode arrays. Functional Electrical Stimulation is relatively well understood and applied in the fields of prosthetic devices such as the retinal prostheses system mentioned in chapter 1, cochlear implants, cardiac pacemakers, urinary incontinence devices, etc. This research is a first step in proving the duality between Functional Magnetic Stimulation (FMS) and FES for implantable devices. As described in section 2.1, there is a large body of literature that proves that externally induced magnetic fields are an effective method to stimulate neural tissues or affect human functions. However, to the best of our knowledge, there are no previous attempts that can be found in the literature to use implanted microcoils for neural stimulation. We believe that the reasons for this are the following:

1. It is substantially easier to design and fabricate arrays of microelectrodes than arrays of microcoils and, therefore, in the neural stimulation field that has traditionally been driven by the need to provide effective devices and solutions and prove ideas with a relatively quick turn-around time and limited engineering complexities, widely available electrode arrays have been universally used for just about any implantable neural stimulation application;
2. There is a tremendous amount of knowledge and literature on stimulating electrode arrays with a number of books and papers that provide guidelines for their design;
3. Retinal prosthetics are relatively new and they are particularly amenable, in our opinion, to the use of microcoils for magnetic stimulation because the target cells (ganglion and bipolar cells) are only 30 to 50 µm below the microcoils that are placed on the surface of the retina (which is 200 µm thick).

4. Even in a retinal prosthetic application, simple coil geometries will probably not induce eddy currents in the tissue which are large enough to elicit vision.

Several important questions must be answered, however, before micromagnetic stimulation of the neurons can be achieved. Specifically, what current levels in the microcoils will be needed to stimulate ganglion and bipolar cells? What shapes and physical characteristics of coils will allow us to effectively induce sufficient eddy currents in the targeted cell layers to generate controlled stimulation? What will be the drawbacks associated with micromagnetic stimulation, including potential thermal increase on the surface of the concerned tissue?

This activity seeks to answer these important questions. At the same time, in this research we will provide preliminary (theoretical, numerical and finally experimental) data that we believe supports our idea that a class of microcoils for micromagnetic stimulation will prove a viable and effective solution to the neural stimulation problem. Through this research, we propose new geometries and devices that can significantly increase the current density induced in the tissue region with respect to traditional coils, thus enabling the concept of micromagnetic stimulation. Further, we will investigate the effect of variation of stimulation frequency on the induced fields and currents and the control and “steering” capabilities that they offer.

In the following chapters, we will present numerical and experimental results toward the development of micromagnetic neurostimulators. It should be noticed that the smallest of coil which could be hand wound with facilities and technology at our disposal have a diameter between 2mm and 5mm. Since we were successfully able to stimulate rat sciatic nerve in vivo with voltages two orders of magnitude lower compared to data found in the literature, our future work will focus on fabricating smaller micromachined coils. The final
implantable coils we intend to build in future would be made out of MEMS technology. A detailed discussion will be presented in the final chapter.

The rest of this thesis is organized as follows: Chapter 2 presents defines the problem of magnetic coils carrying time varying currents. In this chapter induced electromagnetic quantities are theoretically calculated for simple coil geometries. Chapter 3 introduces a novel Finite Difference scheme to compute induced electromagnetic quantities when the source coils have complex geometries including ferrite cores, figure-of-eight configurations, and array of coils. Chapter 4 explores the possibility of using magnetic stimulation of neural tissues in implantable devices. In this chapter we consider the retinal prosthetic system as an example where micro coil arrays can be implanted inside the eye to elicit visual responses in the retina. Chapter 5 concentrates on experiments with Rat Sciatic Nerve. A novel boot strap stimulator circuit will be discussed, inductors fabricated in the lab would be analyzed, and brief description of evoked neural responses would be presented and finally the experimental results on Rat Sciatic Nerve would be presented.
Chapter 2

Theoretical Analysis

The possibility of neural micro magnetic stimulation relies on success in achieving high magnetic fields (and hence high induced electric fields and eddy current densities) in the vicinity of the micro inductor coils, since the eddy currents induced by magnetic stimulation are much smaller than the electric currents being injected by electrode arrays of existing neural prosthetic devices. This chapter is intended to describe the underlying concepts and the basic mathematics involved in the solution of the considered problem. As an example of neural tissue we consider here the Retina and the Retinal Ganglion Cell Layer (GCL). GCL is the region of retina where neurons are still intact even if the photoreceptor cells are not functioning. In the case of the artificial retina, the intention is to induce a neural response from ganglion and bipolar cells.

2.1 Single Coil Calculations

Figure 5 depicts a typical configuration of an array of microinductor coils carrying time varying magnetic fields placed in front of the neural tissue (retina in this case). The time varying magnetic fields induces eddy currents inside the retina.
We start investigating the electromagnetic behavior of our proposed configuration by considering a single-turn coil. A cross-sectional view of such a coil in front of the retina is depicted in Figure 6. A coil carrying a time-varying current is placed on the retina. The time-varying current in the coil induces eddy currents inside the retina that, for simplicity, is modeled as an infinite slab. The coil dimensions are of 100 microns while the diameter of the eye is 25 mm, hence a valid assumption. To calculate the induced eddy currents we must solve the diffusion equation for the magnetic vector potential:

$$\nabla^2 \mathbf{A} = \mu \sigma \frac{\partial \mathbf{A}}{\partial t} - \mu \mathbf{J} \quad \text{................................(1)}$$

Where

$$\mathbf{J}_{\text{eddy}} = -\sigma \frac{\partial \mathbf{A}}{\partial t} \quad \text{........................(1.1)}$$

We know that for a uniform stimulating current distribution the vector potential is directly proportional to the stimulus current. Defining $\mathbf{A}_0$ as the potential due to unit current and $I(t)$
as the current in the stimulus coils, which is a function of time, equation (1.1) would be suitably modified as:

$$J_{\text{edd}} = -\sigma A_0 \frac{\partial I}{\partial t} \quad \text{................. (1.2)}$$

Equation (1.2) becomes the governing equation, and we have to delve into the appropriate mechanism to get a suitably high rate of change of current in the stimulating coil.

We start off investigating this problem by considering a low frequency sinusoidal time-varying current in the coil. We assume quasistatic behavior and ignore the first term in the right side of equation (1). This leads to:-

$$\nabla^2 A = -\mu J \quad \text{.................................(2)}$$

The basic configuration is shown in Figure 6. Here:

- $\mu_0 = 1.26 \times 10^{-6}$ (permeability of free space)
- $f=100$ Hz
- $\sigma = 0.5$ (conductivity of the Retina)
- $I = 1$ A.
\[ r_i = 100 \text{ microns (inner radius of the simulating coil)} \]
\[ r_o = 110 \text{ microns (outer radius of the simulating coil)} \]
\[ z' = 30 \text{ microns (depth in the retina where we calculate induced eddy currents)} \]

In these calculations we assume a coil thickness of 10 microns, and therefore, 
\[ l = 10 \text{ microns (thickness of the coil)} \]

The analytical solution to (1) has been presented in [45] and is given by:
\[ \mathbf{A}(r,z) = \mu \int_{r}^{\infty} \frac{1}{x^2 (x^2 + \sqrt{x^2_1})} \left( \int_{r_{1x}}^{r_{2x}} w J_1(w) dw \right) J_1(rx)(1 - \exp(-lx))(\exp(-x_1z)dx) \]
\[ x_1 = \sqrt{(x^2 + j\omega \mu \sigma)} \]

For the particular data mentioned above the resultant induced eddy current at \( z' = 30 \text{ microns} \) and \( r \sim 100 \text{ microns} \) is approximately \( 1e-8 \text{ A/m}^2 \).

This induced eddy current is relatively low. Thus we investigated ways to increase such induced currents. Some of the ideas we explored and implemented were:

1. Using a pulsed discharge circuit to drive the coils instead of the sinusoidal source as considered above.
2. Using coils embedded with ferrite cores. Ferrites increase the induced magnetic fields and also focus the fields in the vicinity of the coil. Details will be presented in chapter 3.
3. Using ferrite slabs at the ends of the coil configuration.
4. Using two coils carrying antisymmetric currents arranged in a figure-of-eight configuration.
5. Using four coils carrying alternate anti parallel currents arranged in two figure-of-eight configurations attached together.
2.2 Analytical and Numerical Solution to the Poisson Equation Involving the Magnetic Vector Potential for a Coil Carrying a Current and Fitted with a Long Ferrite Core

The analysis for magnetic vector potential and the on axis magnetic fields for a coil encircling a long cylindrical core is performed for the static case. The diffusion equation for the magnetic vector potential has been previously solved in [45] for regions of different conductivities but with the same permeability. We are interested in configurations with different magnetic permeabilities and in the static case, which may be further extended to quasistatic conditions. This is an effort to show the efficacy of embedding a ferrite core in boosting the magnetic fields. Further, this chapter proves that even for simple discontinuities in permeabilities the theoretical analysis becomes extremely cumbersome. Hence we need to formulate a Finite Difference Code to solve the electromagnetic problem involving coil configurations with various discontinuities in permeability.

Figure 7 shows a single coil carrying a time-varying current encircling a infinitely long ferrite core. The radius of the coil is \( r_0 \) while the radius of core is \( a \). We present here the
analytical solution for the diffusion equation for the magnetic vector potential for the configuration of Figure 7.

**Analytical Solution**

We wish to solve the diffusion equation for the magnetic vector potential, viz.:

\[
\nabla^2 \mathbf{A} = \mu \sigma \frac{\partial \mathbf{A}}{\partial t} - \mu \mathbf{J} \tag{4}
\]

Since we are interested in frequencies of the order of 100 Hz (biomedical) we assume the quasistatic behavior and drop the first term in right side of (1).

\[
\nabla^2 \mathbf{A} = -\mu \mathbf{J} \tag{5}
\]

First we consider the delta function coil carrying a current I. (2) then becomes:

\[
\nabla^2 \mathbf{A} = -\mu I \delta(z-z_0)\delta(r-r_0) \tag{7}
\]

For most of the region we consider the Laplace equation and cast (7) in cylindrical coordinates as:

\[
\frac{\partial^2 A}{\partial r^2} + \frac{1}{r} \frac{\partial A}{\partial r} - \frac{A}{r^2} + \frac{\partial^2 A}{\partial Z^2} = 0 \tag{9}
\]

We use separation of variables. Writing \( A(r,z) = R(r)Z(z) \) leads to eigenfunction equations for \( R(r) \) and \( Z(z) \) as:

\[
\frac{1}{Z(z)} \frac{\partial^2 Z(z)}{\partial z^2} = const = -\alpha^2 \tag{10}
\]

\[
\frac{1}{R(r)} \frac{\partial^2 R(r)}{\partial r^2} + \frac{1}{r R(r)} \frac{\partial R(r)}{\partial r} - \left( \alpha^2 + \frac{1}{r^2} \right) = 0 \tag{11}
\]
The reason behind choosing negative constant in (10) is to give rise to a cosine function in \( z \) for \( A \) considering the symmetry of the system about \( z_0 \). As for (11) the solution involves a linear combination of modified Bessel functions of the first kind. Combining the two solutions we can write the general solution as:

\[
A^i(r, z) = \int_0^\infty \left( C_i(\alpha)I_1(\alpha r) + D_i(\alpha)K_1(\alpha r) \right) \cos(\alpha(z - z_0)) \, d\alpha \quad \text{.........(12)}
\]

Where the subscript \( i \) denote various regions according to

<table>
<thead>
<tr>
<th>( i )</th>
<th>( r )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( 0 \leq r \leq a )</td>
</tr>
<tr>
<td>2</td>
<td>( a \leq r \leq r_0 )</td>
</tr>
<tr>
<td>3</td>
<td>( R_0 \leq r &lt; \infty )</td>
</tr>
</tbody>
</table>

From the finiteness of \( A \) as \( r \to 0 \) and \( r \to \infty \) we obtain the following formulation for \( A(r, z) \) in different regions:

\[
A^1(r, z) = \int_0^\infty C_1(\alpha)I_1(\alpha r)\cos(\alpha(z - z_0)) \, d\alpha \quad \text{.........(13)}
\]

\[
A^2(r, z) = \int_0^\infty \left( C_2(\alpha)I_1(\alpha r) + D_2(\alpha)K_1(\alpha r) \right) \cos(\alpha(z - z_0)) \, d\alpha \quad \text{.........(14)}
\]

\[
A^3(r, z) = \int_0^\infty D_3(\alpha)K_1(\alpha r) \cos(\alpha(z - z_0)) \, d\alpha \quad \text{.........(15)}
\]

Taking into consideration boundary conditions, we obtain the following:

At \( r = a \)
\[ A^1(a, z) = A^2(a, z) \] 

\[
\left. \frac{1}{\mu} \frac{\partial r A^1}{\partial r} \right|_{r=\theta} = \left. \frac{\partial r A^2}{\partial r} \right|_{r=\theta} \] 

(17)

At \( r = \theta \) we have:

\[ A^2(r, z) = A^3(r, z) \] 

(18)

\[
\left. \frac{\partial r A^2}{\partial r} \right|_{r=\theta} = \left. \frac{\partial r A^3}{\partial r} \right|_{r=\theta} \] 

(19)

Using Fourier formula:

\[
\pi^{-1} \int_0^\infty f(\alpha) \left[ \int_0^\infty \cos(\alpha \alpha) \cos(\alpha z) dz \right] d\alpha = f(\alpha') \] 

(20)

and the following properties of modified Bessel function:

\[
\frac{d[x I_1(x)]}{dx} = x I_0(x) \] 

(21)

\[
\frac{d[x K_1(x)]}{dx} = -x K_0(x) \]

and solving for the unknowns \( C_i \) and \( D_i \) we have:

\[ A^1(r, z) = \mu_i I_i \int_0^\pi \frac{K_1(\alpha r)}{I_1(\alpha r) K_0(\alpha r) + K_1(\alpha r) I_0(\alpha r)} \int_0^\infty \frac{1}{\alpha} \left[ 1 + \frac{(\mu - 1)K_1(\alpha \alpha) I_0(\alpha \alpha)}{\mu I_1(\alpha \alpha) K_0(\alpha \alpha) + K_1(\alpha \alpha) I_0(\alpha \alpha)} \right] I_1(\alpha r) \cos(\alpha(z - z_0)) d\alpha \] 

(22)
Thus the on axis magnetic field can be written as:

\[ |B_r|_{r=0} = \left| \frac{1}{r} \frac{\partial r A}{\partial r} \right|_{r=0} \]

Using \( I_0(0) = 1 \) and the recurrence relations for modified Bessel functions we obtain:

\[ B(0, z) = \frac{\mu_0 I}{\pi} \int_0^\infty \frac{1}{\alpha l_0(\alpha a)} \left[ \frac{1}{1+D_1} \left[ 1 + \left( \frac{\mu-1}{1+D_2} \right) \right] \cos(\alpha(z-z_0))d\alpha \right] \]

\[ .........................(23) \]

where

\[ D_1 = \frac{I_1(\alpha a)K_0(\alpha a)}{I_0(\alpha a)K_1(\alpha a)} \]

\[ D_2 = \frac{I_1(\alpha a)K_0(\alpha a)}{I_0(\alpha a)K_1(\alpha a)} \]

\[ .........................(23.1) \]

**Results:**

We compared the above-mentioned analytical results with the finite-difference code developed by us to model regions of different permeabilities in the axisymmetric case. We had a coil core configuration in which the core tightly fit into the coil.

Approximating the radius of the core with that of the coil:

\[ B(0, z) = \frac{\mu_0 I}{\pi} \int_0^\infty \int_0^\infty \frac{1}{\alpha l_0(\alpha a)} \left[ \frac{1}{1+D_1} \left[ 1 + \left( \frac{\mu-1}{1+D_2} \right) \right] \cos(\alpha(z-z_0))drdzd\alpha \right] \]

\[ .........................(24) \]

We used:

\( r_1 = 3.02 \text{ mm} \)

25
\( r_0 = 4.42 \text{ mm} \)
\( z_0 = 8.1 \text{ mm} \)
\( I = 1 \text{ A.} \)

MATLAB’s “triplequad” function was used to evaluate (24) on various points of \( z \) axis.

1. **Air core**

A direct solution to the \( B \) field on the \( z \) axis for this case can be obtained using the Biot-Savart law. The magnetic field as a result of such calculation is given by:

\[
B = \frac{\mu_0 I}{2} \left[ l_2 \log \frac{r_0 + \sqrt{r_0^2 + l_2^2}}{r_i + \sqrt{r_i^2 + l_2^2}} - l_1 \log \frac{r_0 + \sqrt{r_0^2 + l_1^2}}{r_i + \sqrt{r_i^2 + l_1^2}} \right]
\]

Thus calculated fields using equations (24) and (25) are plotted below. Clearly we see that setting \( \mu = 1 \) in (24) reduces this equation to the normal equation (25).

*Figure 8. \( B_z \) vs \( z \) from equation (24) as calculated and (25)*
2. **Long Core tightly embedded in the above coil**

We developed a finite-difference scheme to model the magnetic vector potential in axisymmetric cases for regions of different magnetic permeabilities. This will be presented in the next chapter. Extending our idea, we simulated a long ferrite core by extending the core all the way up to its boundary. Though the results are expected to diverge, the error as can be seen below is only approximately 15%.

*Figure 9. Results Verifying $B_z$ vs $z$ for a coil encircling long ferrite rod*
Conclusion

To induce neural stimulation using coils, we need to induce in the neural tissue as high an eddy current as possible. Thus, the idea of using ferrite cores with solenoid coils to increase the fields and induced currents is numerically and analytically explored. Here we have formulated an analytical method to obtain fields and vector potentials due to a long ferrite core encircled by a current carrying coil. These results appear to corroborate our idea of using ferrites. In the next chapter we formulate numerical methods to investigate more complicated geometries.
3.1 Method of Finite Differences to Solve Problems with Axial Symmetry in Cylindrical Coordinates

Since the analytical solution of (1) in closed form is very difficult to obtain even for simple geometries, we have devised a finite difference solution to the same problem involving axial symmetry. We shall first formulate the difference scheme and then test it for two cases for which analytical solutions already exist.

Formulation

We wish to solve:

\[ \nabla^2 A = -\mu J \]

(2)

Since we are interested in geometries with axial symmetry we cast (2) in cylindrical coordinates. Then we have

\[ J = J_\phi \phi \]

so that

\[ A = A_\phi \phi \]

This makes all derivatives of \( A \) w.r.t. \( \phi \) vanish. Hence (2) in cylindrical coordinates becomes:

\[ \frac{\partial^2 A}{\partial r^2} + \frac{1}{r} \frac{\partial A}{\partial r} - \frac{A}{r^2} + \frac{\partial^2 A}{\partial Z^2} = -\mu J \]

(26)

To efficiently incorporate boundary conditions across materials of different permeabilities in (2) we do the following transformation:
\[ \Psi = 2\pi r A \]

so that (26) now becomes:

\[
\frac{\partial^2 \Psi}{\partial r^2} - \frac{1}{r} \frac{\partial \Psi}{\partial r} + \frac{\partial^2 \Psi}{\partial Z^2} = -2\pi \mu_r J \quad \text{.....(27)}
\]

\[
H_r = \left( \frac{1}{2\pi \mu_r} \right) \frac{\partial \Psi}{\partial z} \quad \text{.....(28a)}
\]

\[
H_z = \left( \frac{1}{2\pi \mu_r} \right) \frac{\partial \Psi}{\partial r} \quad \text{.....(28b)}
\]

Consider the following mesh and the nodes as shown below. (27) can be formulated using the finite difference approximation as

\[
\Psi_1 \left( 1 + \frac{h}{r_0} \right) + \Psi_2 \left( 1 - \frac{h}{r_0} \right) + \Psi_3 + \Psi_4 - \Psi_0 = 0 \quad \text{.....(29)}
\]

\[\text{Figure. 10. FD Mesh for space with no discontinuities in magnetic permeabilities}\]
To incorporate discontinuities in permeability we make use of the integral equation:

\[ \oint H \cdot dl = I \] \hspace{1cm} (30)

Consider the following mesh

![FD Mesh for space with magnetic discontinuities](image)

**Figure. 11.** *FD Mesh for space with magnetic discontinuities*

We integrate (30) along the inner loop and the inner nodes are exactly midway through the corresponding 0 node and the outer node.

\[
\frac{1}{2\pi} \left( \frac{1}{r_5} \frac{\partial \Psi_5}{\partial r} \frac{h}{2} \left( 1 + \frac{1}{\mu} \right) + \frac{1}{r_0} \frac{\partial \Psi_7}{\partial z} + \frac{1}{r_6} \frac{\partial \Psi_6}{\partial r} \frac{h}{2} \left( 1 + \frac{1}{\mu} \right) + \frac{1}{r_0} \frac{\partial \Psi_8}{\partial z} \right) = 0
\]

Which leads to the boundary condition:

\[
\frac{\Psi_1}{2} \left( 1 + \frac{h}{2r_0} \right) \left( 1 + \frac{1}{\mu} \right) + \frac{\Psi_2}{2} \left( 1 - \frac{h}{2r_0} \right) \left( 1 + \frac{1}{\mu} \right) + \Psi_3 + \frac{\Psi_4}{\mu} - 2\Psi_6 \left( 1 + \frac{1}{\mu} \right) = 0 \] \hspace{1cm} (31)

A Finite ferrite core would have several interfaces as shown below:
Similarly the boundary condition for the corner of the ferrite core (figure. 12) leads to:

\[
\frac{\Psi_1}{2} \left(1 + \frac{h}{2r_0}\right) \left(1 + \frac{1}{\mu}\right) + \Psi_2 \left(1 - \frac{h}{2r_0}\right) + \frac{\Psi_3}{2} \left(1 + \frac{1}{\mu}\right) - \Psi_0 \left(3 + \frac{1}{\mu} - \frac{h}{4r_0} \left(1 - \frac{1}{\mu}\right)\right) = 0 \quad (32)
\]

and the boundary condition for right side of ferrite-vacuum interface leads to:

\[
\frac{\Psi_1}{2} \left(1 + \frac{h}{2r_0}\right) \left(1 + \frac{1}{\mu}\right) + \Psi_2 \left(1 - \frac{h}{2r_0}\right) + \frac{\Psi_3 + \Psi_4}{2} \left(1 + \frac{1}{\mu}\right) - \Psi_0 \left(2 \left(1 + \frac{1}{\mu}\right) - \frac{h}{2r_0} \left(1 - \frac{1}{\mu}\right)\right) = 0 \quad (33)
\]

Other interfaces can be taken care of by symmetry considerations.

This discretization leads to a linear system of equations:

\[ AX = B \]

We used the quasi-minimal-residual iterative scheme to solve the linear system. Since the solution is perfectly symmetric about the r axis and perfectly antisymmetric about the z axis,
we modeled only the 1st quadrant of the r-z plane. We used a cell space of N=350 in both directions and a cell width of h=2e-6 m.

**Verification of the Finite Difference Scheme**
We verified the newly developed FD scheme with three cases for which analytical solution exist. We present the result for each case:

1) In section 2.1, *Figure 6*, we analytically solved for the induced eddy currents induced due to single coil carrying a time-varying current. We modeled the same problem using the FD formulation. The problem was first solved for static case and resultant was multiplied by the frequency (100 Hz in this case as in section 2.1) in accordance with the quasistatic assumption (equations (1.2) and (2)). The results are in good agreement with the analytical results.
We see that an induced eddy current of ~7e-9 is obtained at z=20, r=100 in good accordance with the analytically obtained value ~1e-8 in section 2.1.

2) Magnetic Fields for a coil in Free Space
We consider a coil as shown in Figure 1. The coil had dimensions of 100 microns diameter and a rectangular cross section of thickness 10 microns and length 200 microns. The magnetic fields induced on the z axis by the configuration of Figure 1 were used to compare the analytical and numerical results. Obtained results are plotted in Figure 14.
Figure 14. Analytical and Numerical results for $B_z$ Vs $z$ in free space

3) Sandwich Inductors
Next we verify the FD scheme by modeling a circular coil sandwiched between two infinite slabs of infinite permeability. The configuration is shown in Figure 15. Coil diameter for this case was 100 microns and length was 20 microns. In these calculations $z_1 = z_2 = 50$ microns. This configuration has an exact solution that can be obtained using the method of images [46]. Comparisons of analytical and numerical results are presented in Figure 16 and Figure 17 respectively.
Figure 15. Cross-sectional view of sandwich inductor model carrying current I [46]

Figure 16. Analytical results of $B_z$ vs $z$ for sandwich coils
We observe the close proximity of numerical results with exact analytical results and doubling of fields in both cases.

3.2 Coil Array

*Figure 2* depicts an existing stimulating electrode array for retinal prosthetic system. After having analyzed the behavior of a single micro coil carrying current with ferrite core embedded and sandwiched between infinite ferrite slabs we now consider an array of such stimulating coils, which may in the future replace the electrode array shown in *Figure 2*. *Figure 18 depicts a typical 4X4 array of figure-of-8 coils that we wish to explore.*
Figure 18. A 4X4 array of figure-of-8 shaped micro stimulator coils

A single stimulator in this array is shown in Figure 19.

Figure 19. A single micro stimulator

We wish to solve for the induced current density inside the GCL obtained by such an array of stimulating coils placed just the retinal surface.
**Approach: Principle of Linear Superposition**

In the previous chapters we used the cylindrical symmetry of the circular coils to formulate a Finite Difference scheme to solve the Poisson equation involving magnetic vector potential. The symmetry allowed us to cast the 3D problem in 2D since the potential is independent of the azimuth when the z axis is situated on the axis of symmetry. By considering an array of electrodes the symmetry is however lost in the overall frame of reference.

To circumvent this problem we use the superposition principle of the vector potential viz.

\[ \mathbf{A} = \mathbf{A}_1 + \mathbf{A}_2 + \mathbf{A}_3 + \ldots \ldots \ldots \quad (34) \]

The net potential due to n coils is the vectorial sum of potentials obtained due to individual coils.

Since the induced current is vector given by

\[ \mathbf{J} = -\sigma \omega \mathbf{A} \quad \ldots \ldots \ldots \quad (35) \]

we would expect \( \mathbf{J} \) to obey the principle of superposition as well.

First, we compute the induced current density profile at a depth \( z \) just inside the retina as a function of radial distance \( r \). This calculation is done in the symmetry axes of the coil. By doing so we can compute \( \mathbf{J}(r,z) \). At a particular \( z \), \( \mathbf{J} \) becomes a function of the radial distance \( r \). We use a cubic spline interpolation to compute \( \mathbf{J} \) as a function of any \( r \) instead of the discrete FD grid points. The graph of \( \mathbf{J} \) and its interpolant is shown *Figure 20.*
Figure 20. Cubic Spline interpolation of Induced current density as a function of $r$

We can use the following coordinate transformation:

Figure 21. Coordinate transformation.
\[ \mathbf{J} = \mathbf{J}(\mathbf{r}') = |\mathbf{J}(\mathbf{r}')| \hat{\varphi} \] .............................. (36)

\[ \mathbf{J} = |\mathbf{J}(\mathbf{r} - \mathbf{s})| \{-\sin \hat{\varphi} x + \cos \hat{\varphi} y\} \] ............. (37)

In x, y coordinates:

\[
\mathbf{J}(x, y) = \left| \mathbf{J} \left( \sqrt{(x-x_1)^2+(y-y_1)^2} \right) \right| \left\{ -\frac{y-y_1}{\sqrt{(x-x_1)^2+(y-y_1)^2}} \hat{x} + \frac{x-x_1}{\sqrt{(x-x_1)^2+(y-y_1)^2}} \hat{y} \right\} \] ...... (38)

where we obtain the |J| values for various (x,y) from the interpolant.

We have solved the problem in a generic coordinate system while still retaining the symmetry and simplicity of our 2D code. The net \( \mathbf{J} \) would be a vector addition of all such individual currents from different coils.

We will now consider the current density profiles obtained by superposition of coils in an array. In chapter 4 we will consider current densities for various configurations of coil arrays. The goal will be to maximize current densities near the individual stimulators so that only those nerve cells which are just below individual stimulators are excited.
Chapter 4

MicroMagnetic Stimulation of the Retina-Numerical Predictions

In this chapter we present the possibility of using microcoils to stimulate neural tissue. The idea here is to explore the possibility of using such coils for implantable devices. As an example we consider in this chapter the Retinal Ganglion Cell layer. The concepts explored in this chapter are applicable to any neural tissues, since these have a relative magnetic permeability of 1. We have considered the retina as a special case because it presents the worst-case scenario, in the sense that neurons in GCL are relatively more difficult to stimulate than other neural systems (for example peripheral nervous system or brain cortex) because of their small sizes (Retinal Ganglion Cell of a human retina is only 30 microns in width). Further, we have to use much smaller coils (few hundred microns in diameter) for a retinal prosthetic system to be possible. The Peripheral Nervous system is likely to be easier to stimulate and allows for relatively larger size of the implantable coil. In this chapter we used a constant frequency of 100Hz for our predictions of neural stimulation. In chapter 5 we will explain the use of a pulsed discharge circuit instead of a sinusoidaly varying current. Since the dominant frequency in the Fourier spectrum of pulsed currents is still in the order of few KHz, quasistatic conditions hold and equation (1.2) can be accordingly modified.
4.1 Induced eddy current calculations inside the retinal ganglion cell layer

Figure. 22. Various layers of tissue that compose a human retina [figure taken from http://en.wikipedia.org/wiki/File:Gray881.png]

Figure 22. shows the anatomical structure of the human retina. Light enters the eye through the cornea, passes through the lens and vitreous humor which forms the bulk volume of the eye. Once it reaches the retina, it travels through the retina thickness and reaches the photoreceptor cells (layers of rods and cones) located at the outer retinal region just under the pigment epithelium. The photoreceptor cells comprise of rods and cones which contain a photopigment which enables the conversion of the light signal to electrical and chemical signals (neural signals). These signals travels via the retinal layers to reach the ganglion cells which links to the optic nerve, as shown in the flowchart in figure 23.
Retinal degenerations, such as Retinitis Pigmentosa (RP) or Age Related Macular Degeneration (AMD), the retina experiences a progressive loss of photoreceptor cells that eventually leads to blindness. Even though the photoreceptor cells are lost, most of the remaining neural pathway is still largely intact. This gives the motivation for artificially
eliciting neural responses in the GCL while the rest of the process in the neural signal remains essentially the same.

This chapter describes the induced current densities due to small coils carrying time-varying currents placed on the retina. Various designs are considered that will enhance the induced eddy currents and focus the induced fields in the vicinity of the individual coil. We use the numerical code developed in chapter 3 to calculate the induced current densities.

We will focus on distances $z = 130$ microns, $140$ microns, and $150$ microns (at which we wish to know the eddy currents) from the center of the coil. This means a distance of 30 microns (start of retinal GCL), 40 microns and 50 microns inside the retina. Retinal Ganglion Cell layer start at 30 microns depth and end at 60 microns from the surface of the retina.

**Configuration 1: Single Coil carrying time varying current placed on the surface of retina**

Figure 6 shows a single coil carrying a sinusoidally varying current placed on the retinal surface. The coil details are as follows:

- Inner radius of the stimulating coil ($r_i$) = 100 microns,
- Outer radius of the stimulating coil ($r_o$) = 110 microns,
- Coil thickness = $2l = 200$ microns.
- Sinusoidal Current Amplitude in the coil = 1A.
- Frequency of the sine wave ($f$) = 100 Hz.
- Conductivity of the Retina ($\sigma$) = 0.5 S/m.

The induced current densities are shown in figure 24. Induced current densities as a function of radial distance ($r$) from the centre of the coil for the different depths ($z$) are plotted in here.
Figure 24 Plots of eddy currents induce in GCL by a coil configuration of figure 6.

Configuration 2: Circular Coil Embedded with a Ferrite core placed on the Retinal Surface

*Figure* 25 depicts a coil with a tightly embedded ferrite cored placed in front of the retina. The magnetic permeability of this core was assumed high (1000). *Figure* 26 depicts the plot of induced eddy currents in the GCL as a function of r for this configuration. Notice the rise in induced currents (~ 3 times) due to the embedding of the ferrite core.
Figure 25. Cross section of Coil with ferrite embedded. The inner picture shows a n turn coil with a core inside.

Figure 26. Eddy currents for coil+core combination
Configuration 3: Coil Embedded with Ferrite core Surrounded by End Ferrite Plates

We considered the possibility of introducing two ferrite plates (one in epiretinal space and the other in subretinal space). This configuration is similar to sandwich inductors considered earlier. This further enhanced the concentration of fields in GCL and hence the induced eddy currents. Also important to note is factor that due to the symmetry of the end plate ferrites the decay of fields with z is much less in this case than due to the other two case. Figure 27 depicts configuration 3. Figure 28 is the plot of induced eddy currents as a function of r for various z.

Figure 27. Depicts Coil-core-slab configuration. The two end plate ferrites place on either side of the retina effectively enhance the induced currents and also focus the fields.
Figure 28. Eddy currents for coil-core-slab combination. Notice that decay of the induced eddy currents with depth is much less in this case.

It is interesting to observe that the general shape of the current induced in the ganglion cell layers by this family of coils is a donut-like shape in the x-y plane for a particular z. This is shown in Figure 29 for the case of a ferrite core tightly fitted and end-plates. However, this can change to a bell curve with figure-eight coils or by simply feeding two adjacent coils out of phase. This simple observation proves how versatile the pattern of induced currents can be with this technology.
4.2 Array of coils

In this section we investigate the effect of a combination of coils, the effect of inter coil spacing, and the effect of the phase of the current in the coils. The technique of interpolation and vectorial addition of fields described in chapter 3 is exploited here. This investigation is necessary to arrive at a final configuration of microcoil stimulators that will effectively focus induced eddy currents right beneath each individual stimulator. This is essential for the reason that in an array of stimulators, neurons just below individual stimulators need be excited by that particular simulator with least interference from other members of the array. In the discussion that follows the inter edge separation between the stimulator coils is designated as ‘s’. Three values of ‘s’ are considered viz. s = 100 microns, 300 microns and 500 microns.
1) Four coils with centers on the x axis carrying parallel currents

Consider the configuration shown in figure 30. Four coils (with the same dimensions as used for individual core with coil and end plate ferrites in section 4.1) are placed on the retinal surface. In this case the stimulator coil carries parallel currents (which means in phase).

Figure 31 depicts the induced current densities inside the GCL layer with respect to x for various y. The plot with circles are at y = radius of the coils, while the blue line is on the x axis (y=0). We see that the constructive interference is uniform at the coil radius but on the x axis two extreme peaks are much more prominent then the small peaks. At exactly x = 0 the current is zero because the currents on the left side of the y axis cancel those produced by their right hand side counter parts. With increasing ‘s’ we see a local minimum in the extreme peaks and rise in the central peaks. This is because of the destructive interference occurring at x = ~ coil edges of the inner coils.
2) Four coils with centers on the x axis carrying anti parallel currents

![Diagram of antisymmetric coil configuration]

_Figure 32. Antisymmetric coil configuration_

*Figure 32* depicts a coil combination in which adjacent coils carry antisymmetric currents (out of phase). Rest of the configuration is exactly as described in *figure 30*. Corresponding plots for induced current density are plotted in *figure 33*. We notice that the focus just below
the coils increases significantly as compared to the parallel current configuration. Further, we note that this focus is maximum when ‘s’ is minimum. This trend is expected since we rely on the destructive interference of the anti parallel currents to give rise to sharp peak. This destructive interference is diminished when we increase the distance between the coils. This suggests that even better focus can be achieved if two adjacent could be combined together.

Figure 33. Current Density profile for antisymmetric coil configuration
3) Figure 8 coils

Figure. 34 introduces the concept of figure-of-8 coils. In this configuration two coils in figure-of-8 shape carrying antisymmetric currents act as a single stimulator. Figure. 36 depicts the induced current profiles due to such configuration. We observe that most of the current is concentrated just below the meeting point of the figure-eight coils. Also the peaks tend to increase in magnitude with increasing s. This is expected because as s increases each figure-eight pair tends to behave as individual entity and the effect of other coils is drastically reduced.
4) **A 4X4 array of figure 8 coils**

In chapter 3 *figure 18* we depicted a configuration a 4X4 array of microcoil stimulator in which each individual stimulator was a figure-of-eight coil. *Figure 36* depicts a 3D plot of induced currents just inside the GCL as a function of x and y, due to the coil configuration of *figure 18*. s was taken to be 500 microns We see a perfectly symmetrical current distribution with very sharp peaks in the vicinity of the fig8 coils.
Figure 36. Induced current density as a function of $x$ and $y$ for an array of microcoils

Magnitude of induced current density

We note that a typical array of fig8 coils give rise to peak current density of $\sim 4.5 \times 10^{-4}$ Am$^{-2}$. With a 100 turn coil we would have current densities of the order of 40 mAm$^{-2}$. Notice the sharp focusing of the induced currents. This is likely to be desirable since individual stimulators should elicit neural responses in neural cells just beneath it and not interfere with neural cells which are at a distance from the stimulator. This is currently the problem with electrode array since current tends to flow in all directions as current injected by the electrode array follows a path of minimum resistance.
Chapter 5

Experiments on Rat Sciatic Nerve

Introduction
This chapter presents magnetic coil stimulation results from the experiments on rat sciatic nerve. Description of rat sciatic nerve, action potentials involved in cellular reactions, magnetic coils fabricated in the lab, a new boot strap circuit to drive the magnetic coils, and finally experimentally obtained results for the evoked action potentials in the rat sciatic nerve using the stimulus from fabricated magnetic coils will be presented.

5.1 Brief Description of a Nerve Cell and Transmembrane Potentials

Figure 37. Cell membrane with intracellular and extracellular part is depicted
58

Figure 37 shows the relevant parts of a cell involved in neural stimulation. Cell typically consists of an intracellular space (cytoplasm). The intracellular space is separated from the extra cellular space by a rigid plasma membrane. This membrane is selectively permissive to flow of ions (Na\(^+\), K\(^+\), Ca\(^{++}\), Cl\(^-\) being the main ones) from intracellular space to extracellular space and vice versa. Individual ions are allowed to pass selectively through the membrane from small pores. These are termed Ion Channels. At rest, the intracellular space is at 65 mV bellow the extracellular space. This is called the rest potential of the cell. The ion channels activity depend on the voltage difference between the intracellular and extracellular space. Hence they are called Voltage Gated Ion Channels. Any external stimulus may change the potential difference and the cell membrane becomes active and selective passage of ions start across the membrane. The intracellular potential starts rising. This process is called the depolarization of the cell. Once the intracellular potential goes above that of the extra cellular potential the cell the cellular mechanism try to get back to equilibrium and the intracellular potential starts decreasing, goes below the rest potential and finally attains the equilibrium. If enough stimuli are provided, the intracellular potential can abruptly shoot more than 100 mV above their resting potential triggering an action potential. This is called as nerve being stimulated. This action potential then propagates across the whole nerve giving rise to various functions of the body (for example vision, motion etc.). A detailed description of this whole process can be found in [57].

In a normally functioning body the excitable nerve cells are naturally triggered by stimulus like reflexes, light, sound etc. But in organs affected by degenerative diseases the nerve cells are not triggered naturally. In such cases artificial stimulus may be provided to the neural cells to partially restore the functions.

5.2 Model for Stimulation of Nerve Cell

The mechanism of neural stimulation is not well understood. In typical electro neurostimulation a current is injected across the cell membrane that is believed to elicit neural responses. The strength of the injected current and time for which it is applied determines the neural response. Different neurons have different threshold values of injected
current and pulse widths for excitation. Over past few years it is being proposed that the spatial gradient of the electric field in the direction parallel to the nerve is the main quantity which determines the neural excitation. While others believe that the transverse component of the electric field is important too.

Mechanism of neural stimulation by magnetic induction is even little understood. Since in this research the experiments were performed on long sciatic nerve, a model of neural stimulation proposed in [24] was used to simulate evoked action potentials due to coils fabricated in lab and new stimulator circuit devised in the process of this research.

The typical cell and its behavior can be modeled, to first approximation, by a resistance-capacitance model. The cell membrane described above can be modeled as a voltage dependent resistor and capacitor in parallel as shown in Figure 38.

**Figure 38.** An electrical circuit representing the passive cable. The intracellular space is modeled by a resistance per unit length $r_i$, the membrane by a resistance times unit length $r_m$ and capacitance per unit length by $c_m$. The extracellular potential is assumed to be zero. The axial intracellular current $I_i(x)$ is related to the intracellular potential $V(x)$ by Ohm's law, and related to the membrane current per unit length, $i_m(x)$ by the equation of continuity [24]
Figure 39. An active cable with Hodgkin-Huxley membrane. The membrane is now represented by three voltage and time dependent conductances, representing the sodium, potassium, and leakage channels.[24]

Applying basic circuit laws and after a few modifications we arrive at the following equation for the transmembrane potential:

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} - V = \tau \frac{\partial V}{\partial t} + \lambda^2 \frac{\partial E_x}{\partial x} \ldots \ldots \ldots \ldots \ldots (39)$$

This is modified passive cable equation known from transmission line theory.

To get better accuracy in understanding the neural behavior the voltage dependence of the ion channels (and hence the membrane resistances and capacitances) are modeled by incorporating the Hodgkin-Huxley model of cell membrane. This results in active cable equation for action potential evoked across the nerve membrane given by:
\[
\frac{a}{2R_l} \frac{\partial^2 V}{\partial x^2} - (g_{Na} m^3 h (V - E_{Na}) + g_k n^4 (V - E_k) + g_L (V - E_L))
= C_m \frac{\partial V}{\partial t} + \frac{a}{2R_l} \frac{\partial E_x}{\partial x} (x,t). \quad (40)
\]

where:

\(g_{Na}, g_k, g_L\) are peak sodium, potassium and leakage membrane conductance per unit length and \(E_{Na}, E_k\) and \(E_L\) are the sodium, potassium and leakage Nernst potentials. The gating variables \(m, h\) and \(n\) are dimensionless functions of time and voltage varying between 0 and 1. Each gating variable follows a first order differential equation given by:

\[
\frac{\partial m}{\partial t} = \alpha_m (1 - m) - \beta_m m \quad \ldots \quad (41)
\]

\[
\frac{\partial h}{\partial t} = \alpha_h (1 - h) - \beta_h h \quad \ldots \quad (42)
\]

\[
\frac{\partial n}{\partial t} = \alpha_n (1 - n) - \beta_n n \quad \ldots \quad (43)
\]

where the \(\alpha\)s and \(\beta\)s are given by:

\[
\alpha_m = \frac{0.1[-40 - V]}{\exp \left(\frac{-40 - V}{10}\right) - 1} \quad \ldots \quad (44)
\]

\[
\beta_m = 4.0 \exp \left(\frac{-65 - V}{18}\right) \quad \ldots \quad (45)
\]

\[
\alpha_h = 0.07 \exp \left(\frac{-65 - V}{20}\right) \quad \ldots \quad (46)
\]
\[ \beta_h = \frac{1}{\exp\left(-\frac{35-V}{10}\right) + 1} \] ...

\[ \alpha_n = \frac{0.01[-55-V]}{\exp\left(-\frac{55-V}{10}\right) - 1} \] ...

\[ \beta_h = 0.125 \exp\left(-\frac{65-V}{80}\right) \] ...

The boundary conditions for solving the above set of equations comprise: 1) initial rest condition of the membrane 2) far from the site where stimulus is applied the axial gradients of V, m, n, h vanish.

To solve the set of coupled differential equations (40)-(43) and correspondingly obtain the transmembrane potential due to an externally obtained stimulus, \( E_x(x,t) \) has to be specified. The spatial part and temporal part of the electromagnetic quantities can be variably separated and hence the following relation is obtained:

\[ E_x(x,t) = F(x)G(t) \] ...

where \( F(x) \) is the spatial part of \( E_x \) obtained for a coil carrying unit current changing at a unit rate and \( G(t) \) is the time dependence of the current in the stimulating coil. As described in previous chapters \( F(x) \) is obtained by using the FD code described in chapter 3. \( G(t) \) depends on the driving circuit and type of inductors being used as magnetic stimulators.

### 5.3 Stimulator Circuit

Earlier we numerically solved the diffusion equation for the magnetic vector potential under quasistatic conditions rendering it into a Poisson equation viz.

\[ \nabla^2 A = \mu J \] ... ... (1)
We had solved (1) assuming a unit current uniformly distributed inside the coil and sinusoidal oscillating at 100 Hz. So that the induced eddy currents were given as:

\[ \mathbf{J} = -\sigma \omega \mathbf{A} \] .......................... (2)

In chapter 1, table 3, we showed that the pulse widths and induced current densities required to elicit a neural response vary a lot in magnitudes depending on the tissue being excited. In Chapter 3 a sinusoidally time varying current with frequency 100Hz was used and we obtained peak induced current densities of the \(~ 45 \text{ mAm}^{-2}\).

We can further enhance the induced currents and other electromagnetic fields by using a magnetic stimulator circuit which uses a Pulsed discharge as used in current TransCranial Magnetic Stimulation. In this, input pulses comprise of very sharp rise of current in the stimulating coil and then a slow drop. This sharp rise of current may have sharp slope with respect to time that would render very high induced current for a very small time. So we do a brief modification to our equations as following. The equation (2) is actually:

\[ \mathbf{J}_{\text{eddy}} = -\sigma \frac{\partial \mathbf{A}}{\partial t} \] .......................... (51)

Now we know that for a uniform stimulating current distribution the vector potential is directly proportional to the stimulus current. Let’s say \(A_0\) is the potential due to unit current and \(I\) is the current in the stimulus coils which of course is a function of time. Then equation (3) would be suitably modified as:

\[ \mathbf{J}_{\text{eddy}} = -\sigma A_0 \frac{\partial I}{\partial t} \] .......................... (52)

Equation (52) then becomes the governing equation and we have to delve into appropriate mechanism to get a suitably high rate of change of current in the stimulating coil.

The circuit shown in figure.40 forms the base of any pulsed magnetic stimulation with modification taking place in the frequency of charging and discharging giving rise to monophasic, biphasic and polyphasic pulses [39,48,49,50]. A capacitor is charged to supply voltage through the switch S2. The switch S2 opens and switch S1 closes and capacitor is discharged through the inductor.
Charging circuit
The charging part follows a simple RC charging principle. The instantaneous charging voltage and charging current are given as:

\[ V_c(t) = V_0 e^{-\frac{R_c}{C}t} \quad \ldots \ldots \text{(53)} \]
\[ I(t) = \frac{V_0}{R_c} (1 - e^{-\frac{R_c}{C}t}) \quad \ldots \ldots \text{(54)} \]

Theory of LCR Discharge Circuit
The LCR discharge circuit follows a second order partial differential equation. We can formulate the equation of this circuit as follows:

At any given instant of time the LCR circuit obeys the following equation:

\[ \frac{\int idt}{c} + L \frac{di}{dt} + R_L i = 0 \quad \ldots \ldots \text{(55)} \]
Differentiating gives:

\[
\frac{d^2i}{dt^2} + \frac{R}{L} \frac{di}{dt} + \frac{i}{RcC} = 0 \quad \ldots \ldots \ (56)
\]

Equation is a well know damped oscillator equation in variables \(i\) and \(t\). Making a small transformation:

\[
\alpha = \frac{R}{2L}
\]

And

\[
\omega_0 = \frac{1}{\sqrt{LC}}
\]

\[
\frac{d^2i}{dt^2} + 2\alpha \frac{di}{dt} + \omega_0 i = 0 \quad \ldots \ldots \ (57)
\]

\(\alpha\) is the attenuation and is a measure how the current in the circuit will die down, \(\omega_0\) is the natural frequency of the circuit. We define:

\[
\gamma = \frac{\alpha}{\omega_0} = \frac{R}{2} \sqrt{\frac{C}{L}}
\]

The current in the inductor coil is depended on whether \(\gamma\) is >, = ,or <1.

1.) Overdamped Condition \(\gamma > 1\):

We define:

\[
\omega_1 = \sqrt{\left( \left( \frac{R}{2L} \right)^2 - \frac{1}{LC} \right)}
\]
The current in the circuit is given by:

\[ i(t) = V_0 C \omega_1 e^{-\alpha t} \left( \left( \frac{\omega_0}{\omega_1} \right)^2 - 1 \right) \sinh(\omega_0 t) \ldots \ldots (58) \]

2.) Underdamped Condition \( \gamma < 1 \):

\[ \omega_1 = \sqrt{\left( -\left( \frac{R}{2L} \right)^2 + \frac{1}{LC} \right)} \]

The current in the circuit is given by:

\[ i(t) = V_0 C \omega_1 e^{-\alpha t} \left( \left( \frac{\omega_0}{\omega_1} \right)^2 + 1 \right) \sinh(\omega_0 t) \ldots \ldots (59) \]

The case of critical damping, when \( \gamma = 1 \), is very difficult to achieve practically and shall not be considered. \( \alpha \), the attenuation constant, is the measure of how fast the waveform will go to zero. The time constant for pulsed discharge circuits is \( 1/\alpha = 2L/R \). Typically the current in the inductor lasts for 3-4 times the time constant. At the initial moment, when discharge of the capacitor through the inductor begins, the voltage across of the inductor is same as voltage of the capacitor, which in turn is the charging source voltage. Hence we get a peak \( di/dt = V/L \).

**Boot Strap Driving Circuit**

As discussed in previous chapters, TMS stimulator circuits use high voltages (1kV) and large inductor coils to obtain a high rate of change of current in the stimulating coil (\( 10^8 \) As\(^{-1} \)) which in turn induce large eddy currents inside the tissue to be stimulated. Using larger coils has the advantage that magnetic fields diffuse slowly with increasing depth from the coil. Also larger coils have larger inductance and lower resistance giving rise to higher \( di/dt \) and larger pulse widths (\( \alpha = R/2L \) being the attenuation factor).
In general the strength duration curve for a neural response to be elicited demands a high induced currents and a large pulse width. Even in the pulse width the first positive lobe of the waveform is deemed important as any negative going $\frac{di}{dt}$ induces a negative current which tend to hyperpolarize the nerve. Figure 41 depicts typical waveforms of electromagnetic quantities involved in TMS [41].

But since this research is aimed at exploring the possibility of using magnetic stimulation for implantable devices coils need to be much smaller in dimensions and the source voltages need to be scaled down drastically. Making coils smaller renders smaller inductances and larger resistances and hence shorter pulse widths. Hence we used ferrite cores to enhance the inductance values. At the frequencies concerned and the strength of the B fields generated in this range the hysteresis losses are negligible and hence the resistance is not affected by the incorporation of ferrite.

Considering the above factors and to make the circuit as small as possible we designed a new boot strap circuit to drive the inductor coil. The layout of the circuit is depicted in figure 42. Switches S1 and S2 are very low resistance power mosfets FDP 047N10. The on resistance of these transistors is $\sim 4 \text{ m}\Omega$. The maximum drain to source voltage can be 100V. While the maximum gate to source voltage can be 20 V. When the transistors are on the source gets connected to the drain and hence can a have voltage more than the gate. Since for a mosfet to operate the gate voltage need be more than the source voltage more than a least value (threshold voltage) we need a gate drive circuit. The gate driver chip shown here is FAN 7390 from fair child semiconductors. The chip has a drive voltage of 15 Volts (pin 5). We feed complementary signals (5 V square wave pulses) to pins 1 and 2. The chip converts this to a 15 V complementary square wave pulses and transfers it to pin 7 and pin 4 respectively. The internal circuit of the gate drive chip maintains pin 7 (gate of switch S1) 15V above pin 6 (source of switch S1) when pin 1 is high. When pin 2 is high the internal circuit of the gate drive chip maintains pin 4 (gate of switch S2) 15V above pin 3 (source of switch S2).
When switch S1 is on the gate charge is provide by the boot strap capacitor when S1 is on.

**Figure 41**: Depicts various electromagnetic quantities involved in TMS as a function of time [39]

**Figure 42**: Boot strap circuit to drive the inductor coil
Usually a boot strap circuit operates a pull down circuit in which the lower switch is directly connected to ground and hence all grounds can be united. But in our circuit S2 is connected to the inductor. This calls for the ground of the drive circuit being totally different from the circuit being driven. Hence G1 and G2 are mentioned as two different grounds. A 10W 25Ω charging resistance was used to charge the capacitor C. C was chosen 1000 µF so as to obtain an over damped oscillation. Charging voltage was varied from 0-50V.
Inductors Fabricated in Lab

Figure 43. Various hand wound coils embedded with ferrite made in our lab

Figure 43 shows some of the coil configurations that were made in our lab. All the coils are embedded with ferrite cores generously supplied to us by Fair-Rite Corporation. The initial permeability of the cores was 2300. Details of the coils are given in Table 4. We mention the details of individual coil in the coil configuration. All length dimensions are in mms.

Table 4. shows the properties of coils shown in figure 43.

<table>
<thead>
<tr>
<th>N</th>
<th>$D_{core}$</th>
<th>$D_{wire}$</th>
<th>N</th>
<th>$D_{total}$</th>
<th>Length(l)</th>
<th>L(µH)</th>
<th>$R_O$(Ω)</th>
<th>$R_C$(Ω)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>0.75</td>
<td>4</td>
<td>13</td>
<td>14</td>
<td>47</td>
<td>0.2</td>
<td>0.09</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>0.4</td>
<td>2</td>
<td>3.9</td>
<td>15</td>
<td>26</td>
<td>0.6</td>
<td>0.10</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>0.4</td>
<td>2</td>
<td>3.9</td>
<td>15</td>
<td>26</td>
<td>0.6</td>
<td>0.10</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0.22</td>
<td>4</td>
<td>3.5</td>
<td>10</td>
<td>45</td>
<td>0.5</td>
<td>0.53</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0.22</td>
<td>2</td>
<td>2.5</td>
<td>10</td>
<td>15</td>
<td>0.3</td>
<td>0.21</td>
</tr>
</tbody>
</table>

$D_{core}$ = Core diameter

$D_{wire}$ = Cross sectional diameter of winding wire

N = Number of layers of wire.

$D_{total}$ = Outer diameter of the coil

Length = Length of the coil
L = Inductance of the coil
R₀ = Observed Series Resistance of the coil on a LCR meter
Rₐ = theoretically calculated Series resistance of the coil

Current Waveforms in the Fabricated Inductor coils

Current waveforms in the inductor coil in a pulsed discharge circuit are governed by equation (58). We used a capacitance of 1000 µF and source voltage of 50 V. This gives to overdamped LCR discharge. Currents as a function of time for the above mentioned coils are plotted in figure 44. It is the rate of change of current (dI/dt) in the inductor coils that determines the time dependence of induced electromagnetic quantities. dI/dt wave forms for the respective fabricated inductors are plotted in Figure 45. Inductor 1, which has the largest inductance, has largest pulse width for di/dt even though the peak di/dt is the lowest. But for comparable magnitudes of peak di/dt (and hence peak induced fields and induced current densities), larger pulse widths are better suited for neural stimulation.

![Figure 44. Current (I) vs Time(t) for various inductors.](image)
5.4 Simulation Results for Transmembrane Potential

To compute the transmembrane potential from the set of coupled differential equation (40-43) $E_x = F(x)G(t)$ has to be specified. Case of fabricated inductor 1 from Figure 43 is considered.

The inductor coil is placed on a nerve cell as shown in Figure 46.
During the experiments the coil was placed right above nerve fiber. The coil is placed such that the circumference of the coil is tangential to the nerve fiber. Assuming that the nerve fiber forms a part of the rat sciatic nerve which is roughly 1-2 mm in diameter we simulated the electric field and gradient of the electric fields at a distance of $z=2$ mm below the coil using the FD scheme described in chapter 3. Figure 47 shows the x component of electric filed profile in x,y plane at $z=2$mm. Figure 48 shows the corresponding spatial gradient of x component of the electric field ($E_{xx}$) in the x,y plane. Since $E_x$ is dual lobed $E_{xx}$ assumes a 4-lobed profile. At $y=r$ the spatial gradient of the electric field parallel to the nerve axis has form depicted in Figure 49.
Figure 47. Component of the induced electric field parallel to the nerve axis ($E_x$) is plotted in the $x,y$ plane.

Figure 48. Spatial gradient of the induced electric field in the direction of the nerve fiber ($E_{xx}$) is plotted in the $x,y$ plane.
Figure 49. Spatial gradient of the induced electric field in the direction of the nerve fiber ($E_{xx}$) Vs $x$ at $y = r_c$ (radius of the coil)

A gaussian approximation was performed on the plot shown in figure48 and continuous Gaussian function for $F(x)$ was obtained. For $G(t)$ the overdamped LCR discharge function from equation (58) was used. Thus $E_{x}(x,t) = F(x)G(t)$ was finally obtained and was used to calculate the transmembrane potentials by solving Equations 40-43.

The resultant transmembrane potential is plotted in figure 50.
Figure 50. Transmembrane potential evoked across a nerve fibre using time varying current from inductor 1 as stimulus.
Figure 51. Transmembrane potential evoked across a nerve fibre using time varying current from inductor 1 as stimulus Vs time(t)
5.5 Experimental Results

Sciatic Nerve

Figure 52. Schematic diagram of a Sciatic nerve and its branches[51]

Figure 53. Rat Sciatic Nerve exposed for experimentation purpose

The sciatic nerve is a large nerve fiber in humans and other animals. It originates from the lower back of the body running down to the lower limb. It is the longest and widest single
nerve in most animals and human beings. The sciatic nerve consists of several hundreds of nerve fibers varying in their sizes and diameters. Typically larger fibers are easier to stimulate than the smaller ones. A schematic diagram of Rat Sciatic Nerve is shown in Figure 52.

Experiments on rat sciatic nerve were done with our collaborators in Department of Biomedical Engineering, University of Utah. A dissected rat with the sciatic nerve exposed is shown in Figure 53. The objective of the experiment was to see if the nerve reacts to induced electric fields due to the stimulator circuit described in section 5.3 and if the simulated results using first approximations presented in section 5.4 could be corroborated.

One main difference in recording the nerve response experimentally was that instead of directly measuring the transmembrane potential, Compound Action Potentials (CAPs) are measured. The compound action potential (CAP) represents the activity of many axons in the nerve. The CAP results from near-simultaneous action potentials in many fibers, rather than from an action potential in a single fiber (as simulated in section 5.4). The CAP recorded extracellularly is much smaller in amplitude (a few mV) than an individual action potential recorded intracellularly (over 100 mV), and exhibits a reversed polarity (negative rather than positive). These additional differences arise because extracellular recording does not measure the transmembrane voltage directly; rather, it measures voltage drops generated by current flows across resistances in the extracellular space. Nevertheless an evoked CAP is in correspondence with the depolarization (described in section 5.1) of many nerve fibers. Hence any observed CAP would corroborate the numerical predictions from section 5.4.

While performing the experiment, twitches in rat leg were observed in intervals of 1 sec. This was in perfect accordance with the frequency of the inductor activity. Figures 54 and 55 show the Electromyography response of recorded CAP from the rat sciatic nerve recorded at different times and varying stimulus voltage.
Figure 54. Compound Action Potential (EMG response) of the Rat Sciatic Nerve due to an external stimulus obtained from Stimulator Circuit described in section 5.3 and inductor coil 1. Stimulus voltage was 45 V
Figure 55. Compound Action Potential (EMG response) of the Rat Sciatic Nerve due to an external stimulus obtained from Stimulator Circuit described in section 5.3 and inductor coil 1 recorded at a different time and lower strength of the stimulus voltage compared to Figure 54

Figures 54 and 55 experimentally verify our predictions that Inductor coil would elicit neural response in nerve fibers with voltages much lower than those in the existing literature. Rat sciatic nerve is very small in diameter when compared to other mammals. We believe that the stimulus voltages can be further reduced and inductor sizes can be further cut down to elicit neural responses in bigger animals.
Chapter 6

Conclusions and Future Work

This research focused on exploring the feasibility of using small coils carrying time varying currents as a viable alternative to electrode arrays in neural stimulations. Magneto stimulators have been shown to have many advantages over the corresponding electroneurostimulators. Theoretical analysis was performed to calculate induced electromagnetic quantities in neural tissues due to magnetic coils. A Novel Finite Difference Code was formulated to compute induced electromagnetic quantities for complex geometries. An example application of implementing an array of microcoils in implantable devices was explored using Retinal Prostheses system. Very small prototype inductors were fabricated in the lab. A novel Boot Strap Circuit was devised to drive the stimulating inductor coils. Experiments were performed on Rat Sciatic Nerve using this new circuit. Twitches and corresponding EMG pulses were obtained by exciting the nerve using the designed stimulator circuit. The neural responses were obtained at 40V of stimulus supply as compared to 1-2kV used in existing technologies. Inductor sizes were narrowed down to maximum 1.5 cm diameter as compared to 5-10 cm in existing Transcranial Magnetic Stimulation. These results indicate toward possible success in realizing a implantable prosthetic device using an array of microcoils carrying time varying currents.

Inductor coil labeled 1 was able to elicit neural response in a rat sciatic nerve. While the strength of peak $\frac{dl}{dt}$ in other inductor coils was much higher than that of inductor 1, the pulse width in these coils was much lesser. Measured values of the resistance considerably differed from the calculations. Moreover, if the cable model for neural response were to be proven true the figure-of-8 coils should stimulate the nerve at much lower stimulus voltages as compared to single coil, since they have higher electric fields and corresponding spatial gradients compared to single coil. But since we had only one opportunity to work with rat sciatic nerve, we were unable to test figure-of-eight version of inductor coil 1. Moreover
heavy lead resistances from the stimulator circuit to the inductor coils (which was placed on the sciatic nerve) tremendously increased the resistance of the inductors. This rendered the pulse width very small. For example the inductor coil labeled 4 theoretically have a positive dI/dt for approximately 200uS. But in effect during the experiment on the nerve, the pulsed decayed with 100uS. Hence these coils were unable to elicit any response from the sciatic nerve.

Future work in this research is focused on building an on-chip stimulator circuit. This would remove any unwanted contact resistances. Also the chip could directly be placed on the nerve thus eliminating the need for inductor leads. This would tremendously increase the pulse width of the small inductors and hence enabling them to possibly elicit neural responses in future.

Since not enough data regarding in vivo experiments involving magnetic stimulation of neural data are available in literature, a definite mechanism for neural stimulation is not understood. Our future work will focus on using coils of different sizes, different stimululs voltages, and experimenting with different neurons from different animals. This would help us in establishing a relationship between stimulus strength threshold and minimum pulses width needed for excitation depending on the type of nerve. Once such relationships are established, we will be in a better position to create an accurate model of neural stimulation depending on which type of nerve we are exciting.

Future implantable devices need to be much smaller than our prototype devices. We are collaborating with fellow researchers at the University of Utah on the possibility of using MEMS to fabricate coils with diameters in the range of 100-500 microns. A driver circuit would be designed which can selectively drive some or all of the micro coils in an array. This would accomplish our goal of implementing an implantable prosthetic device using an array of microcoils as neural stimulators.
References


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