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**The pulse clamp method for analyzing neural stimulating
electrodes**

Bonner, Matthew David, Ph.D.

Case Western Reserve University, 1991

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**THE PULSE CLAMP METHOD
FOR ANALYZING
NEURAL STIMULATING ELECTRODES**

by

MATTHEW BONNER

Submitted in partial fulfillment of the requirements
for the Degree of Doctor of Philosophy

Thesis Advisor: Dr. J. Thomas Mortimer

Department of Biomedical Engineering
CASE WESTERN RESERVE UNIVERSITY
May 1991

CASE WESTERN RESERVE UNIVERSITY
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THE PULSE CLAMP METHOD FOR ANALYZING NEURAL STIMULATING ELECTRODES

Abstract
by
MATTHEW BONNER

The Pulse-Clamp (P-C) method was developed and used to analyze the electrochemical behavior of neural stimulating electrodes on the same time scale as typical neural stimulating pulses. The P-C method consists of applying a controlled current stimulating pulse, followed by a controlled potential pulse. The instrumentation, cell, and technique were shown to measure accurately electrochemical processes for times greater than $10\mu\text{S}$. These experiments were performed with uniform current distribution at 1 Hz pulsing.

The P-C method of analysis was applied to gold, platinum, and SS316 electrodes. The charge recovered during the controlled potential pulse was divided into three segments based on time. A 3 element model was derived using these three time segments. The behavior of this proposed 3 element model was compared with the observed electrode behavior. The model could imitate most of the observed electrode behaviors for changes in the pulse width, delay, and clamp potential.

The difference between the three materials was in the relative amount of charge found in the three time segments. From these finding it was deduced that gold stored the majority of charge in double layer, while platinum stored most of the charge in the hydrogen adsorption reaction. Almost two thirds of the evolved hydrogen on platinum could be reoxidized during the reversal phase. SS316 primarily stored the charge in the oxide reduction process.

The response of the three electrode materials was similar in that the electrode potential during an electrochemically reversible pulse was substantially more negative than the H_2 evolution potential as determined by slow cyclic voltammetry. An estimate of the safe charge injection limits was based on the measurement of unreversed electrochemical products. On gold unrecoverable charge was detected above $-75\mu\text{C}/\text{cm}^2$. On SS316 the safe limit is unknown, but it was in excess of $-150\mu\text{C}/\text{cm}^2$. The safe limit was also not reached on platinum, but it was in excess of $-300\mu\text{C}/\text{cm}^2$. The optimal reversal waveform was found to be a large current spike containing the double layer charge followed by a exponentially decaying current timed to the rate of the reversal processes for the particular material.

Dedication

I dedicate this work to the women in my life.

First and foremost, I dedicate this work to my wife Mary Jo Bonner. Her unending love, support, and help made the undertaking and completion of my doctoral work possible.

I also dedicate this work to my long time friend Naomi Franklin. Her continual care, concern, and prodding have helped me make many important decisions that ultimately allowed me to undertake this graduate program.

I further dedicate this work to Lizbeth Kraft who has provided me with sound advice at critical turning points in my life.

Last, but certainly not least, I dedicate this work to my late mother Miriam Bonner. Her high standards, both academic and personal, were always a source of inspiration and drive.

I thank you for your love and support in the past, present, and future.

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1. Introduction and Work to Date

1.1 Introduction

The field of applied neural control attempts to restore lost body functions by electrically stimulating selected neurons. In theory, a neural prosthesis could restore virtually any lost ability. The most successful prosthetic to date is the cardiac pacemaker. The auditory prosthesis, another commercially available product, can significantly improve speech recognition in deaf patients. These prostheses operate by passing electrical current between two metal electrodes implanted in the body. The electrical current causes the adjacent neurons to fire in a normal fashion.

As promising as electrical stimulation is, fundamental problems exist in some applications. The main issue is tissue damage to the cells surrounding the electrode. Death or disruption of these cells removes the ability to stimulate them, and results in prosthesis failure. To pass current from an electrode to the tissue requires electrochemical reactions. These reactions, under certain conditions, may generate noxious products that could damage the adjacent tissue. Another problem is corrosion of the stimulating electrode. It has been found that injecting too much charge using the standard waveform causes electrode corrosion. Stimulation levels must stay between two limits. The lower limit is the minimum level that causes neuron firing, and the upper limit is the level that causes electrode corrosion.

It is the overall goal of this study to understand how the processes store charge during a stimulus pulse. Charge is injected into the electrode, as it is done during neural

stimulation. We then analyze how the charge is stored during the pulse. Avoiding possible electrochemically induced tissue damage depends on understanding the electrochemical processes occurring during stimulation at the electrode/tissue interface. Further, some of the processes consuming charge may not damage cells. Optimizing the use of these processes may increase the safe charge injection levels. Corrosion of the electrode may effect prothesis function, but it will not be directly considered in this study. The advantage of using charge measurements is that they directly relate to the amount of electrochemical products generated. Measuring charge allows us to study the amount of electrochemical products created and reversed.

This work uses the Pulse-Clamp (P-C) method to study the electrochemical behavior of stimulating electrodes on a time scale consistent with stimulation. The primary advantage of the P-C method is that it can be used to evaluate the nature of the processes occurring on the electrode during a typical neurostimulation pulse. This technique can also be used to measure the level of unrecovered charge that is critically important to understanding the electrochemical impact on tissue damage. Using this method, the charge going into the specific processes is inventoried. A method did not previously exist to measure the charge stored by individual electrochemical reactions on this time scale. We also examine safe charge injection limits, and optimal reversing pulse shapes. An electrical analog model that mimics observed electrode behavior is also presented. Finally, the charge stored by various processes during a pulse is measured. This information is then used to discuss the design of an ideal system.

1.2 Principles of Stimulating Electrode Operation

1.2.1 Action Potential Creation

The ability to control body functions with neural prostheses is based on creating an action potential using an electrical current. An action potential is an electrical impulse that flows down the length of a neuron. It is generated by a spatially varying electric field. Any current flowing through a resistive media, such as tissue, creates a spatially varying electric field. When current is pulsed between two implanted electrodes, the field can be created artificially. An action potential generated this way is indistinguishable from one generated by normal nerve function.

Electrically induced action potentials can recreate the same effect as normal neural impulses. The electrically induced action potential is indistinguishable from a biologically induced one, and will cause the same response. A neurotransmitter is released by the action potential at the neuron terminus. This chemical can then cause the release of a hormone, the contraction of a muscle, or the firing of another neuron. The function depends entirely on the transmitter and receptors at the terminus, not on the action potential. The result is the same regardless of how the action potential is initiated.

Many different body functions can then be controlled depending which neurons are stimulated. If the excited neuron ends at a neuromuscular junction, then acetylcholine is released causing the contraction of a group of muscle fibers. Stimulation of a group of motoneurons results in the contraction of the entire muscle. If the stimulated neuron ends in the visual cortex of the brain, a white dot or phosphene appears in the visual field. Stimulation of nerves in the auditory canal results in a tone being perceived. Ideally, any function under nervous control can be affected by stimulating the proper group of neurons.

1.2.2 Current versus Potential Control

The most consistent stimulation threshold over time is achieved if the stimulating pulse uses controlled current rather than controlled potential pulses. Stimulation threshold is the minimum value of current or potential required to stimulate the neurons. Current control varies the potential between the electrodes to maintain the desired current, while potential control maintains the desired potential by varying the current between the two electrodes. Remember, that it is the current that creates the spatially varying field necessary to cause an action potential. Controlling the electrode potential assures the potential difference between the two electrodes is constant, but the current will depend on the impedance of the tissue. It turns out that tissue impedance does change over time. Thus, the current will vary over time given the same potential. It is important to maintain a constant stimulus threshold. Changes in the stimulation threshold may change the performance. Sometimes no stimulation may occur, while other times overstimulation may occur. Thus, controlling the current instead of the potential will maintain a more consistent stimulus threshold over time.

1.2.3 Stimulation Waveforms

The current passed through the electrodes to achieve neural stimulation is referred to as the stimulation waveform. The typical stimulation waveform is two opposite polarity current controlled pulses separated by a period of no current flow. A typical waveform is shown in Figure 1-1. The first negative pulse is the stimulation pulse. The second positive pulse is used to reverse the electrochemical processes that occur during the first pulse. The charge contained in the first pulse is matched to that in the second pulse. The waveform shows that the negative and positive polarity pulses are separated by an open circuit delay.

Figure 1-1 - Typical stimulation controlled current biphasic waveform.

The delay avoids quenching the nascent action potential created by the first pulse with the second opposite polarity pulse. This waveform has become the defacto stimulation standard. As will be shown, it is not necessarily the best waveform for reversing the products created during stimulation.

The average duration of most stimulation pulses is around 100 μ S. Durations range between 10 μ S and 200 μ S. These limits result from a compromise between two opposing constraints. The first is to minimize the charge required to achieve threshold. Passing the minimum charge into the body is desirable both to reduce the electrochemical products, and to maximize the battery life of the stimulators. The second constraint is imposed by a limit on the practical current available to most systems. To create large currents one must have large potentials and more power. The opposition of these two constraints is shown in Figure 1-2. This figure shows the threshold current and charge versus pulse duration. Shorter durations require larger currents, and less charge. Longer durations require increasing charge and some minimum current. Thus, to minimize the charge one should use short pulse widths, while to keep the current small one should use long pulse widths. A compromise is reached between the conflicting demands at around 100 μ S.

1.2.4 Electrode Configurations

The stimulus current is passed through the body via metal electrodes. Electrodes come in many shapes and materials to accommodate the many different applications. The disk electrode, for example, is a simple cylinder in which one end is generally insulated (see Figure 1-3). This electrode is used for cortical and muscular stimulation. A barb electrode consists of a helical coil of metal with a barb at the end to hold the electrode in place. This electrode is intended for implantation in tissue that undergoes much physical

A

B

MEMBRANE STRENGTH-DURATION

Figure 1-2 - A) Charge duration curve. The charge to just stimulate a neuron.
B) Strength duration curve. The current required to just stimulate a neuron.

Figure 1-3 - Four Types of Stimulating Electrodes

displacement such as muscle contraction. Electrodes in a muscle can easily undergo a 180 degree flexion. The nerve cuff electrode contains a metal band. This thin strip of metal wraps around the nerve being stimulated. The metal must be very compliant so it does not damage the nerve. Many new micro electrodes come in the shape of a spike. The end is the only uninsulated portion, and they are intended for use in cortical stimulation.

1.2.5 Faradaic Processes

The passage of current through the metal electrodes to achieve stimulation requires Faradaic processes. For current to flow between the electrodes, electrons must be transferred between the metal electrode and the solution. This transfer creates ions in the solution. Thus, electrons carry the current in the wire, and ions carry the current in the tissue. The electron transfer processes are called Faradaic processes. Faradaic processes have reactants and products as do all chemical reactions. However, all electrochemical reactions must take place at the electrode surface. This means reactants must diffuse to the surface, and products must diffuse away. It also means that most reactions will create some electrochemical product that can diffuse into the adjacent tissue.

Each Faradaic reaction has associated with it an energy level required to drive the reaction. The energy is supplied by the electrode potential. The larger the absolute value of the electrode potential, the more energy supplied to the interface to drive these reactions. Each reaction occurs at the potential supplying the necessary energy to drive the reaction. Electrode potential is, therefore, a key parameter in the study of electrochemical reactions.

Like all other chemical reactions, Faradaic reactions also have an associated rate for each reaction. The farther the potential exceeds the minimum necessary to drive the

reaction, the faster the reaction will go. How the reaction velocity varies with potential is different for each reaction, and is referred to as the reaction kinetics. Thus, kinetics control the reaction rate through the electrode potential. However, the reaction rate can also be controlled by other factors. The reaction will slow down when the reactants adjacent the electrode have been consumed, and when the products become concentrated near the electrode. Thus, the reaction velocity is controlled by kinetics, and reactant and product concentration.

1.3 Background

Electrical stimulation of nervous tissue has been accomplished for centuries, but only recently have health care products based on this principle been available. Muscle contraction was the first application of electrical stimulation. In the eighteenth century scientists such as Benjamin Franklin and Luigi Galvani investigated these phenomena. By the nineteenth century the use of electrical stimulation was refined to study the functional anatomy of individual muscles. Its general use was probably limited by the lack of small stimulators. By the 1900s, people were experimenting with stimulation that included virtually every part of the body. It was used as a cure for everything from headaches to impotence.

Since then the physiological mechanisms underlying electrical excitation of nervous tissue have been elucidated. This understanding and the advent of modern miniature electronics have made possible completely self contained implantable systems. However, the electrochemical mechanisms underlying charge transfer during the stimulus pulse are still not well understood. The pertinent research about these mechanisms will now be discussed.

1.3.1 John Lilly

John Lilly discovered the relation between stimulation pulsing and tissue damage. Others before him knew that direct current could induce lesions (Ranson & Ingram, 1932), and this technique was used to produce brain deficits in specific areas. However, no one had linked the damage created during current pulsing to the damage produced by direct currents. For years the stimulus pulses used were of single polarity. Lilly found that the tissue adjacent stimulating electrodes showed abnormal histology and neuronal death after many hours of stimulation with these monopolar pulses (Lilly et al, 1952). He postulated that the damage may be due to the dislocation of proteins and other charged molecules from their proper locations around the cells. This dislocation resulted from the net direct current that resulted from continuous pulsing with a single polarity. From this he derived the idea that a balanced current passed in both directions would eliminate any permanent displacement of these molecules, because no net direct current would flow. In a later paper (Lilly et al, 1955) he showed that using "balanced biphasic stimulation" achieved by quasi differentiating a rectangular current pulse reduced the associated damage. A similar waveform has become the defacto standard for neurostimulation. However, the rationale for using this waveform has changed from balanced molecule displacement to balanced electrochemistry at the electrode interface.

1.3.2 Anthony Dymond

Anthony Dymond was one of the first researchers to bring electrochemical ideas into the biomedical research effort. In a review of the pertinent literature to date (Dymond, 1976), he discussed many aspects of the electrode/tissue system. Most work at this point focused on the impedance of this system. The voltage across, and the current through the two electrodes were measured, and their dividend was denoted the impedance. The use of

transient measurements allowed separation of a resistive and a capacitive component. In general, the resistive component decreased with both the frequency and amplitude of the stimulus pulse. The capacitive component decreased with frequency, but increased with increased amplitude. The changes were unexplained, but concepts such as frequency dispersion due to microcracks and surface nonuniformity were discussed.

The concept of impedance of the electrode/tissue system has not proved fruitful in elucidating mechanisms, and has generally been abandoned. While there is still much speculation about the processes responsible for tissue damage, the elucidation of these mechanisms has yet to be done. A technique only briefly mentioned in his paper is polarization studies. For these studies a constant current pulse was applied, and the electrode potential during the pulse was measured. Much of the work after this time used polarization studies to examine electrode behavior, and workers including Greatbatch, Robblee, and Donaldson continue to use this technique.

Some speculation was made about the possible processes responsible for the observed tissue damage. Most discussion centered around the positive potential processes. The possible culprits included oxychloride species, changes in pH, and the precipitates involving ions such as calcium, magnesium, and carbonate. It was found that electrodes causing damage in one location could be moved to a new location, and cause further damage without passing current. This gave weight to the idea of an electrochemically generated product causing the damage rather than thermal or field effects. The second or reversal pulse can remove these generated species to some extent, but as Dymond pointed out, charge balance across the interface does not necessarily dictate electrochemical balance. This was explained using the concept of Faradaic rectification in which the net current is

zero yet the electrode polarization undergoes a net change over times much longer than the stimulus pulse.

About this time, the pulse duration came under scrutiny. Previously, the pulse durations used were many milliseconds long. Questions were raised about the charge efficiency of these waveforms. The result of the strength duration studies was to establish the use of pulse durations in the 100 μ S range. However, the change from 10 mS pulses to 100 μ S pulses could easily change the electrochemical behavior of these neural stimulating electrodes. This is because the current density increased, and the time decreased by a couple orders of magnitude. Both of these factors can affect electrochemical behavior.

1.3.3 Barry Brummer

Barry Brummer was one of the first to study the basic reactions in a classical electrochemical manner. He approached the problem in a more rigorous and systematic fashion than had been done previously. Brummer and Turner studied primarily platinum electrodes in both acid and physiological saline media. They discussed the individual reactions consuming charge during a pulse that changed the electrode potential across the entire water window¹. This was the first attempt to quantify the safe charge injection limits based on the likely reversible reactions.

Three papers came out in the same year describing results from studies on platinum electrodes (Brummer & Turner, 1977 a, b, c). All used the same setup that included uniform current distribution on a spherical electrode, clean electrolytes including HClO₄,

¹ The water window is generally defined as the potential limits imposed by water electrolysis. In this case it is the window between the potential for hydrogen evolution and oxygen evolution as determined by CV.

(perchloric acid) H_2SO_4 (sulfuric acid), and phosphate buffered saline. The procedure consisted of applying a constant current pulse, and measuring the potential excursion during the pulse. The pulse durations they used varied between 5 and 25 mS. During the current controlled pulses, Brummer & Turner studied the potential plateaus that indicated the occurrence of a reaction. The reactions occurring at specific potentials were known from other electrochemical studies. The charge going into each reaction was measured from the time between changes in slope and the known constant current. From these studies the available charge in each reaction could be measured. The major drawback with these studies is that they used low currents and long pulse durations. The current densities are within the range of a moderate stimulus pulse, but they do not probe the limiting values. To inject the $350 \mu\text{C}/\text{cm}^2$ Brummer associates with the hydrogen adsorption reaction, during a typical $100 \mu\text{S}$ pulse requires a current density of $3.5 \text{ A}/\text{cm}^2$. The currents used in these studies had a maximum of $450 \text{ mA}/\text{cm}^2$. The problem with very high current densities is that the different reactions, many of which occur simultaneously, are very difficult to separate.

The possible reactions and their relevance to biomedical stimulation were discussed (Brummer & Turner, 1977a). The conclusion was drawn that anodic potentials should be avoided because of platinum dissolution in a chloride containing media. Not much had been studied about the kinetics of oxidation and corrosion on platinum in phosphate buffered saline, and they concluded that more work was required to measure the products of these reactions under typical stimulation regimes. The hydrogen plating reaction appeared unaffected by the presence of chloride, and was, therefore, a good candidate for reversible charge injection on these electrodes. He repeated the concerns of Dymond that charge balanced biphasic stimulation did not necessarily balance the electrochemistry. Further work

(Brummer & Turner, 1977b) used the consistency of the hydrogen plating reaction to establish the real area of the electrodes. They went on to measure the charge available in hydrogen adsorption (Brummer & Turner, 1977c), and found that hydrogen adsorption contained approximately $350 \mu\text{C}/\text{cm}^2$. Because the pulse parameters he used were quite different than those of a typical neural stimulation pulse, this number may not represent the value during a stimulus pulse.

1.3.4 Wilson Greatbatch

Wilson Greatbatch began by surveying seven different metals and their potential response to a constant current pulse (Greatbatch, 1967). He has continued the same type of research over 20 years (Piersma & Greatbatch, 1987) while refining the technique and changing the electrode materials, solutions, and gases. Greatbatch is a cardiologist, and the aim of most of his work is to improve the performance of cardiac stimulating electrodes for the pacemaker industry. He has generally been interested in positive current pulses, although his more recent work includes both positive and negative current pulses.

The experiments involved the use of a metal wire electrode held in "physiological saline" at 37 degrees Centigrade. The electrodes were pulsed with constant current pulses of 1.6 to 2.6 mS duration and from 6 to 56 mA/cm² amplitude. Thus, the maximum charge delivered to these electrodes is $146 \mu\text{C}/\text{cm}^2$. The potential of the electrode at the end of the pulse was the parameter in which he was interested. The electrodes are sometimes coiled as for implanted electrodes, and sometimes they are straight wires. His measurements showed less than 5% difference in the electrode potential between coiled and straight electrodes (Greatbatch, 1967). A concern with these studies is that the potential may not be accurate due to the non uniform current distribution over the electrode surface. The

current distribution on a straight wire with no insulating endplates is not uniform. The cut and insulated end each have significantly higher current than the rest of the electrode. Electrode potential is a function of the current passed across the interface. Non uniform current distribution means the electrode potential will also not be uniform over the surface of the electrode. Also, different reactions may be occurring on different parts of the electrode due to the different potentials. The potential measurements made under these conditions will therefore be some spatial average of the different potentials on the surface. The potentials measured in this study are unlikely to provide reliable information about the electrochemical reactions occurring. Comparing the results and looking for electrodes with smaller potential excursions is one way to use these results.

1.3.5 Nick Donaldson

Donaldson was the first to question the defacto necessity of the "Lilly" charge balanced biphasic waveform (Donaldson & Donaldson, 1986a-d). He wanted simpler circuitry so more stimulation channels could be packed in the same size stimulator box. For example, a cortical stimulator needs hundreds of channels, and it would require a very large box for the stimulator alone. Much of the circuitry is required by the secondary reversing pulse. If a way can be found to avoid the use of this pulse then the stimulator size can be reduced. The idea was to short the two stimulating electrodes at the end of the stimulus pulse. In general, one electrode is very large and changes potential very little during the pulse. The other is much smaller and can change potential a great deal. Shorting these two electrodes would force the smaller electrode to the potential of the larger electrode, and cause some electrochemical reversal. While it is not clear from Donaldsons' results that this method achieves electrochemical reversal, questioning the "Lilly" waveform is long overdue.

Since Donaldson showed that simply shorting the two electrodes affects some potential and charge reversal, more people may now consider alternate methods of charge reversal.

1.3.6 Lois Robblee

Lois Robblee has continued the work of Barry Brummer in trying to define safe charge injection limits for stimulating electrodes. She recognized the problem that the slow cyclic voltammetry predicted the charge available at slow speeds, but kinetics can easily affect how the charge is stored during a very rapid pulse. Slow cyclic voltammetry is a technique in which the current is measured while the electrode potential is slowly moved between two limits. The approach she and her colleagues have taken is to provide two numbers that bracket the likely real safe charge injection limits. The first, based on slow cyclic voltammetry, gives the maximum number. The minimum number is based on potential transients resulting from constant current pulses. The charge required to depolarize the electrode to the safe potential determined by slow cyclic voltammetry gives a minimum safe charge. The two numbers she gives as bracketing values, however, differ substantially on platinum. The lower limit provided by potential transient measurements show that the safe injectable charge is about $74 \mu\text{C}/\text{cm}^2$ (Kelliher & Rose, 1989). This compares with the value of $350 \mu\text{C}/\text{cm}^2$ determined by slow cyclic voltammetry. Thus, there is a large variation between the maximum and minimum limits, and the choice of a safe charge injection limit is not clear.

1.4 Objectives of this study

Reviewing the research to date we find there is consistent use of very long pulse widths and low currents. The reactions occurring during very short pulses may be different than during long pulses. The use of nonuniform current distribution by other researchers

makes interpretation of potential measurements very difficult. Also, no one to date has actually measured the occurrence of specific reactions during typical pulses. To address these issues, we have developed a new method, the pulse-clamp technique, to examine the electrode behavior during a typical stimulus pulse.

The principle behind the pulse-clamp method is to measure the available recoverable charge after a stimulus pulse. We can use the amount of recoverable charge and the rate of charge recovery to indicate what processes occurred during the stimulus pulse. Each process will store some amount of the injected charge. If the charge injected during the stimulus pulse exceeds the charge recovered during the reversal pulse, we know that some electrochemical products were permanently created. We assume unreversed products are the cause of electrochemically induced tissue damage.

With this method, the electrochemical reversal was accomplished by returning the electrode to its initial potential immediately after the stimulus pulse was applied. The only reactions occurring during the reversal pulse will be the reverse of processes initiated during the stimulus. The recovered charge, then, will only be that associated with the reversal of processes. This charge recovery technique is quite different from the typical biphasic pulsing that forces charge balance, but ignores electrochemical balance. Keeping the electrode interface in electrochemical balance is an important criteria for safe charge injection. The ability to measure the recoverable charge will tell us the level of electrochemical balance. It will also indicate stimulation waveforms that are more likely to cause damage by passing charge that cannot be recovered. The recoverable charge technique can establish the difference in the various metals' ability to store and return charge during a pulse.

Using this charge measuring idea, we can examine how the charge is stored during typical neural stimulation. The recovered charge can be measured and compared for pulses with increasing injected charge levels. Studying the pulse in this way allows us to take apart the processes that occur during a stimulus pulse. It also allows us to study how the processes change with increasing charge injection. Understanding how the processes change can lead to understanding of how the processes operate during high charge density pulses. Also by measuring the unrecoverable charge with increasing increments of injected charge, we will know at what total charge levels the unrecoverable charge, and possibly tissue damage, begins.

1.5 How this Document is Organized

The first part of this study involves developing the Pulse-Clamp (P-C) method. The development and verification of the instrumentation and methodology are detailed in chapter 2. The instrumentation and electrochemical cell are tested using impedance analysis with both electronic and electrochemical test loads. The ability of the P-C method to measure accurately load capacity is tested using electronic loads with varying capacity. The P-C technique is also compared with two other established techniques to measure the double layer capacity that has been well established from other studies. The technique is then applied to an electronic load that mimics a gold electrode, and to an actual gold electrode. The results are presented in chapter 2.

In chapter 3, we look at the behavior of three electrode materials, gold, platinum, and stainless steel. From these data, we discuss which processes are occurring, the safe charge injection limits, and the best reversal pulse to minimize leftover products. The

ability to reverse the electrochemistry occurring during the stimulus pulse is critical for safe charge injection. The shape of the reversal pulse can effect how complete the reversal is. Several researchers have already questioned whether it is. Our work will attempt to decide if the Lilly waveform is appropriate, and if not, what shape recovers the most charge. The safe charge injection limits are critical for long lasting neural prostheses. If the tissue is damaged because the safe threshold is breached, then the prosthesis will fail.

An electrical analog model is presented in chapter 4. The behavior of this model is compared with various electrode behaviors. We use the concept of the model to study whether certain expected model behaviors can be found with the actual electrodes. This will be done by varying the post stimulus clamp potential on a gold electrode in sulfuric acid. The expected model behaviors are also compared to electrode results when the pulse duration and the delay between the stimulation pulse and initiation of the reversal pulse are varied. We compare the patterns of charge recovery with these parameter variations to those expected of the analog model. This is done on gold and platinum electrodes in a phosphate buffered saline solution.

The last study, in chapter 5, investigates how much charge is actually going into each reaction during a typical cathodic pulse. This is done by creating an inventory of charge consumption for each reaction participating in cathodic pulses on gold and platinum electrodes. Gold and platinum electrodes in phosphate buffered saline are pulsed with increasing amounts of charge. The amount and rate of charge recovery is combined with other knowledge about the reactions known to occur during these pulses. By doing this, we are able to quantify the charge going into each of the reactions.

2. The Pulse Clamp P-C Method

2.1 Introduction

We have developed a method for studying the electrochemical processes occurring on an electrode under typical neural stimulation conditions. This method is unique in its ability to study the electrode under the same pulse conditions as those encountered in a neural prosthesis. The method is called the pulse clamp (P-C) technique. Applying the P-C instrumentation and technique to an electrode, the different electrochemical processes occurring on the electrode surface during a pulse can be distinguished from each other. Further, this can be accomplished within the typical parameters of a neural stimulating pulse. A typical prosthesis will use a 100 μ S pulse duration and a current density in excess of 1A A/cm².

From in vivo work, we know that the amount of charge injected during a neurostimulation pulse is an important parameter influencing the electrochemically induced tissue damage. Tissue damage is usually identified with a threshold charge below which no damage occurs. The association of damage with a specific charge injection level means that either the processes responsible for damage are beginning after a given level of charge has been exceeded, or that the quantity of electrochemical products are exceeding the toxic threshold in the adjacent tissue. Both damage mechanisms can be examined with P-C method using the charge measurements. First, charge is injected into the electrode, and then a reversal pulse is applied to examine how much and how fast the charge can be recovered. If some the injected charge is not recovered during the reversal pulse, it is because the charge still resides in some product. This unrecovered charge can be measured by

comparing the injected to the recovered charge. Thus, an increase in the unrecoverable charge will indicate when a process begins. A constantly increasing level of unrecoverable charge with increasing total charge signifies an accumulation of the product.

At the very high current densities and short durations typical of a neural stimulating pulse, the reactions will be dominated by double layer charging. The double layer separates the charge on the metal electrode and the charged species in the solution. The current going into this process is proportional to the rate of change of potential. At very large charge injections, the electrode potential changes very rapidly, and the double layer current will be very large.

Many researchers use slow cyclic voltammetry to study electrochemical reactions. This method indicates at what potential reactions occur, but the current levels typically used are orders of magnitude lower than those found during a typical stimulus pulse. If the rate of potential change for cyclic voltammetry is increased to a similar rate as that observed during stimulation, then the double layer current dominates and makes the other processes difficult to see. With the P-C technique, we do not have this limitation. We are able to study the reactions that are occurring by separating the double layer current from the other processes.

The P-C technique removes the double layer current using a controlled potential after the stimulus pulse. With this P-C method, a controlled current pulse, identical to a neural stimulation pulse, is first delivered to the electrode. The potential during this pulse is controlled only by the electrochemical processes that are occurring. After the pulse, the potential is forced back to its prestimulus value. With a constant potential, the double layer

current will be zero. So the double layer current is removed by the controlled potential pulse after the stimulus pulse.

The work in this chapter will use two different types of test load systems. One type will be an electronic circuit that is designed to mimic some aspect of electrode behavior. The advantage of an electronic circuit test system is that the parameters are completely known, and can be used to test the accuracy of the experimental system. The other type of test system we will study is that of a gold electrode in sulfuric acid. Electrochemically, this is a simple and well understood system on which to build the P-C method. Very few reactions occur in this system and they have all been thoroughly studied using many electrochemical techniques.

2.2 Pulse Clamp Technique

2.2.1 Description

For a P-C experiment, a test electrode is placed in an electrochemical cell that controls the electrode's environment. A current controlled pulse, or current clamp, is then applied to the electrode. A clamp is defined, for this work, as a control system that maintains either the current or the potential at a constant value. The current clamp reproduces a typical neural stimulation pulse. This portion of the experiment is referred to as the stimulating pulse phase. After the given length of time, the current clamp is then switched to a potential clamp. By applying the potential clamp after the stimulating pulse, we force the electrode potential back to its prepulse potential. The potential clamp phase of the experiment reverses the electrochemical reactions occurring during the stimulus phase. The potential clamp mimics the current controlled reversal pulse used by many neural prostheses. The recovered charge during a potential clamp reversal pulse is

determined by the ability of the electrochemical processes to reverse. By contrast, a controlled current reversal pulse forces the reversal charge onto the electrode. The amount of recovered charge is determined by the current and duration of the reversal pulse. By forcing the charge onto the electrode, reactions may occur during the reversal pulse that are not the reversal of reactions occurring during the stimulus pulse.

The charge measurements contain information about the electrochemical reactions that took place during the stimulus pulse. While the stimulus pulse is being applied, electrochemical processes are occurring. By measuring the charge during this phase, we have a reference of the quantity of charge injected during the stimulation pulse. The clamp is then applied. The charge is also measured during the potential clamp for a fixed period. The charge injected during the pulse phase is compared with the charge measured over the clamp phase. The difference between them gives the amount of unrecoverable charge.

For an ideal neural stimulating electrode, the unrecoverable charge measurement should be zero. This would indicate that all the electrochemical processes that occurred during the stimulus pulse, were completely reversed during the potential clamp. In actuality, some unrecoverable charge will always be measured. By measuring the unrecoverable charge, the processes occurring during the pulse can be deduced.

Across a general electrode/electrolyte interface, there are a number of reactions that can occur. These reactions are shown schematically in Figure 2-1. The fastest reaction will be double layer charging. Ideally, we would like to isolate the charge returned from this reaction to the period between the application of the potential clamp, and when the electrode is returned to a stable prestimulus potential. A perfect P-C experiment would

Figure 2-1 - System of processes representing charge injection for pulse clamp method.

create the potential step instantaneously. In reality, there will always be some stabilization time. Some reactions, other than double layer charging, may be fast enough to reverse during this stabilization period. The charge associated with these reactions would be included in, and contaminate the double layer charge measurement. At the other end of the time spectrum, some process may reverse more slowly than the allotted unrecoverable period. Although some of these processes may be reversible, they may not reverse within the measurement time. To account for both possibilities, the recovered charge measurement has been divided into time divisions.

For all the experiments, the charge measured during the clamp portion is divided into three time divisions. These are, as shown in Figure 2-1, the fast recoverable, slow recoverable, and unrecoverable time segments. The fast recoverable portion shows the charge returned between the time when the potential clamp is applied and when the potential stabilizes. In many cases, double layer charging will dominate this measurement. Because some fast processes other than double layer charging can be included in the fast recoverable measurement, we fixed the time period to 50 μ S. This way, any offset in the recovered charge measurement introduced by the inclusion of other fast recoverable processes will now be consistent. At some charge injection levels, less time was required for the potential to stabilize. To maintain consistency, the 50 μ S time period was used.

The unrecovered charge time was set at 20 mS. This was the minimum time between pulses, or the interpulse interval, for a typical maximum neural stimulator frequency of 50 Hz. The unrecoverable charge measurement included irreversible processes, as well as very slow processes. The remaining time segment, between the two extremes of fast recoverable and unrecoverable, was designated the slow recoverable segment.

We further defined a parameter we call virtual capacity. This parameter gives an indication of the charge storage capacity at the electrode interface. Virtual capacity is simply the charge returned during the fast recoverable portion divided by the magnitude of the potential step. The potential step was the difference in the potential before and after the potential clamp was applied. By including the potential measurement in evaluating our results, the capacity of the electrode was more clearly indicated. Some processes may store much charge with little change in potential. Other processes may store the same charge over a large potential range. The virtual capacity quantifies to what extent the fast recoverable charge behaves like an electronic capacitor.

2.2.2 Instrumentation

A custom instrument was built for these studies. A block diagram of the custom instrument is shown in Figure 2-2. (A complete schematic of the instrument is detailed in Appendix A) The instrument can be operated in either a current controlled mode (galvanostat), or in a potential controlled mode (potentiostat). Control can be switched between current control and potential control very rapidly ($2\mu\text{s}$). A key component in this instrument is the operational amplifier. This element supplies the command potential that controls how much current flows through the electrode. The command potential is dependent on both a command input, and on feedback from the potential and current monitors.

In the current control mode, the command potential controls the output current via a voltage to current converter, and an output stage. The converter drives the output stage with a closed-looped controlled current. Feedback from the closed-loop current control is

Figure 2-2 - Instrument Block Diagram

delivered to the primary operational amplifier by the voltage to current converter. The control of the current through the load is open-loop. Thus, the current monitor does not detect the actual load current, but rather the current that drives the output stage.

In the potential control mode, feedback to the primary operational amplifier is the potential difference between the reference electrode and the working electrode. Any difference between the desired potential, and the actual potential results in a non zero command potential that causes current to flow through the load.

A third mode can be considered in which the output is held in an open circuit condition. In this mode no current can flow through the electrode. This mode is generally referred to as the delay mode. The feedback in the delay mode does not matter because the command potential is set to zero regardless of the feedback.

Switching between control modes is accomplished by changing the source of the feedback to the operational amplifier. The feedback can come from either the current ("a" in the figure) or the potential ("b" in the figure) monitors. A pattern of mode changes, or a waveform, can be initiated with the push of a button. This is the manual initiation mode. The waveform can be also be repeated automatically in the automatic initiation mode. The waveform can be divided into as many as five independent stages. All stages within the pulse period can be current controlled mode, potential controlled mode, or delay mode. All stages have continuously variable amplitude of both polarities provided by a dial setting. One stage differs from the other four only in its duration. This different stage is the interpulse interval, or the resting time between pulses. The interpulse stage can last from 1 mS to 10 S, in 1 mS increments. This allows continuous pulsing at a rate from 1 kHz

down to 0.1 Hz in the automatic repetition mode. The other four stages can last from 0 μ S to 1 mS, in 1 μ S increments. The five stages are sequentially cycled for each waveform period.

A low impedance reference electrode is necessary to achieve potential stability very quickly after the potential clamp is applied. The low impedance is essential because the reference electrode is in the feedback path. The electrode impedance combines with the input capacitance of the electronic buffer, and creates a feedback time constant (Cahan et al, 1972). Delays in the feedback cause instability as the feedback becomes -180 degrees out of phase with the command potential. The operational amplifier already provides a -90 degree phase shift, so the reference electrode needs to provide only another -90 degrees phase shift for the system to become unstable. For example, a -90 degree phase shift would take only 2.5 μ S for a potential step that occurs in 10 μ S. The saturated calomel electrode (SCE) has an impedance of approximately 100k ohm. This resistance combined with a typical buffer input capacitance of 10 pF results in a feedback time constant of 1 μ S. This allows only 2.5 time constants for the system to achieve stability. The charged palladium reference electrode used by our system has an impedance of 10 ohms or less, so it causes very little phase shift. A typical time constant for a charged palladium reference electrode and buffer is 100 pS (10 ohms*10 pF).

The instrument provides complete IR correction and IR compensation up to 100 ohms. The IR correction removes the potential drop between the test and reference electrodes from the potential waveform. I stands for current, R for resistance, and IR is a potential by Ohms's law. The potential comes from the passage of current through the access resistance. The access resistance results from the solution between the test and

reference electrodes. The potential we are trying to measure is that exactly adjacent the test electrode. Physically, the reference electrode cannot be placed this close to the working electrode. Thus some access resistance always exists, and the potential measurement is distorted by the current flow through this access resistance. IR correction removes this distortion by subtracting the potential resulting from the current flowing through the access resistance from the potential waveform.

IR compensation increases the current drive during the potential clamp to reduce the time constant associated with charging the double layer through the access resistance. The access resistance slows the rate at which the electrode can be charged. By adding positive feedback related to the current flowing through the electrode, we can remove the effect of the access resistance. Since IR compensation adds positive feedback, IR compensation cannot exceed IR correction or the system becomes unstable.

The operational parameters of the instrument are shown in table 2-1. The maximum current output is 600 mA during the potential clamp. The transient peak current depends on the applied load, but is limited to 600 mA. The output power supplies are $\pm 75\text{V}$ so the total load resistance should be less than 125 ohms. The output current in the current controlled mode is 80 mA. The IR correction and compensation network can accommodate up to 100 ohms, but electrochemical loads with IR corrections in excess of 30 ohms tend to destabilize the instrument. The instrument then loses potential control during the clamp, and the electrode is subjected to potential oscillations between the power supply limits. The reason for the loss of control during the potential clamp is unknown. The 30 ohm IR correction limit was determined empirically from solutions of varying conductivity. In general, load capacities of 1-10 μF and load access resistances of 5-30 ohms will give the

Table I - Parameters of instrument design.

	Maximum (resolution)	Minimum (resolution)
Number of phases	4 (+ interpulse phase)	0
I_{MAX}	600 mA	0.1 mA
Q_{MAX}	14 μC	0.01 μC
V_{MAX}	+/- 75 V	-
IR_{CORR}	100 ohms	0.1 ohms
IR_{COMP}	100 ohms	0.1 ohms
V_{CLAMP}	+/- 2 V	1 mV
I_{CLAMP}	+/- 320 mA (pulse)	-
	+/- 80 mA (DC)	-
PW/Delay Interval	9999 μS	1 μS
# Repeat Pulses (Manual)	99	0
Pulse Interval (Non Man)	9999 mS	1 mS
(Frequency)	0.1 Hz	1 kHz
T_{clamp}	30 μS	10 μS
(Fully compensated; Uncompensating can increase clamp time even more depending on access resistance and load capacitance)		

maximum stability during the clamp. Electrode areas in excess of 0.1 cm^2 are not generally recommended. This is because of the 600 mA maximum current limit. Areas less than 0.01 cm^2 are also not recommended, because the access resistance becomes prohibitively high. This instrument will operate satisfactorily within these constraints.

Data collection involves taking digitized waveforms from a Tektronix 6303 scope with a 7D20 plug in. The scope has an 8 bit vertical resolution, and can sample at 10 nS/pt with no interlace. Each waveform contains 1024 points. Two charge and two potential waveforms are taken for each experimental test. The waveforms are taken in pairs, with one potential and one charge waveform per pair. The first pair uses a long measurement to capture the unrecoverable time segment. These waveforms are always 20 mS in duration. The second pair of collected waveforms are taken for a much shorter time. The duration of the measurement for these waveforms depends on the pulse width. For example, for a $100 \text{ }\mu\text{S}$ pulse, the measurement time might be $200 \text{ }\mu\text{S}$, while for a $500 \text{ }\mu\text{S}$ pulse the measurement time would probably be $1000 \text{ }\mu\text{S}$. Thus, 4 different waveforms, a long charge and potential pair, and a short charge and potential pair, are taken for each test pulse.

2.2.3 Electrochemical Cell

The electrochemical cell designed for these experiments is based on a standard three electrode configuration. A three electrode cell consists of a test or working electrode, a counter electrode, and a reference electrode. The current passes between the working and counter electrodes. The counter electrode is usually much larger than the working electrode so that the potential will change very little on this electrode. As a consequence, very few electrochemical reactions will occur on the counter electrode. The working electrode is the electrode being tested. The significant reactions should all occur on the working electrode.

The reference electrode maintains a stable electrochemical reference potential against which the potential of the working electrode can be compared. No current flows through the reference electrode.

In the cell used for these experiments, the working and counter electrodes are cylindrically oriented. This orientation provides uniform current distribution over the working electrode surface. The configuration was developed and shown to have uniform current distribution by Kasper (Kasper, 1940). A schematic drawing of our cell can be seen in Figure 2-3. The inner cylinder was the electrode wire, the outer cylinder was a ring of gold foil. The insulating endplates were provided by gas on one side, and a glass disk on the other. The wire was attached to the disk using an ultraviolet curing polymer (Hysol Globtop from Dexter). The insulating endplates each contained a small meniscus. Impedance measurements on gold electrodes in sulfuric acid showed the phase angle to be 87 degrees. This indicates that the effect of these menisci on the current distribution was small. The reference electrode tip was removed from the current path by sensing the potential from the top of the solution. The reference electrode was touched to the top of the solution, and lowered until the tip was just visible when sighting along the bottom of the solution meniscus. Thus, the reference electrode tip caused little disruption of the current. Sensing the potential from the top of the solution also reduced the stray capacitance that can occur between the reference electrode and both the working and counter electrodes (Cahan et al, 1972). The cell was made from glass. Nitrogen gas was bubbled through an electrolyte reservoir prior to passing it over the working electrolyte to avoid evaporation of the electrolyte. The effective area of the electrode was controlled by changing the height of the liquid in the dish. The liquid was typically 5mm deep, making the effective electrode area 0.04 cm^2 . All electrodes were of 0.25 mm diameter gold wires, 99.99% pure or better. The

Figure 2-3 - Cross Sectional Schematic of Electrochemical Cell

electrodes were sonicated in ethanol before use. The electrolyte is 0.1M H_2SO_4 (Ultrax from J.T.Baker) in ultra pure reverse osmosis distilled water.

The reference electrode was a charged palladium ($\alpha\text{-Pd/H}$) electrode. The palladium reference electrode was charged by creating hydrogen gas on the surface using a constant negative current. The diffusion of hydrogen into the metal lattice is called charging the electrode. The palladium reference electrode was charged with a current of -1 mA/cm^2 for 1 hour. This charging protocol created a reference electrode that drifted less than 10 mV/hr over a 6 to 12 hour period. A saturated calomel electrode (SCE) was connected to the palladium compartment via an electrolyte bridge (three way stopcock in Figure 2-3) for two reasons. As mentioned above, the reference electrode maintained a stable potential based on a reference electrochemical reaction. No such reference reaction occurs on the palladium electrode. Comparing the palladium and the SCE potentials connected the palladium electrode voltage to a known electrochemical reference potential. The SCE, also, provided a way to detect and correct for any slow drift in the palladium reference electrode potential. Once the potential drifted more than 50 mV the palladium electrode was recharged.

2.3 Instrument and Technique Verification

The development of any new technique requires validation and corroboration with existing methods. The major functions performed by the instrument and technique were to evaluate load capacity and recoverable charge. For this reason we will test the accuracy of load capacity measurements using electronic capacitors as loads. Further, we will measure the recoverable charge contained in the double layer, and compare these results with those of other well developed methods. The primary parameter used for these capacity

measurements was the virtual capacity. We will show that the instrument accurately evaluated both the electronic and double layer load capacities.

2.3.1 Electronic Load

An electronic load (shown in the inset of Figure 2-4) was used in this section to test the general instrument response versus frequency using impedance analysis. We used this method to examine resistor/capacitor networks. We compared the results with the actual load values. This was done with the instrument in the controlled potential (potentiostat) mode.

The instrument/load response to a small signal input is shown in the Bode plot in Figure 2-4. This plot was derived using a Solatron 1255 frequency analyzer to perform the impedance analysis. A 50 mV sinusoid output from the Solatron was electronically added to the clamp potential of the instrument. The Solatron evaluates the 0 and 90 degree phase response of the current and potential outputs over a broad frequency range. From these data, a Bode plot was drawn that shows the impedance and phase of the instrument/load response. In the Bode plot we know a horizontal line represents a purely resistive load, because resistance does not depend on frequency. A negatively sloped line shows a capacitive element dominates the impedance. This can be seen by the capacitor impedance equation $z=1/j\omega C$, in which z is the impedance, j is the square root of -1 , ω is the frequency in radians, and C is the capacity. From the figure we can see that a 260 ohm resistor dominates the response at low frequencies. At middle frequencies, a 2.5 μF capacitor is the primary element. At the highest frequencies, a different 10 ohm resistor dominates the behavior. From these data we could deduce the circuit shown in the inset of Figure 2-4. Thus, the instrument accurately evaluates the load response up to 10^5 Hz.

Figure 2-4 - Bode Plot for Response of electronic and electrochemical Load.

Electrochemical load is Gold, 0.15M Sulfuric, N2, 4 sq. mm.

The P-C method was then used to examine electronic loads. Electronic load capacities from 0.01 μF to 10 μF were tested. The measured capacities were taken directly from the virtual capacity parameter. To see the effect of instrument parameters on the measured load capacity, the IR correction, IR compensation, and clamp speed were all varied for each electronic load. Clamp speed, remember, is simply the time between when the potential was applied and when the potential became stable. The results of testing of the various electronic loads are shown in Figure 2-5. IR correction had the most effect. The effect was most pronounced with large capacitors, because they need larger charging and discharging currents than small capacitors to make the same potential change. Since IR correction is a current dependent potential, larger currents will cause larger errors when the correction is set improperly. The effects of clamp speed and IR compensation, as shown in the figure, are very small. These results indicate that the measurements of an unknown load capacity could be in error up to $\pm 20\%$ if the IR correction is off by ± 2 ohms. The IR correction of an electrochemical load, though, was easily set to within 1 ohm or less. Thus, the error of the electrochemical virtual capacity measurement will not exceed $\pm 10\%$.

2.3.2 Electrochemical Load

Impedance

The instrument was examined again, but this time using an electrochemical load. The test system response is shown in Figure 2-4. The electrochemical load was a gold electrode in 0.1M H_2SO_4 clamped at a potential of 0V versus the SCE under nitrogen atmosphere. This electrochemical system was completely capacitive for small potential disturbances around 0V SCE. Thus, the response to the 50 mV perturbation provided by the Solatron should be similar to that of a capacitor. This can be seen by the very linear

Figure 2-5 - Measurement of Electronic Capacitor Loads

response over the entire frequency ranges tested. Thus, the instrument provides no distortion of the measurement up to a frequency of 10^5 Hz.

Double Layer Measurements

The electrochemical load was then examined in detail using three different techniques. This was done to qualify the P-C technique. The first two methods were traditional electrochemical methods. They were the impedance technique used above, and the fast cyclic voltammetry technique. For a purely capacitive load, using the impedance technique, the load capacity can be determined by the impedance equation $Z=1/j\omega C$. Since Z can be measured, and ω is known, then C could be calculated. An example of the impedance measurement technique is shown in Figure 2-6.

The second traditional method used was fast cyclic voltammetry. In cyclic voltammetry the potential is controlled and swept linearly between two limit potentials. The result is a triangular potential waveform. The current flows in response to the electrochemical reactions that are occurring. In these experiments, the electrode potential was fixed at +0.2V versus the SCE. A 35 mV triangular wave was added to this steady state potential. The frequency was 5 kHz. Thus, the potential change versus time was 350V/S. The capacity of the electrode interface can then be determined from the equation $I=CdV/dT$. Here, I is the current, C is the capacity, V is the voltage, and T is time. We measured I and V over time, so C can be calculated as shown in Figure 2-7. Finally, the P-C method was applied. With the P-C method, the virtual capacity will be the same as the double layer capacity in this system. The electrode was clamped at a potential of 0.5V SCE, and pulsed with sufficient charge to achieve a 0.5V potential excursion. The virtual

Figure 2-6 - Example of double layer capacity measured by impedance.
Gold, 0.15M sulfuric acid, 4mm area, Nitrogen gas

Figure 2-7 - Double layer capacity measurement by fast cyclic voltammetry.

Gold, 0.15M sulfuric acid, 4mm area, Nitrogen gas. $C=i/(dV/dT)$

Vertical: 40 μA and 1.9 mV per major div. Horizontal: 17 μsec per major div.

capacity was then determined. The results for the P-C are plotted with the other two methods as shown in Figure 2-8.

The three methods agreed well as shown in Figure 2-8. The mean and standard deviation for each method on six electrodes are included in the left hand portion of the graph. For each method six tests were performed, each with a different electrode. Notice, that while the double layer capacity was similar for each method, none of the measured charge capacities matched the commonly accepted double layer capacity for gold in sulfuric acid. A literature study revealed that gold must be "electrochemically" cleaned to yield the value of $25 \mu\text{F}/(\text{real cm}^2)$ for the double layer capacity on gold (Laitinen & Chao, 1961). The real designation is included here to differentiate it from the geometric area used in the rest of this study.

We tested various cleaning procedures to find the best one for our system. Anodic cleaning has been shown to work well in the absence of chloride (Laitinen & Chao, 1961). However, phosphate buffered saline contains chloride, and that would corrode both the gold and platinum electrodes. Thus, cathodic cleaning procedures were also tested. The results are shown in Figure 2-9a. Both anodic and cathodic cleaning processes could achieve at least $25 \mu\text{F}/\text{cm}^2$ double layer capacity for some of the paradigms. Potentials that are very positive can create some surface alterations. The capacity becomes very large for the most positive cleaning potential at the longest time. In general, both cleaning methods required times in excess of 1 second to achieve sufficient cleaning. Another finding of this cleaning study was that the electrodes become recontaminated quite quickly (Figure 2-9b). They must therefore, be cleaned consistently throughout an experiment. The cleaning

Figure 2-8 - Double layer capacity measured by three methods.
Gold, 0.15M Sulfuric, N2, 4 sq. mm.

Figure 2-9 - Cleaning and recontamination.

Gold, 0.15M sulfuric acid, 4mm area, Nitrogen gas.

A) Cleaning: cleaned at designated potential for various times.

B) Rate of recontamination after clamping at 1.4V SCE for 1 minute.

procedure adopted for sulfuric acid electrolytes was to clamp the electrode at a potential of 1.2V SCE for at least one minute. Continuous cleaning was provided during the experimental run by clamping the electrode at a potential of 1.2V for 10 mS after each test pulse.

Once the cleaning procedure was perfected, the double layer charge capacity was again determined using the P-C and fast cyclic voltammetry methods. In this case the double layer charge capacity was determined at different potentials. This was done to see if the double layer capacity changed with potential as expected from the electrochemical literature. The experimental results are shown in Figure 2-10. Both curves agree with each other, and they change capacity as expected for polycrystalline gold surfaces (Bard, 1986). Thus, the P-C method mimics other methods in its examination of the electrode interfacial capacity and behavior.

2.4 Pulse Clamp Experiments

2.4.1 Electrochemical Load

Methods

The electrochemical application of the P-C method was on a gold electrode in 0.15M H_2SO_4 (ultrex, J. T. Baker) in ultrapure reverse osmosis distilled water under nitrogen. To start this experiment, the palladium electrode was charged, and the oxygen was removed from the electrolyte by bubbling nitrogen through the electrolyte reservoir. The working electrode, after being sonicated in ethanol and placed in the cell, was clamped to the initial clamp potential of -0.225V SCE. The pulse width was set to 100 μs , and the IR correction and IR compensation were set (see Appendix D). The charge necessary to perturb the electrode potential by 50 mV was used as the initial charge level. We set the

Figure 2-10 - Double layer vs. potential for fast CV and P-C.

Gold, 0.15M Sulfuric, N₂, 4 sq. mm., n=5

charge based on potential changes because the potential is an important factor in determining which reactions occur. It is important, therefore, to control the potential to which the electrode moved during the pulse. The charge and potential waveforms were recorded at this initial charge level. The charge level was increased such that the potential excursion during the pulse increased by 50 mV. The charge and potential waveforms were again recorded. This process was repeated up to a charge level of $-37 \mu\text{C}/\text{cm}^2$.

Interpretation of Collected Data and Results

When the gold electrode was pulsed with a constant current pulse, and then clamped back to the prestimulus potential, charge, current, and potential waveforms were generated. Typical experimental waveforms are shown in Figure 2-11. A 100 μS pulse is illustrated by the constant current between 20 and 120 μS . The potential during the constant current phase depends on the reactions occurring on the electrode. When the potential clamp is applied after 120 μS , a very large current spike ensues. In this simple system, the current passed during this step is entirely due to double layer charge. After a stable potential is achieved, some current still flows. The very small currents passing during the slow recoverable segment can be more easily seen by examining the slope of the charge waveform (Figure 2-11a).

The four categories of charge can be calculated from the collected waveforms shown in Figure 2-12. Total charge is defined as the amount of charge delivered during the stimulus pulse (point 5). Fast recoverable charge is charge returned 50 μS after application of the potential clamp (point 5 - point 6). Slow recoverable charge consists of that charge returned between 50 μS and 20 mS after application of the potential clamp (point 6 - point 8). Unrecoverable charge is charge that is not returned within 20 mS after application of the potential clamp (point 8). The ratio of the fast recoverable charge to the

Figure 2-11 - Charge, current, and potential waveforms for P-C experiment.
Gold, 0.15M sulfuric acid, 4mm area, Nitrogen gas.

Figure 2-12 - Collected waveforms for P-C experiments.

A) 20 mS waveforms, B) high resolution waveforms.

Gold, 0.15M sulfuric acid, 4mm area, Nitrogen gas.

potential excursion during the clamp is designated virtual capacitance. It is calculated from Figure 2-12 as $(\text{point 5} - \text{point 6})/(\text{point 2} - \text{point 3})$. Virtual capacity is a measure of the storage capacity of an electrode.

To examine the electrode response for a series of increasing charge density pulses, the four charge segments are graphed against the electrode potential at the end of the stimulus pulse. The four charge segments include the total charge, the fast recoverable charge, the slow recoverable charge, and the unrecoverable charge. These data are collected into plots we call charge-potential plots. These plots are how our final data will generally be presented. An example of the four charge and the potential measurements for a single test pulse are shown by the stars in Figure 2-13. The potential is plotted on the abscissa, to be consistent with the following electrochemical results.

Another way we will plot the data is to graph the percent of the total charge in fast recoverable, slow recoverable, and unrecoverable portions against the total charge. From the neurostimulation viewpoint the total injected charge is a key parameter, so the percent total charge graphical format displays electrode behavior in a more useful way for the prosthesis designer. Both the charge-potential plot and the percent charge plot will be used to present the experiments for this entire study.

Results

The charge-potential diagram in Figure 2-14a presents the data collected in this experiment. The slope of the fast recoverable charge is constant and indicates a capacity of $31 \mu\text{F}/\text{cm}^2$. The double layer process is very fast, and can easily operate within the fast recoverable time segment. The double layer capacity measured here is consistent with a

Figure 2-13 - Example of how a charge potential graph is generated from the collected waveforms.

Gold, 0.15M sulfuric acid, 4mm area, Nitrogen gas.

Fig 2-14 - A) Charge potential, B) Percent total charge graphs for gold in 0.15M sulfuric acid, N₂, 4 mm area, Mean of 5 Electrodes

capacity between 10-40 $\mu\text{F}/(\text{real cm}^2)$ with a surface roughness factor of 2 (Bard, 1986). The real area designation is used to differentiate it from the geometric area used in the rest of this study. Any electrode surface, when examined on the microscopic scale, will exhibit some roughness. This increases the real area of the electrode. The roughness factor for an electrode is determined from the ratio of the actual double layer capacity to the double layer capacity measured for a perfectly smooth electrode. The roughness factor generally falls between 1 and 2. Thus, a double layer capacity of 25 $\mu\text{F}/(\text{real cm}^2)$ translates to approximately 50 $\mu\text{F}/\text{cm}^2$ assuming a roughness factor of two. Since the double layer capacity depends on potential and the potential excursions are large during P-C experiments we will use 25 $\mu\text{F}/(\text{real cm}^2)$ as the double layer capacity, and assume a roughness factor of 2. There is a small amount of slow recoverable charge that is unaccounted for in the slow recoverable charge curve. In a clean system, such as this one, two main reactions are expected to occur. They are double layer charging and hydrogen gas (H_2) evolution. Double layer charging will be seen in the fast recoverable charge segment, and H_2 evolution will be seen in the unrecoverable charge segment. The largest amount of slow recoverable charge constitutes only 5% of the total charge so these processes are small contributors. Possible candidates for this slow process are sulphate adsorption, or hydrogen adsorption.

The unrecoverable charge curve indicates at what potential hydrogen evolution begins under these conditions. This is shown by the change in slope of the unrecoverable charge curve. It does not begin until potentials more negative than -0.6V SCE. This value can be compared with -0.325V measured by slow cyclic voltammetry. Thus, during these very fast pulses H_2 evolution does not begin until almost 300 mV negative of the value determined with slow cyclic voltammetry. The major differences between these gold electrodes, and ones in the body are the presence of chloride and a much higher pH.

Therefore, the increase in H_2 evolution potential observed in this experiment may likely be found for electrodes in the body. Using the P-C method to measure the processes occurring on the gold electrode, we find that significant H_2 evolution does not begin until potentials well negative of hydrogen evolution potential determined by slow cyclic voltammetry.

The fast, slow, and unrecoverable charge are all displayed as a percentage of the total injected charge in Figure 2-14b. This graph shows that over 90% of the total charge goes into fast recoverable processes at total charge magnitudes less than $-10 \mu C/cm^2$. After $-15 \mu C/cm^2$ of charge has been injected, the fast recoverable charge decreases while the unrecoverable charge increases. This is consistent with the hydrogen evolution beginning. The slow recoverable charge increases up to about 5% of the total charge at $-10 \mu C/cm^2$. It increases no further beyond this value.

The gold in sulfuric system has very few reactions. Double layer charging is the primary reaction at potentials more positive than $-0.325V$. Hydrogen evolution is the only process likely to occur at more negative potentials. The results from experiments on this system provide a baseline result against which other more complicated systems can be compared.

2.4.2 Electronic Load

Methods

The second application of the P-C method was on the electronic load shown in Figure 2-15. In this experiment, the clamp potential was 0V. The IR correction and compensation were set as shown in Appendix D, and the access resistance was around 10 ohms. The pulse width was set to 100 μS . The slow electronic was pulsed with the

Figure 2-15 - Circuit used in electronic load experiment.

minimum charge level. The charge and potential waveforms were recorded at this initial charge level of $-0.2 \mu\text{C}/\text{cm}^2$. The charge was then increased to $-0.4 \mu\text{C}/\text{cm}^2$, and the charge and potential waveforms were recorded. The process was repeated with the equal charge increments of $-0.2 \mu\text{C}/\text{cm}^2$ until the maximum charge level was injected. The load with no slow recoverable component was tested in the same manner. The initial charge level was $0.1 \mu\text{C}$, the charge increments were $0.1 \mu\text{C}$, and the maximum charge level was $1.5 \mu\text{C}$.

Results

The charge-potential graph for the electronic load is shown in Figure 2-16. The total charge and fast recoverable charge increase together up to -1.0V . At this potential, the slope of the total charge curve increases while the fast recoverable curve does not. Up to the change in slope of the total charge, only the capacitor and resistors are passing current. The size of the capacitor is shown by the slope of the fast recoverable curve, and is $0.94 \mu\text{F}$. After the slope changes, the diodes begin to conduct. We can also examine where the charge goes from the percent charge curves. Looking at the percent charge curves in Figure 2-16b, we see most of the charge is fast recoverable up to slightly less than $-1.0 \mu\text{C}$. Increased charge injection beyond $-1.0 \mu\text{C}$ goes primarily into unrecoverable charge as shown by the increase in slope of this curve. There is very little slow recoverable charge at any total charge level. This makes sense because no capacitor existed that could store slow recoverable charge.

The results shown in this chapter demonstrate the value of the P-C method in elucidating the electrochemical behavior of electrodes at very fast times. The method has been shown to accurately evaluate load capacity. Further, the proper response of resistor/capacitor/diode networks is found with the P-C technique. On gold electrodes, we

Figure 2-16 - A) Charge potential, B) Percent total charge graphs for electronic load in figure 2-15.

find that hydrogen evolution potential is more negative during stimulus pulses than predicted by slow cyclic voltammetry. In the next chapter we will use the P-C method to study the response to stimulation pulses of three different metals in a physiologic saline solution. We will also discuss the safe charge injection limits, and the most efficient reversal pulse to minimize unrecoverable charge.

3. Analysis of Three Metals Using the Pulse Clamp Method

3.1 Introduction

Using the P-C method, we observe the electrochemical behavior of electrodes when a typical neural stimulus pulse is applied. The processes occurring during the stimulus pulse can be resolved. Also, important operational parameters can be deduced from these resulting data. We can determine the maximum amount of charge that can be safely injected into the tissue. Also, the least damaging reversal pulse shape can be estimated. The electrode materials, gold, platinum, and stainless steel, will be tested in a physiological saline solution.

The processes occurring during typical neurostimulation pulses will be identified. From the slow cyclic voltammogram, we know the potentials at which the processes can occur. We generated slow cyclic voltammograms to find the exact potentials of the reactions in our system. Combining this information with the observed changes in the charge categories measured with the P-C technique, we can deduce which reactions are actually occurring during the stimulus pulse.

Assuming unreversed products are responsible for the observed tissue damage, a safe charge injection limit can be taken directly from the P-C results. The safe charge injection limit for this study is defined as the total charge at which $20 \mu\text{C}/\text{cm}^2$ unrecoverable charge is measured. Our $20 \mu\text{C}/\text{cm}^2$ limit is based on the monophasic

stimulation work Mortimer et al (1980). Since we can measure the unrecoverable charge, the safe total limits comes straight from the P-C results.

Using information about the current collected during the P-C reversal pulse, we can optimize the shape of the stimulation reversal pulse. It is commonly assumed that charge balanced biphasic stimulation is the best way to reverse the electrochemical processes. We can test the validity of this assumption. Since we are measuring the charge levels during the clamp portion, and because the clamp simulates a reversal pulse, we can deduce what reversal pulse will leave behind the least amount of unrecoverable charge. The unrecovered charge is a direct indication of unreversed electrochemical processes.

We examine three electrode metals platinum, and stainless steel 316LVM (SS316), and gold. The most common material used for stimulation electrodes is platinum. It has been found to be relatively inert, and has been widely used with few complications. It is also the most widely studied metal with a fairly large safe charge injection level. The main drawback is platinum's softness, and this eliminates its use in situations requiring high mechanical strength. By contrast, a material with high mechanical strength is SS316. SS316 is typically used in intramuscular stimulation applications (Mortimer, 1981). The electrochemical properties of this material are not well known, but, empirically, it has been found to be safe at moderate charge levels. Gold is not commonly used in electrodes as it has a very low safe charge injection level (Dymond, 1970). Gold is included in our work because it is a well understood system with few electrochemical reactions.

3.2 Cyclic Voltammetry

3.2.1 Methods

Slow cyclic voltammetry was briefly introduced in chapter 2. It was used to establish the hydrogen evolution potential using a known method. As slow cyclic voltammetry is an important part of this chapter it will be discussed in more detail here. The equipment and materials are the same as those outlined in the Pulse Clamp methods section (3.3.1). During slow cyclic voltammetry experiments the electrode potential was controlled, and the potential was swept slowly and linearly between 0V SCE and the hydrogen evolution potential. The current was measured during the potential sweep, and was a function of the reactions occurring. A cyclic voltammogram plots the measured current against the potential. An example showing how the cyclic voltammogram is generated is given in Figure 3-1. When a reaction begins, the current increases, either positively or negatively, depending on the nature of the reaction. This can be seen as peaks in the current curve.

Slow cyclic voltammetry tell us at what potential reactions occur. The nature of each reaction on the 3 metals has been determined by others through a variety of other electrochemical methods. It has been shown that the negative current on gold near -0.6V SCE is due to H_2 evolution. Similarly, the hydrogen adsorption reaction is associated with the two current peaks slightly more positive than the hydrogen evolution reaction. Thus, slow cyclic voltammetry provides information about which reactions can happen. Other factors such as diffusion or kinetics may change the reaction behavior under the high current conditions of typical neural stimulation pulses. Therefore, we can use slow cyclic

Figure 3-1 - Cyclic voltammogram of gold in sulfuric acid.
20 mV/S, 4mm area, N₂ gas, 0.05M sulfuric

voltammetry to predict which reactions can occur, but not necessarily which reactions do occur during stimulation pulses.

3.2.2 Results

A cyclic voltammogram for gold is given in Figure 3-2a. The H_2 evolution reaction is known to begin near $-0.659V$ SCE (CRC Handbook) at pH 7.0. This is shown on the plot by the negative current beginning peak at $-0.65V$. The chloride adsorption reaction is marked by the very rounded peaks near $-0.3V$. Double layer charging is always present whenever the electrode changes potential. The only way to measure the double layer capacity is in the absence of any other reaction. We will use the $50 \mu F/cm^2$ described earlier. The double layer charging current can be calculated from the equation $i=C(dV/dT)$, in which C is the double layer capacity, and dV/dT is the sweep rate. The double layer current for the gold cyclic voltammogram is $\pm 2.5 \mu A/cm^2$ calculated using the $50 \mu F/cm^2$ double layer capacity and a $0.05 V/S$ sweep rate. Thus, on gold, the three possible reactions are hydrogen evolution, chloride adsorption, and double layer charging.

The platinum cyclic voltammogram is shown in Figure 3-2b. The very large negative peak at $-0.65V$ represents the hydrogen evolution reaction. The two large current peaks at -0.4 and $-0.5V$ are known to be the hydrogen adsorption reaction. Chloride adsorption can only be determined by comparing the cyclic voltammogram in the presence and absence of chloride. This has been done by Bagotzky et al (1970), and chloride adsorption is known to occur between the potentials of $0.15V$ and $-0.6V$ SCE. As with gold, the double layer charging current occurs at all potentials. The double layer charging current can be determined from the double layer capacity ($50 \mu F/cm^2$) and the sweep rate ($0.05V/S$) as above, and is found to be $\pm 2.5 \mu A/cm^2$. The possible reactions occurring on a platinum

Figure 3-2 - Cyclic voltammograms for gold, platinum, and SS316.
50 mV/S, 0.3M phosphate buffered saline, N₂ gas, 4mm area

electrode pulsed from 0V are hydrogen evolution, hydrogen adsorption, chloride adsorption, and double layer charging.

The cyclic voltammogram for SS316 is shown in Figure 3-2c. The H_2 evolution reaction is shown by the large negative current around -0.8V. Like platinum, chloride adsorption cannot be determined from this graph. The double layer current can be calculated if we assume a double layer capacity of $50 \mu F/cm^2$. The resulting the double layer current is $2.5 \mu A/cm^2$ for this graph. The reaction occurring around -0.2V is oxide reduction.

3.3 Pulse Clamp

3.3.1 Methods

The P-C technique was applied to electrodes in a saline solution (For a complete description, see chapter 2). The 0.25 mm diameter wire electrodes were tested using typical neural stimulating pulses. The pulses were current controlled, and were 100 μS in duration. The charge was injected, as in chapter 2, to achieve potential excursions that were integer multiples of -50mV. The charge injections were varied from $1 \mu C/cm^2$ up to $175 \mu C/cm^2$. The pulse was then followed by a potential clamp that returned the electrode to its' prestimulus potential. No delay was imposed between the stimulus pulse and application of the potential clamp. The electrolyte used was 0.3M NaCl with 30 mM phosphate buffer in ultrapure reverse osmosis distilled water. This was chosen to simulate the extracellular body fluid. The atmosphere was 100% ultrapure nitrogen. The electrodes were sonicated in ethanol and rinsed in ultrapure water prior to use. The electrodes were not electrochemically cleaned to simulate an electrode starting from rest in the body.

The cell diameter was reduced from 3 cm. to 1 cm. for only the experiments in this chapter. The instrument was not stable during the potential clamp using 0.15M NaCl. It was found that increasing the electrolyte conductivity solved this problem. However, it was desirable to keep the electrolyte similar to that of the human body, so we reduced the cell diameter. The radial symmetry of the cell makes the solution resistance a function of the natural log of the cell radius ($\text{Resistance} = \int (\rho \cdot dr / 2 \cdot \pi \cdot r \cdot h)$) Here, ρ is the conductivity, dr is the incremental radius, r is the radius, and h is the height. The solution resistance is reduced by a factor of 1.37 by reducing the cell diameter from 3 cm. to 1 cm. Changing the diameter, though, does not effect the interfacial ohmic drop that turned out to be the primary problem. The stability was not improved, and the instrument remained unstable during the clamp at high charge densities. Therefore, the sodium chloride concentration we used (0.3M) was actually higher than that in the body. However, comparison of the results from tests that used the actual body concentration to those using up to 1M NaCl, showed no qualitative or quantitative difference in the charge-potential diagrams. The increased conductivity provided by the higher concentration of the electrolyte improved the stability during the very rapid clamp.

All of the electrodes were pulsed from an initial potential near 0V SCE. Additionally, both platinum and SS316 were pulsed from an initial potential of -0.5V. With these two metals, it was not possible to detect any amount of unrecovered charge when they were pulsed from a neutral potential. By offsetting the value to -0.5V, the unrecoverable charge could be detected. The potential of an implanted electrode can fluctuate, so our offset is within the actual operational parameters of a stimulating electrode. The offset value was chosen to be close to the hydrogen evolution potential as determined by slow cyclic voltammetry for platinum, about -0.65V SCE.

3.3.2 Results

An example of the electrode response to a single pulse is shown for each metal in Figure 3-3. The electrode potential, fast recoverable charge, slow recoverable charge, and unrecoverable charge are derived as shown in the figure (see chapter 2 also). The charge, current, and potential for each metal are shown on these graphs. The upper plot is the charge measured during the pulse and clamp. Notice how the charge returned is similar for SS316 and platinum, but smaller for gold. The middle plot shows the current waveform. The first portion is the controlled current or stimulus pulse. It is followed by a large current spike during the potential clamp. The spike contains a majority of the injected charge indicating most of the charge was stored or transferred using very fast reversible processes. The bottom plot is the electrode potential. The potential is governed by the electrochemical processes during the controlled current pulse, and it is constant during the potential clamp.

Gold

The gold electrode was found to always display a cleaning phenomenon during the first experimental run. This is shown by the change in slope of both the fast recoverable, and the slow recoverable charge curves around a potential of -1.0V in Figure 3-4a. The cleaning phenomenon involves no unrecoverable charge. This is shown by a lack of change in slope of the unrecoverable charge curve around the potential at which the cleaning process occurs. After $175 \mu\text{C}/\text{cm}^2$ of charge was applied, the behavior of the electrode changed, as shown by the return curve in Figure 3-4a. When the same experiment was immediately repeated in Figure 3-4b, the cleaning phenomenon was no longer displayed. The curve became linear out to a potential of -1.5V. The unrecoverable charge behavior

Figure 3-3 - Charge, current, and potential waveforms.
Gold, platinum, SS316 in 0.3M PBS under nitrogen.

Figure 3-4 - Charge, current and potential waveforms.
Gold, 0.3M phosphate buffered saline, 4mm area, Nitrogen gas.
A) Contaminated (First Run), B) Clean (Second Run)

was identical for the contaminated gold electrode and the clean gold electrode. The platinum and SS316 electrodes, as will be shown, did not display this behavior.

For a clean gold electrode, the electrode potential at which hydrogen evolution began could be determined from the charge-potential plot. The hydrogen evolution potential, as determined by slow cyclic voltammetry for a clean gold electrode, was about -0.65V SCE. The electrode potential when hydrogen evolution was detected by the P-C clamp method was about -1.6V SCE. This is read from the figure by locating the increase in the slope of the unrecoverable charge curve. Notice that hydrogen evolution did not begin until $120\text{ }\mu\text{C}/\text{cm}^2$ of charge had been injected. Thus, hydrogen evolution was not found during P-C stimulus pulses until the electrode potential was over 900 mV more negative than that predicted by slow cyclic voltammetry. Recalling the results presented in chapter 2, the electrode potential when hydrogen evolution was detected in the acid electrolyte was also more negative for P-C stimulus pulses than for slow cyclic voltammetry. The difference was specifically 900 mV more negative in saline and 300 mV more negative in acid.

The virtual capacity can also be determined from these data. Recall that we have defined the virtual capacity as the ratio of the fast recoverable charge to the magnitude of the potential step during the clamp. The ability to store charge in fast processes is a characteristic we wish to maximize for reversible charge injection on neural stimulating electrodes. A change in virtual capacity may indicate the gain or loss of a process in the fast recoverable charge segment. The virtual capacity for a contaminated gold electrode changes with electrode potential at the end of the pulse. A virtual capacity of $59\text{ }\mu\text{F}/\text{cm}^2$ was determined from the mean fast recoverable curve of the clean gold electrodes over the range 0V and -1.5V .

The relative proportions of charge stored by processes during the pulse can be found by examining the percent of charge in fast recoverable, slow recoverable, and unrecoverable charge portions. The percentages will be compared when $20 \mu\text{C}/\text{cm}^2$ of unrecoverable charge has been detected for each electrode. The $20 \mu\text{C}/\text{cm}^2$ limit was chosen as it is the maximum charge density that can be injected during monophasic stimulation with no tissue damage to muscle (Mortimer et al, 1980). When $20 \mu\text{C}/\text{cm}^2$ of unrecoverable charge had been detected on a contaminated gold electrode the fast recoverable portion stored 69% of the total charge. On a clean gold electrode the fast recoverable portion stored 79% of the total charge. Thus, the majority of charge was found in the fast recoverable charge segment.

Platinum

Platinum is known to have a more complex system of processes that can store charge during a pulse. The hydrogen evolution potential determined by slow cyclic voltammetry was about -0.65V SCE. The results of the P-C experiments on platinum are shown in Figure 3-5. In the top plot, a platinum electrode pulsed cathodically from a potential near 0V SCE showed no unrecoverable charge up to $150 \mu\text{C}/\text{cm}^2$ of total charge. While, each electrode was subjected to charges up to $175 \mu\text{C}/\text{cm}^2$, the way the experiment was run made it impossible to average the results above $150 \mu\text{C}/\text{cm}^2$ of total charge. Since no unrecoverable charge was detected, the hydrogen evolution potential during pulses from 0V cannot be determined from these data. In the bottom plot, unrecoverable charge was detected at a potential of approximately -1.25V on a platinum electrode pulsed from a potential of -0.5V . We assume the presence of unrecoverable charge indicates the occurrence of H_2 evolution. Comparing -1.25V with that from slow cyclic voltammetry

Figure 3-5 - Charge, current and potential waveforms.
Platinum, 0.3M phosphate buffered saline, 4mm area, Nitrogen gas.
A) 0V clamp potential, B) -0.5V clamp potential

measurements, we see the electrode potential when hydrogen evolution is detected during a neural stimulus pulse is 0.6V more negative than that determined with slow cyclic voltammetry. This means the hydrogen evolution potential determined by slow cyclic voltammetry underestimates the potential at which hydrogen evolution occurs during a typical stimulus pulse.

The virtual capacity at -1.0V on a platinum electrode pulsed from 0V was about 100 $\mu\text{F}/\text{cm}^2$. When the electrode was pulsed from -0.5V, the virtual capacity at -1.0V was reduced to 52 $\mu\text{F}/\text{cm}^2$. Thus, some fast process that stored charge during pulses from the more positive clamp potential was lost when the electrode was pulsed from more negative potentials.

When platinum was pulsed from 0V SCE, the charge consuming reactions were found to be dominated by fast recoverable processes. At the maximum charge injection from 0V, we found 65% of the charge was fast recoverable and 35% was slow recoverable. Unrecoverable charge could not be detected. When the electrode was pulsed from a potential of -0.5V, 35% of the injected charge was fast recoverable while 52% was slow recoverable when 20 $\mu\text{C}/\text{cm}^2$ of unrecoverable charge was measured. Thus, during pulses from a clamp potential of 0V, most of the injected charge is fast recoverable, while during pulses from a clamp potential of -0.5V SCE, slow recoverable processes store most of the injected charge.

Stainless Steel 316LVM

SS316 displayed a response more like platinum, than like gold. The hydrogen evolution potential determined by slow cyclic voltammetry for SS316 was approximately

-0.8V SCE. The results for P-C experiments on SS316 are shown in Figure 3-6. A SS316 electrode pulsed from a potential of 0V SCE displayed no unrecoverable charge over the range studied. Therefore, the hydrogen evolution potential for short duration high current density pulses must be more negative than -1.2V SCE. A SS316 electrode pulsed from -0.5V SCE displayed some unrecoverable charge. Assuming the unrecoverable charge measurement represents H_2 evolution, the potential for hydrogen evolution determined by the P-C method was approximately -1.6V. Thus, during P-C stimulus pulses, the hydrogen evolution potential moves 800 mV more negative of the hydrogen evolution potential as determined by slow cyclic voltammetry.

The virtual capacity at -1.0V of a SS316 electrode pulsed from 0V was 178 $\mu F/cm^2$. The virtual capacity at -1.0V reduced to 39 $\mu F/cm^2$ when the same electrode was pulsed from a potential of -0.5V SCE. As for platinum, some fast charge consuming process occurring near 0V SCE was lost when the electrode was pulsed from a potential of -0.5V SCE. For SS316, though, the virtual capacity changed by a factor of four, instead of the factor of two for platinum.

From the charge-potential plots, we can find that SS316 electrodes pulsed from 0V displayed no unrecoverable charge over the range studied. This was also found for platinum electrodes. The total charge from 0V was divided between fast recoverable and slow recoverable charge. The fast recoverable processes stored 78% of the charge and the slow recoverable processes stored 22% of the charge when 150 $\mu C/cm^2$ of total charge was injected. When the SS316 electrode was pulsed from -0.5V SCE, unrecoverable charge was detected. When 20 $\mu C/cm^2$ of unrecoverable charge was detected, 58% of the charge was fast recoverable, while 21% of the charge was slow recoverable. The unrecoverable charge

Figure 3-6 - Charge, current and potential waveforms.
SS316, 0.3M phosphate buffered saline, 4mm area, Nitrogen gas.
A) 0V clamp potential, B) -0.5V clamp potential

observed during pulses from the more negative clamp potential apparently replaced the fast recoverable charge observed during pulses from the more positive clamp potential. This is because the percent of slow recoverable charge was very similar during pulses from the two clamp potentials. This observation reinforces the finding using virtual capacity that a fast recoverable process was lost by pulsing the electrode from a more negative potential.

3.4 Discussion

From the test results on gold, platinum, and SS316, we conclude that during a typical stimulating pulse, most of injected charge was accommodated by rapidly reversible processes. This is because most of the injected charge was recovered in the fast recoverable portion. Comparing Figures 3-3b, 3-4a, and 3-5a, we find that 88% of the injected charge is rapidly reversed for the "clean" gold electrode (-1.5V Figure 3-3b), 75% for the platinum electrode (-1.25V SCE Figure 3-4a), and 78% for the SS316 electrode (-1V SCE Figure 3-5a). Even when sufficient charge was injected to detect unrecoverable charge on gold and SS316, the majority of charge was still fast recoverable. On platinum, by contrast, when sufficient charge was injected to detect unrecoverable charge most of the charge was recovered in the slow recoverable portion. The important point is that even at potentials far negative of hydrogen evolution potential as determined by slow cyclic voltammetry, we measured no unrecoverable charge on any of the metals.

Three topics will be covered using the results. First, the electrochemical processes that occur during stimulation will be discussed. Processes will be categorized based on the known relative rates of the reactions, and the charge measured in the three charge segments. The safe charge injection limits will be covered next. These can be interpreted directly from the data. Lastly, the optimal reversal pulse will be examined. These are

derived using the information we have gained about the processes occurring during the pulse and the currents measured when the potential clamp is applied.

3.4.1 Processes Occurring During Stimulation

Studying both the cyclic voltammograms and the P-C results, we can begin to understand the processes that occurred during these neural stimulation pulses. The charge-potential graphs tell us at what potential or charge changes occur in the electrochemical processes storing the charge. This determination can be based on changes in the slopes of the four charge curves. For example, if the slope of the recoverable charge curve increases, then a new reaction has likely begun. Similarly, a decrease in the fast recoverable curve matched by an increase in the unrecoverable curve would indicate a fast process was being replaced by an irreversible process.

From the P-C data for clean gold, only two principle processes appeared to be occurring. This is shown by the very large percentage of fast recoverable charge over the entire charge injection range, and the increase in unrecoverable charge around -1.5V. The slope of the fast recoverable charge curve is $59 \mu\text{F}/\text{cm}^2$. This is close to our assumed double layer capacity of $50 \mu\text{F}/\text{cm}^2$, so this process is likely double layer charging. The total charge curve slope increases at potentials more negative than -1.5V, indicating the inclusion of a new reaction. The new reaction, though, must be an unrecoverable process. This is because the unrecoverable curve also changes slope at the same potential. Since we know H_2 evolution is irreversible on gold, this reaction must be H_2 evolution. The only other possible process is chloride desorption. Since double layer charging is very fast, and H_2 is irreversible, the chloride desorption/adsorption process must account for the observed slow recoverable charge. It is unlikely that the slow recoverable charge is part of the H_2

evolution process because hydrogen adsorbs very slightly on gold, and H_2 oxidation on gold is an extremely slow process (Brug et al, 1984).

The processes that can occur on platinum are the same as for gold, but with the addition of hydrogen adsorption. Pulsing a platinum electrode from 0V, the primary charge storing processes are fast, and unrecoverable processes store no charge at all. The double layer charge is found in the fast recoverable portion. However, the virtual capacity of over $100 \mu F/cm^2$ is too large to be accounted for by double layer charging alone. The only other process known to be very fast is hydrogen adsorption. Thus, the extra charge in the fast recoverable portion is likely hydrogen adsorption. The increase in virtual capacity with increasing charge injection, though, indicates that the fast processes can store more charge as more charge is injected. This could be explained by the hydrogen adsorption process by its nonlinear behavior with respect to potential. The inclusion of such a large capacity process will slow down the potential change, and make the virtual capacity increase. The slope of the slow recoverable charge curve also increases with increasing total charge. This may show three things. First, two processes, one fast and one slow, may be involved. Secondly, there may be a single process and the reversal time falls somewhere near the 50 μS fast recoverable time limit. Thirdly, the increasing quantity of slow recoverable charge may indicate that the reversal process is diffusion related. The more product that is generated, the longer it takes to reverse it.

Pulsing the platinum electrode from the more negative clamp potential of -0.5V alters the observed behavior. The proportions of fast recoverable and slow recoverable charge are similar to pulses from 0V, but as the injected charge increases the fast recoverable charge decreases and the unrecoverable charge increases. The unrecoverable

reaction should be hydrogen evolution, as some H_2 should be lost through diffusion. However, on platinum the evolved H_2 can be reoxidized during the reversal pulse. Thus, some of the slow recoverable charge from this potential is likely reoxidization of evolved H_2 . The virtual capacity is also much smaller during pulses from -0.5V. This indicates that the hydrogen adsorption process contributing to the fast recoverable charge is no longer participating in the stimulus pulse. The size of the virtual capacity ($52 \mu\text{F}/\text{cm}^2$) during pulses from the more negative clamp potential is consistent with the charge being entirely double layer charging.

When the SS316 electrodes were pulsed from 0V, the majority of the charge went into fast recoverable processes. The large and constant virtual capacity may indicate that the same process occurred over the total charge injection range. The constant virtual capacity could also mean that the reversal of this process was very rapid with respect to the clamp time. Regardless of how much product was created, it was reversed in the 50 μs fast recoverable time division. As with platinum, though, the charge associated with this process is too large to consist solely of double layer charging. The virtual capacity of $178 \mu\text{F}/\text{cm}^2$ is more than 3 times the size of the typical double layer process. It is possible the process is oxide reduction. From the cyclic voltammogram a cathodic process that is likely oxide reduction begins near -0.2V SCE and is completed by -0.4V SCE. When the electrode was pulsed from -0.5V, the processes changed dramatically. First the virtual capacity dropped from $178 \mu\text{F}/\text{cm}^2$ to $39 \mu\text{F}/\text{cm}^2$. This shows that the fast process consuming charge during pulses from the 0V clamp potential no longer participated during pulses from -0.5V. The virtual capacity ($39 \mu\text{F}/\text{cm}^2$) can now be explained by double layer charging. Also, the presence of unrecoverable charge during pulses from the more negative clamp potential indicates the consumption of charge by a new reaction. This reaction is

likely H_2 evolution. Thus, the processes have been categorized based on the relative rates of the reactions, and the charge measured in each of the three charge segments.

3.4.2 Safe Charge Injection Limits

From our P-C experimental results, we also have the information necessary to estimate the safe charge injection limits for electrochemically induced tissue damage. These limits can be determined assuming that a threshold level of electrochemical products is responsible for the observed damage. The presence of these products can be detected by the measurement of unrecoverable charge. The $20 \mu C/cm^2$ unrecovered charge limit gives an indication of the level of unrecovered charge that can be supported by the body. Mortimer et al (1980) determined that 0.2 mA/mm^2 was the maximum cathodic monophasic stimulation current that could be used during $100 \mu S$ pulses without observing tissue damage in vivo. This corresponds to a charge injection of $20 \mu C/cm^2$. Although our stimulation was not monophasic, we can use their result because monophasic stimulation has no reversal pulse, and passes all of the injected charge irreversibly. The $20 \mu C/cm^2$ charge limit derived from Mortimer's monophasic stimulation study gives a lower limit on the amount of unrecoverable charge that can be safely injected. The tissue can likely accommodate this amount of unrecoverable charge with no ill effects. A safe charge injection limit can then be defined as the minimum total charge at which $20 \mu C/cm^2$ unrecoverable charge is detected.

To determine the safe charge injection limits of the three metals, the amount of charge each metal could inject before the unrecoverable charge reached $20 \mu C/cm^2$ was determined. In table 3-1 the amount of charge in each charge segment is tabulated for the unrecoverable charge level of $20 \mu C/cm^2$. We found that platinum and SS316 electrodes

Table 3-1 - Comparisons of Safe Charge Injection Limits on Au, Pt, and SS316											
Type of Charge	Metal										
	Gold ("clean")				Platinum				SS316 LVM		
	From -0.5V		From 0V		From -0.5V		From 0V		From -0.5V		From 0V
	Charge		% Total		Charge		% Total		Charge		% Total
	Total										
Total	86		147		155		>150		95		>150
Fast Recoverable	65	76	118	80	54	35	NA		55	58	NA
Slow Recoverable	1	1	9	6	81	52	NA		20	21	NA
Unrecoverable	20	23	20	14	20	13	0		20	21	0

Table of charges when the unrecoverable charge was 20 $\mu\text{C}/\text{sq.cm}$.
 No unrecoverable charge was measured on the platinum and SS316 electrodes up to 150 $\mu\text{C}/\text{sq.cm}$.

Thus, these values are not included in this table because the limit was not measured.

The 20 $\mu\text{C}/\text{sq.cm}$. safe limit is based on the measurements of tissue damage using monophasic stimulation.

could accommodate all of the $150 \mu\text{C}/\text{cm}^2$ total charge during pulses from 0V SCE, with no unrecoverable charge. The lack of unrecoverable charge indicates that both platinum and SS316 have a safe charge injection limit in excess of $150 \mu\text{C}/\text{cm}^2$ of total charge when pulsed from 0V. The unrecoverable charge limit may well be much higher. When these two metals were pulsed from a potential of -0.5V SCE, platinum was found to inject a total charge of $155 \mu\text{C}/\text{cm}^2$, and SS316 a total charge of $95 \mu\text{C}/\text{cm}^2$, before the unrecoverable charge limit was reached. Gold, when pulsed from a clamp potential near 0V SCE, was found to accommodate a total charge of $147 \mu\text{C}/\text{cm}^2$ when $20 \mu\text{C}/\text{cm}^2$ of unrecoverable charge was detected. Gold is different from the other two metals, because the $20 \mu\text{C}/\text{cm}^2$ unrecoverable charge limit could be reached during pulses the 0V clamp potential.

The fact that no unrecoverable charge was detected at the hydrogen evolution potential as determined by slow cyclic voltammetry, indicates that the safe charge injection limits may be larger than previously indicated. Determining the safe charge injection limits of neural stimulating electrodes has been a subject of research for many years. Some limits of safe charge injection have been set using the hydrogen evolution potential as determined by slow cyclic voltammetry (Robblee et al, 1984). Our measurements indicate the hydrogen evolution potential as determined by slow cyclic voltammetry can be exceeded by almost 1V on gold electrodes without detecting unrecoverable charge. Brummer, using low current stimulus pulses originally stated that a clean platinum electrode could store $300\text{-}350 \mu\text{C}/\text{cm}^2$ of charge (Brummer & Turner, 1977c). Robblee derived a safe charge limit of $74 \mu\text{C}/\text{cm}^2$ using typical stimulus pulses, and by measuring the charge when the electrode the potential reached the hydrogen evolution potential as determined by slow cyclic voltammetry (Robblee et al, 1986). The authors of both previous papers acknowledged an error due to the lack of kinetic considerations, but no method was available to show at what potential

unrecoverable processes started consuming charge. This study, using the P-C method, is able to estimate the proportions of recoverable and unrecoverable charge. These data suggest a limit of safe charge injection in excess of $150 \mu\text{C}/\text{cm}^2$ for platinum and SS316, and a limit of $150 \mu\text{C}/\text{cm}^2$ for gold electrodes. These data give likely safe charge injection limits based on the measurement of generated unrecoverable charge. Safe charge injection limits are often determined by potential measurements. Our results more likely reflect the actual safe charge injection limits for these materials under uniform current conditions, based on the direct measurement of unreversed electrochemical products.

3.4.3 Optimal Reversal Pulse Shapes

Observations can also be made about the optimal stimulation waveform from these experimental data. Specifically, we can address what the secondary pulse or reversing pulse should look like. We believe the standard charge balanced biphasic stimulation waveform may not be the optimal waveform. By optimal, we mean the best waveform to reverse electrochemical products while avoiding electrode corrosion. Lilly designed his waveform to reverse the "displacement by ionic current of charged particles (ions, enzymes, proteins, and so forth) from their key positions within and around the neurons" (Lilly et al, 1955). This is a very different issue than reversing electrochemically generated products. Thus, the pulse used to reverse the electrochemistry will likely differ from the one used to return the charged molecules to their key locations. The use of the controlled current biphasic stimulus waveform, though, is based on the Lilly waveform. We believe a pulse that mimics the potential clamp will minimize electrochemically induced tissue damage. Since potential is the driving force behind reaction occurrence, returning the electrode potential to its prestimulus value will avoid the creation of additional products.

The reversing pulse should rapidly return the electrode potential to its prestimulus value, in order to avoid continuation of the processes occurring during the stimulation pulse. Once this potential has been achieved, the reversal pulse should return the charge at a rate consistent with that of the processes being reversed. Lets consider three waveforms that illustrate important parameters of the reversal pulse. Our three suggested waveforms and the a typical controlled current biphasic stimulus waveform are shown in Figure 3-7. The general form of the reversal pulses was derived from the current waveforms observed during the P-C experiments. The reversing current for all three electrode materials during the potential clamp was a large spike, followed by a variable amount of current depending on the rate of charge recovery. The first situation we will consider is when the primary process occurring during the stimulus pulse is the double layer charging process. The best reversing pulse under these conditions would be a very large current spike that contained all the injected charge. This is because the double layer charging process can be reversed both completely and very rapidly. Failure to return the electrode potential rapidly to its prestimulus potential, though, may result in the occurrence of irreversible reactions. This is because even though only double layer charging occurred during the stimulus pulse, the electrode potential at the end of the pulse would be negative enough to evolve H_2 given sufficient time. An example of an electrode dominated by this process is a gold electrode with a total charge less than $100 \mu C/cm^2$. A different reversal pulse must be considered if the processes occurring during the stimulus pulse are completely, but not rapidly, reversible. The initial current spike would be necessary to return the electrode to its prestimulus value. The charge in this current spike should only be the charge associated with the double layer. The charge going into the more slowly reversed processes should not be returned as quickly. The studies on platinum show that a large current spike followed by an exponentially decaying current would be ideal for this material. The slow recoverable

Figure 3-7 - Comparison of reversal pulses.

charge cannot be reversed rapidly, and so the reversal pulse should not attempt to restore the charge faster than the processes will allow. Doing so will force the electrode potential more positive than the prestimulus value, and may result in corrosion. While Lan et al (1989) showed that the pitting potential can be exceeded for short times with no corrosion, the potential will not be forced back to the prestimulus value at the end of a biphasic current pulse. Thus, the electrode potential could exceed the corrosion potential for sufficient time to corrode the electrode. The platinum electrodes in this study showed a significant amount of slow recoverable charge, especially with large total charges. In both of these cases, all the charge is recoverable. Therefore, the quantity of charge in the reversal pulse must equal the amount of injected charge.

If some of the injected charge is unrecoverable, then a third type of reversal pulse should be used. In this case, the optimal reversing pulse would contain less charge than the total injected charge. If the injected and recovered charge is balanced, as in the previous waveforms, the electrode potential will be driven to more positive potentials at the end of the reversal pulse. This can result in electrode corrosion. The charge lost electrochemically during the cathodic or stimulating phase will be forced into anodic processes that occur at the more positive potentials. Complete electrochemical balance is rarely achieved in typical neurostimulation paradigms. The reversal charge should, therefore, be less than the stimulus charge.

3.5 Summary

The experiments presented in this chapter show the importance of kinetic considerations, and the value of the P-C method in understanding the electrochemical processes occurring during a typical stimulus pulse. The electrode potentials associated with

H_2 evolution during typical neural stimulation pulses are much more negative than those expected from slow cyclic voltammetry. The three metals studied display similar behavior during rapid pulsing. This work also begins to examine how the processes store charge during a typical neurostimulation pulse. Some processes appear to go fast enough to participate in the stimulus pulse, and be reversed within the 50 μ S fast recoverable charge time. Examples include double layer charging on all three materials, hydrogen adsorption on platinum, and oxide reduction on SS316. Other reactions, such as chloride desorption, go more slowly or not at all. The safe charge injection limit has been found to be larger than that determined with other methods that do not actually measure the charge. The rate of charge recovery and the presence of unrecoverable charge also effect the shape of the ideal reversal pulse. In general, the reversal pulse should contain a large current spike followed by an exponentially decaying current. The latter current should be matched to the rate and amount of recovered charge. These data establish how an electrode will behave starting from a set potential. Electrode behavior during continuous pulsing may differ. In chapter 4 we will further study the electrochemical behavior by varying the stimulus pulse parameters. Specifically, we will examine the effect on the recoverable charge of varying both the duration of the pulse and the time delay before the potential clamp is applied. We will then relate the experimental results to a proposed electrical analog model.

4. Comparison of An Analog Model With Observed Electrode Behavior For Changes in Stimulation Parameters

4.1 Introduction

An electrical analog model is proposed that describes the electrode response to variations in stimulation parameters. The projected model is compared using two different sets of experiments. In previous experiments, the clamp potential was constant, and the clamp was always applied immediately after the stimulus pulse. In the first set of experiments, the clamp potential is varied for gold electrodes in sulfuric acid. This allows us to compare a simple system, with a simple analog model.

In the second set of experiments we use a more complex electrolyte, and include the more electrochemically complex metal, platinum, in addition to gold. In these experiments, the pulse width and delay are varied independently on electrodes in phosphate buffered saline. These experiments test electrode behavior under more physiological conditions. Stainless steel is not included because of its more complex electrochemistry. These experiments also relate to neural prosthesis function in a number of ways. Many prostheses vary the length of the stimulus pulse to change to level of stimulation. Pulses can be as short as 10 μS , or as long as 200 μS . Also, it has been found that when a time delay is imposed between the stimulus and the reversal pulses, smaller stimulus pulses are sometimes needed (Mortimer, 1981). Thus, stimulation may be more efficient with a period of no current flow imposed between the stimulus and reversal pulses. Again, the experimental results will be compared with the projected behavior of the model to tell us how closely the model mimics the observed electrode behavior.

To perform the set of pulse width and delay experiments, the instrumentation was improved. First, the charge injection level was increased four times. We can now inject up to $-12\ \mu\text{C}$ ($-300\ \mu\text{C}/\text{cm}^2$ with $0.04\ \text{cm}^2$ electrodes) of charge during a $50\ \mu\text{S}$ pulse in our system. Also, the fast recoverable time division was reduced from $50\ \mu\text{S}$ to $15\ \mu\text{S}$. The time division was shortened in an attempt to minimize reactions, other than double layer charging, that occur in the fast recoverable segment. With these modifications to the instrument will also help to more accurately elucidate the reactions that are consuming charge on gold and platinum electrodes in chapter 5.

4.2 Presentation of Analog Model

The experimental work presented in this chapter was conducted to see how well our proposed analog model would match the observed electrode behavior. A predictive analog model is desirable to test hypotheses about system functions. The model presented in this section is the first step toward that goal. We have attempted to create a model that mimics the behavior observed for the electrodes under study. This model may not predict electrode behavior under other conditions.

Using three time divisions, fast recoverable, slow recoverable, and unrecoverable, leads to the generation of a three compartment model. A diagram is shown in Figure 4-1. The two recoverable charge divisions must include a capacitor element. The capacitor reflects the electrochemical ability to store and return charge. Referring to Figure 4-1, the fast recoverable charge is stored in C_{DL} , and the slow recoverable charge is stored in C_2 . The slow recoverable compartment also has a resistor associated with it to control the rate of charge storage and recovery. This component is designated transmission element T_2 . The

Figure 4-1 - Proposed analog model to simulate electrode behavior.

C_{DL} is the double layer capacitor.

C_2 is the slow recoverable capacity.

T_1 is the unrecoverable transmission path.

Its conductance depends on the potential of C_2 .

T_2 is the component determining the charge and discharge rate of C_2 .

unrecoverable charge must pass through a resistive pathway. This component is designated transmission element T_1 . The conductance of this element is a function of the potential on C_2 . The current potential characteristics of T_1 could be described by the Butler-Volmer equation. This equation describes the general current potential characteristics of electrochemical reactions. Using the concept of this model we can then see if it behaves in a similar fashion to the electrodes tested in these experiments.

4.3 Variable Clamp Potential in Sulfuric Acid

4.3.1 Experimental Methods

In this set of P-C experiments on gold electrodes, the clamp potential was varied after the pulse. The prestimulus and post stimulus clamp potential were no longer equal. The post stimulus clamp potential lasted for 20 mS after the beginning of the stimulus. The electrode potential was returned to the prestimulus value after 20 mS. The electrode prestimulus potential was clamped at 0.175V SCE. The rest of the methods followed those described in chapter 2.

Five different charge injection levels were used. Each charge level was chosen to achieve a particular electrode potential at the end of the pulse. The potentials were -0.025, -0.225, -0.425, -0.625, and -0.775V SCE. The most negative potential was chosen to exceed the P-C hydrogen evolution potential from chapter 2 of -0.65V SCE. The corresponding charge levels were -14, -25, -43, -56, and 63 $\mu\text{C}/\text{cm}^2$. For each charge injection level, the post stimulus clamp potential was varied in 50 mV increments. The initial post stimulus clamp potential was set 50 mV more positive than the electrode potential at the end of the stimulus pulse. The post stimulus clamp potential for each successive test was increased by 50 mV increments until it matched prestimulus clamp potential. The sequence was repeated

for each of the 5 total charge levels. Pulses achieving more negative potentials required more tests to reach the prestimulus clamp potential. The average current during the clamp was calculated as the slow recoverable charge divided by the time of the slow recoverable period. This experiment was performed on clean gold electrodes in 0.15M sulfuric acid (ultrapure J.T. Baker) in ultrapure reverse osmosis distilled water under nitrogen gas. The procedure was repeated on three different electrodes.

4.3.2 Results

The results of for gold variable clamp potential experiments are shown in Figure 4-2. Five different curves are shown representing the five different total charge densities. The curves to the left use higher levels of total charge than those to the right. The abscissa is the absolute post stimulus clamp potential in volts versus the SCE. The ordinate is the average current measured during the slow recoverable time segment. Only the slow recoverable segment is considered because we are interested in the behavior of this system as it relates to changes in the post stimulus clamp potential. Changes in this potential primarily affect the slow recoverable process in a simple system such as this one. The slow recoverable current increases with increasing post stimulus clamp potential for each curve. Also, when the slow recoverable current is zero, the post stimulus clamp potential is more negative for the higher charge density curves. The slow recoverable charge also increases with increasing total charge, as shown by the increasing magnitude of the currents for the same clamp potential.

To determine if the C_2 element has similar characteristics to an electronic capacitor, the charge versus the potential on the element can be plotted. If the result is linear then C_2 behaves like an electronic capacitor. The slow recoverable charge at the clamp potential

Figure 4-2 - Current during slow recoverable segment versus post stimulus clamp potential. (gold, 0.15M sulfuric acid, N₂ gas, 4mm area)
Mean of three electrodes.

when the average slow recoverable current is zero is plotted against the potential when the slow recoverable current is zero in Figure 4-3. The plot is linear showing the slow recoverable charge process behaves like an electronic capacitor within the tested potential range. The capacity of this component is shown by the slope of the line and is $22 \mu\text{F}/\text{cm}^2$.

Figure 4-4 shows three parameters as a function of the injected charge. The first parameter is the potential at which the slow recoverable current goes to zero ($V(C_2)$). The second parameter the electrode potential at the end of the pulse ($V(\text{Electrode})$). The last parameter is the unrecoverable charge measured when the post stimulus clamp potential matched the prestimulus clamp potential. This plot shows how the unrecoverable charge begins to increase as the "potential" of the slow recoverable process ($V(C_2)$) exceeds the thermodynamic H_2 evolution potential. $V(C_2)$ also appears to level off as it approaches the H_2 evolution potential as determined by slow cyclic voltammetry.

4.4 Variable Pulse Width and Delay in Saline

4.4.1 Methods

For this set of experiments, the pulse duration was changed and a variable delay time was imposed between the end of the pulse and the application of the potential clamp. The electrodes were pulsed with controlled current pulses of variable current amplitude as in chapter 3. In one set of experiments the pulse duration was varied between $25 \mu\text{S}$ and $1000 \mu\text{S}$ using a fixed delay of $0 \mu\text{S}$. In another set of experiments, the delay was varied between $25 \mu\text{S}$ and $1000 \mu\text{S}$ using a fixed pulse width of $100 \mu\text{S}$. The instrument opened the external circuit during the delay time so no current could flow through the electrode.

Figure 4-3 - Calculated charge versus potential for C2 (mean of 3 electrodes)
Gold, 0.15M sulfuric acid, 4mm area, Nitrogen gas.

Figure 4-4 - Plot of the potential of the electrode equivalent of C_2 , the electrode potential at the end of the pulse, and the unrecoverable charge as a function of the total charge. (Gold, 0.15M sulfuric acid, N₂ gas, 4mm area) Mean of three electrodes. HEP CV was determined from appendix B-1A.

Any charge lost from the electrode must have been absorbed by the solution during this open circuit delay.

A delay experiment was started by randomly setting the delay time from a group of test times. The randomization of delay times was done to avoid any trends associated with increasing delay time. The total charge was set to the lowest charge density. The pulse width was fixed at 100 μS for all delay experiments. At the initial charge density, all delay times were tested. The delay times were 0, 25, 50, 100, 200, 500, and 1000 μS . The charge density was increased, and all delay times were tested again. This was repeated up to the highest charge density. The tested charge densities for gold varied from $-12.5 \mu\text{C}/\text{cm}^2$ to $-175 \mu\text{C}/\text{cm}^2$ in increments of $-12.5 \mu\text{C}/\text{cm}^2$. The tested charge densities for platinum were varied from $-12.5 \mu\text{C}/\text{cm}^2$ to $-300 \mu\text{C}/\text{cm}^2$ in increments of $-12.5 \mu\text{C}/\text{cm}^2$. All delay experiments for gold were performed at a clamp potential of 0V SCE gold. All delay experiments for platinum electrodes were performed at the two clamp potentials of 0V SCE and -0.5V SCE.

The pulse width experiments were operated similarly to the delay experiments. A pulse width experiment started by setting the pulse width to the first of the randomized group of pulse durations, and the total charge to the lowest charge density. The delay was fixed at 0 μS for all of the pulse width experiments. At the lowest charge density of $-12.5 \mu\text{C}/\text{cm}^2$, all of the pulse widths were investigated. The pulse widths were 25, 50, 100, 200, 500, and 1000 μS on gold. On platinum the 25 μS pulse width was eliminated because $-300 \mu\text{C}/\text{cm}^2$ of charge could not be injected during this short time. The charge density was then increased, and the all of the pulse widths were tested again. This was repeated for the same charge densities as for the delay experiments on both platinum and gold. The pulse

width experiments on gold were performed at 0V SCE. The pulse width experiments for platinum electrodes were performed at the two clamp potentials of 0V SCE and -0.5V SCE. The solution was 1.0M NaCl with 30 mM phosphate buffer at pH 7. The gas was 100% ultrapure nitrogen. All procedures were repeated on 3 different electrodes. The plots shown are each for a single electrode, but the results were similar for all three electrodes.

Improvements to Instrumentation and Technique

The pulse width and delay experiments required modifications to the cell, the technique, and the instrument. The changes made to the cell included changing the counter electrode material and increasing the electrolyte conductivity. The counter electrode was changed from gold to iridium oxide coated titanium. This was done to avoid corrosion of the gold counter electrode at the much higher charge densities used in these experiments. The iridium oxide electrode will not corrode; it is designed to be a dimensionally stable anode. At positive potentials, the only process occurring on iridium oxide is oxygen evolution. This process should not occur during these experiments. The oxygen evolution potential was measured using slow cyclic voltammetry, and it was found to be approximately 0.9V SCE in the saline solution. Potential transients were measured during positive pulses of the maximum amplitude used in these experiments. The potential transients were found to be no greater than 50 mV. The open circuit potential for the iridium oxide electrode is about 100 mV SCE. The potential transients plus the steady state value, will be far less than the oxygen evolution potential. Thus, the counter electrode will not evolve oxygen during these experiments.

The electrolyte conductivity was increased by replacing the 0.3M NaCl solution, used in the experiments in chapter 3, with a 1.0M NaCl solution. The 30 mM phosphate

buffer concentration was maintained. The 1.0M NaCl electrolyte was necessary for us to maintain potential stability during the clamp segment of the experiment, even though the actual body concentration is 0.15M. The higher current densities used during the experiments in this chapter, required an even more conductive electrolyte to maintain potential control during application of the clamp. Comparing the charge-potential diagrams for a gold electrode in 0.15M phosphate buffered saline, with one in 1.0M phosphate buffered saline showed no differences. Thus, changing to a more conductive electrolyte should not effect the outcome of these experiments.

Two changes were made in the P-C technique. First, the charge and potential waveforms were recorded differently. This will be discussed under results section. For the second change, the surface of the electrodes was kept constant using initial and periodic cleanings during the experiment. In chapter 3 we were interested in how the electrodes behaved without electrochemical cleaning. In the body, any attempt to clean the electrode would likely cause tissue damage or electrode corrosion. In this chapter, the experiments used a higher charge density, causing the surface of platinum electrodes to change slowly over time. This surface change made interpretation of the results impossible. To maintain consistency throughout the experiments, the electrodes were cleaned before each experiment by imposing a constant negative current that caused H_2 to vigorously bubble from the surface. The surface cleanliness was maintained by periodically monitoring electrode using the slow cyclic voltammetry method. Each new cyclic voltammogram was compared with a standard cyclic voltammogram. Each chosen standard was a typical cyclic voltammogram after a long high charge density experiment. The standard cyclic voltammograms used for gold and platinum are shown in Figure 4-5. The electrodes were cleaned, as required, to maintain a match between the experimental and standard cyclic voltammograms. Cleaning

Figure 4-5 - Cyclic voltammograms in 1M PBS, N₂ gas, 4mm area.

A) Gold from 0V at 500 mV/S, B) Platinum from 0V at 150 mV/S

C) Platinum from -0.5V at 150 mV/S

during an experiment was performed by pulsing the electrode at 1 Hz, for up to 1 minute, with sufficient charge to achieve hydrogen evolution.

Two modifications were made to the instrument itself. The first was to increase the current output during a stimulus pulse from 80 mA to 240 mA. This allowed a total charge up to 12 μC ($-300 \mu\text{C}/\text{cm}^2$ for our 0.04 cm^2 electrodes) to be injected into the electrode during a 50 μs pulse. The second change was to reduce the time required to achieve a stable clamp potential from 50 μs to 15 μs . Thus, the time division for the fast recoverable charge portion was reduced to 15 μs . The electrode potential was now stable within this period for all charge densities. The potential was considered stable when it was within $\pm 50 \text{ mV}$ of the target potential.

4.4.2 Experimental Results

For this set of experiments it was necessary to change the way the charge and potential waveforms were collected. Previously, we collected two pairs of waveforms. The charge and potential were measured for 20 mS for the first pair of waveforms. The measurement time for the second pair of waveforms was shorter, and just long enough to measure the stimulus pulse and the potential clamp. For the new method, the first pair of waveforms consisted of a 20 mS measurement of the charge waveform, and a potential waveform measured long enough to include the stimulus pulse and potential clamp. The second pair of measurements started at the end of the stimulus pulse. The duration of this second measurement was always 200 μs . An example of the four waveforms is shown in Figure 4-6. This method of data collection improved the resolution of the clamp interval, and maintained a consistent resolution regardless of the pulse width or the delay time. The interval between when the potential clamp was applied and when the potential became

Figure 4-6 - A) 20 mS charge and higher resolution potential waveforms.

B) 200 μS constant resolution charge and potential waveforms.

stable, was critical in determining the fast recoverable and slow recoverable charge portions. High and consistent resolution during this period was necessary to achieve reproducible results.

Gold

Pulse Width

The effect variations in pulse width had on the response of a gold electrode can be seen in Figure 4-7. The curves show how the electrode potential changes, as a function of the injected charge, for the pulse widths considered. The potential was more negative during shorter pulse widths. The slope for all the curves was very shallow at high levels of injected charge. The key point to be derived from these figures is that the overall shape of the curves is similar, but offset to more negative potentials as the pulse width decreased. The more negative potentials, with decreasing pulse width, are predicted by the Butler-Volmer equation. This equation states that the current supported by an electrochemical reaction is exponentially related to the potential of the electrode. Thus, a larger magnitude current would require a larger magnitude potential. This was seen during the shorter pulse widths in which the current needed to be increased to inject the same charge in the shorter time. For the reactions to accommodate this larger current, the potential must also be larger.

The percent total charge curves, in Figure 4-8, show that the electrode behavior changes after approximately $-75 \mu\text{C}/\text{cm}^2$ of charge has been injected. Below this value, the fast recoverable charge decreases, the slow recoverable charge increases, and the unrecoverable charge increases with increasing pulse width. Beyond $-75 \mu\text{C}/\text{cm}^2$ of total charge, the behavior changes. The unrecoverable charge decreases, and the fast recoverable

Figure 4-7 - Total charge potential curve for pulse width variations.
 Gold, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.
 One of three electrodes: See Appendix E.

Figure 4-8 - Percent total charge curves for changes in pulse width.
 Gold, 0.3M phosphate buffered saline, 4mm area, Nitrogen gas.
 A) Fast recoverable, B) Slow recoverable, C) Unrecoverable charge.
 One of 3 electrodes; see Appendix E.

increases with increasing pulse width at the same charge level. The effect of pulse width on the slow recoverable charge appears unchanged by the level of injected charge.

Delay

The effect of delay on charge recovery is shown in Figure 4-9. The charge potential curves are not shown, because the total charge versus potential curve was unaffected by the delay time. Thus, the charge-potential curve for all delays was the same as the charge-potential curve for a 100 μS pulse width. Increasing delay decreased the amount of fast recoverable charge. At $-100 \mu\text{C}/\text{cm}^2$ injected charge, the fast recoverable charge decreases from 80% with no delay, down to 60% with a 1000 μS delay. The change is similar for all levels of total charge. Increased delay tends to increase the slow recoverable charge. At $-100 \mu\text{C}/\text{cm}^2$ of total charge, the slow recoverable charge increases from about 10% of the total charge with no delay, up to about 20% with 1000 μS delay. Unrecoverable charge also increased with increasing delay at all total charge levels. The largest affect occurred at $-100 \mu\text{C}/\text{cm}^2$ total charge. The unrecoverable charge increased from 5% up to 25% of the total charge when the delay was varied between 0 μS and 1000 μS .

Comparing the effects of pulse width and delay on the charge recovery, we can see that below $-75 \mu\text{C}/\text{cm}^2$ of total charge, the behavior is very similar. The fast recoverable charge decreases, the slow recoverable charge increases, and the unrecoverable charge increases. Above $-75 \mu\text{C}/\text{cm}^2$ total charge the effects of pulse width and delay were opposite for fast recoverable and unrecoverable charge. Apparently, at these higher levels of total charge the mechanism causing the change must be different than for the lower total charge levels. This is because the changes in charge recovery are different above and below

Figure 4-9 - Percent total charge curves for changes in delay.
 A) Fast recoverable, B) Slow recoverable, C) Unrecoverable charge.
 Gold, #1, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.
 One of 3 electrodes; see Appendix E.

-75 $\mu\text{C}/\text{cm}^2$ of total charge. However, the slow recoverable charge does not appear to participate in this process change because none of the slow recoverable curves change slope around -75 $\mu\text{C}/\text{cm}^2$ of total charge.

Platinum

Pulse Width

The effect of pulse width variations on charge recovery for a platinum electrode pulsed from -0.5V can be seen in Figure 4-10. The charge-potential curves do not show a clear change in slope that would indicate when a reaction begins or ends. For all pulse widths, the curves slowly and evenly reduce in slope as the total charge was increased. As was observed with gold, the electrode potential during shorter pulse durations is more negative than those during longer pulse durations. The overall shape of the curves, though, appeared to change very little with changing pulse width.

The percent total charge curves in Figure 4-11 gives a clearer indication of how the charge consumption changed with pulse width. For small charge injections, the fast recoverable charge decreased and the slow recoverable increased with increasing pulse width. At charge injection densities less than 50 $\mu\text{C}/\text{cm}^2$, the fast recoverable charge decreased from over 60% to about 35% as the pulse width increased from 50 to 1000 μs . For similar changes in pulse width the slow recoverable charge increased from about 40% to 65%. This change may be caused by the increased diffusion layer that would be present at the longer pulse widths. It is unlikely the change is due to a change in reactions, because of the smoothly changing slope in the charge-potential curves. However, increasing the injected charge level to -300 $\mu\text{C}/\text{cm}^2$, reduced the variation in fast recoverable and slow recoverable charge to less than 5% over the same pulse width range. Thus, the changes that

Figure 4-10 - Total charge potential curve for changes in pulse width.

Platinum, 1.0M phosphate buffered saline, 4mm area, N2 gas.

Clamp potential: -0.5V SCE.

One of 3 electrodes; see Appendix E.

Figure 4-11 - Percent total charge curves for changes in pulse width.
 A) Fast recoverable, B) Slow recoverable, C) Unrecoverable charge.
 Platinum, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: -0.5V SCE. One of 3 electrodes; see Appendix E.

occurred at low total charge levels became independent of pulse width at high total charge levels.

The changes in the unrecoverable portion with pulse width variations at all charge injections was not obvious from this figure. Plotting the unrecoverable charge versus the pulse width for varying charge densities, as in Figure 4-12, we see there is a minimum occurring around 200 μS . The change is small, but consistent for all charge densities. Apparently, the process responsible for the unrecoverable charge is not strongly dependent on the pulse duration. The unrecoverable process is not strongly pulse width dependent at any level of total charge.

The results on platinum electrodes pulsed from 0V were not included here. This is because they show the same slopes and behaviors as that for the platinum electrode pulsed from -0.5V, and, thus, provided no new insights. Further, the different pulse width curves from 0V fall too close together to resolve any detail on a reasonable scale. We, therefore, chose the results for the platinum electrodes pulsed from -0.5V to discuss the effects of pulse width and delay on charge recovery. All of the results can be seen in Appendix E.

Delay

The effect of delay on a platinum electrode pulsed from -0.5V SCE is presented in Figure 4-13. The charge-potential curves are not shown because they are unaffected by delay since the delay was imposed after the stimulus pulse. The shape of the charge-potential curve is the same as the charge-potential curve for the 100 μS pulse width in Figure 4-10. The fast recoverable charge as a percent of total charge decreases with increasing delay for all total charge levels. At $-50 \mu\text{C}/\text{cm}^2$ of total charge, the percent of

Figure 4-12 - Plot of percent unrecoverable charge versus pulse width.

Platinum, N₂ gas, 4mm area, V_{cl}=-0.5V SCE.

One of three different electrodes. See Appendix E.

Figure 4-13 - Percent total charge curves for changes in delay.
 A) Fast recoverable, B) Slow recoverable, C) Unrecoverable charge.
 Platinum, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: -0.5V SCE. One of 3 electrodes; see Appendix E.

charge in the fast recoverable portion decreased from 35% down to 15% as the delay increased from 0 μS to 1000 μS . At $-300 \mu\text{C}/\text{cm}^2$ of total charge, the fast recoverable charge was 20% and 10%, respectively for the same pulse widths. The percentage of charge found in the slow recoverable portion, by contrast, tends to increase with increasing delay at low levels of total charge. At high total charge injections the slow recoverable charge became independent of the length of the delay. All the slow recoverable charge versus delay curves were found to converge near 65% of the total charge for large total charge injections. The unrecoverable charge portion always had a dependence on both the magnitude of injected charge and the length of the delay. The unrecoverable charge portion increased with higher magnitudes of total charge, and with increases in the length of the delay. Very small total charge levels resulted in no unrecoverable charge. For no delay the unrecoverable portion was 15% at $-300 \mu\text{C}/\text{cm}^2$. At the other extreme, delays of 1000 μS caused the unrecoverable portion to increase to almost 30% at the same total charge level. Thus, longer delay, the larger the levels of unrecoverable charge at all total charge levels.

We can compare the pulse width plots with the delay plots for platinum. The fast recoverable portion decreased very similarly as both pulse width and delay increased for low total charge levels. At high levels of total charge, increases in delay still reduced the percent of fast recoverable charge, but changes in pulse width had almost no effect. The effect on the slow recoverable charge portion was very similar both quantitatively and qualitatively for pulse width and delay variations. At low charge injections the slow recoverable portion increased with increasing pulse width or delay. At higher charge injections, though, the slow recoverable portion became independent of either parameter. The percentage of total charge found in the unrecoverable portion increased only slightly with variations in pulse width, but increased strongly with increases in delay. Thus, the

unrecoverable process appears slightly dependent on pulse width, but strongly dependent on delay.

4.5 Discussion: Electrode Analog Model

The experimental observations of the electrode's behavior can now be compared with the behavior of the three compartment model. First, we must clarify how the measured parameters relate to the model. Experimentally, the electrode potential we measure is the potential across the double layer. The double layer potential drives all electrochemical reactions. Anytime the electrode potential changes, charge must flow into or out of the double layer. The electrode potential measurement is analogous, in the model, to the potential across the double layer capacitor, C_{DL} . This is the only potential in the model that can be directly measured experimentally. The potential across C_2 , in the model, governs whether unrecoverable charge will pass through T_1 . This is because the conductance of T_1 is a function of the potential on C_2 . If a process that behaved like C_2 existed on the electrode, it could be indirectly measured by changing the clamp potential. Variations in potential of this process could be found by checking the clamp potential at which the current through this process was zero. The process would be a slow process, because the element, T_2 , limits the rate of charging and discharging of C_2 . Thus, to find an analogous behavior we must look at the slow recoverable experimental results. The experimental results will now be compared with the model projections.

Variable Clamp Potential in Sulfuric Acid

From the experimental results we find that the model can mimic most of the observed electrode behavior. The results of the variable clamp experiment found that the clamp current changed polarity, as the clamp potential passed through some value. This

behavior will also occur in the model when the clamp potential across C_{DL} is varied through the potential on C_2 . Current will flow into C_2 if the clamp potential is more negative, and out of C_2 if the clamp potential is more positive. Experimentally, we found that the clamp potential at which the current was zero increased as the total injected charge increased. Again, this is how we would expect the model to behave. Increasing the total charge will cause more charge to flow onto C_2 , if all other parameters are kept constant. For any capacitor, the potential must increase as the charge held by the capacitor is increased. Thus, the post stimulus clamp potential at which the slow recoverable current is zero, will increase with increasing total charge in the model.

Another experimental finding is that, as the electrode potential at the end of the pulse neared the P-C hydrogen evolution potential, the clamp potentials at which the current was zero converged on the hydrogen evolution potential as determined by slow cyclic voltammetry. In the model, increases in the potential of C_2 will increase the conductance of T_1 . At some potential T_1 will be sufficiently conductive to carry all the injected current. At this point the potential of C_2 would no longer increase. If we plot the slow recoverable charge versus the clamp potential when the current passed through zero, we would see a linear plot as shown in Figure 4-3. The capacity shown by the slope of this curve is 22 $\mu F/cm^2$.

Lastly, we found experimentally that the electrode potential at which unrecoverable charge was detected, was more negative during P-C stimulus pulses than would be predicted by slow cyclic voltammetry. This is shown by the unrecoverable charge curve in Figure 4-4. In the model, the potential of C_2 will also lag behind that of C_{DL} during short high current pulses. This is because the current through C_2 is limited by T_2 . The potential

of the two capacitors will be very similar, though, during long low current pulses. The potential of C_2 will determine the level of unrecoverable charge via the conductance of T_1 . We would expect the potential across C_{DL} at which unrecoverable charge is detected, to be larger during short high current pulses than slow low current pulses. These data indicate that the experimental behavior of the electrodes in these experiments can be described by the three compartment model.

Pulse Width and Delay in Saline

Increases in either the delay time or the pulse width, in general, decreased the fast recoverable charge, and increased both the slow recoverable charge and the unrecoverable charge. Apparently, increasing the time for the reactions to occur allowed the slower and more irreversible reactions to proceed further. During the longer pulses, the increased charge that went into slow processes showed up in the slow recoverable charge. Similarly, the increased time allows more charge to flow into unrecoverable processes that will show up as unrecoverable charge.

We can also show that the expected model behavior will mimic these experimental observations. Experimentally we found that increasing the pulse duration while maintaining the same charge injection decreased the fast recoverable charge, increased the slow recoverable charge, and increased the unrecoverable charge for low charge injections on gold and all charge injections on platinum. The current must be reduced to inject the same charge while increasing the pulse width. Reducing the current in the model will have the effect of making the potential on C_2 more closely track C_{DL} . The potential on C_{DL} will be lower, and the potential on C_2 will be higher. There will also be an increase of the charge on C_2 to create this higher potential. Since the charge on C_2 represents the slow recoverable

charge, this quantity will increase. Further, the fast recoverable charge will likewise decrease. Although the same charge was injected, more went into C_2 during the lower current pulse. An increased potential on C_2 also means that the unrecoverable charge will increase. This is because the potential of C_2 controls the conductance of T_1 , and a larger potential means a higher conductance and more unrecoverable charge. Thus, the experimental pulse width results can be correlated with the expected model behavior.

In the delay experiments, we observed that increasing the delay time decreased the fast recoverable charge, increased the slow recoverable charge, and increased unrecoverable charge. Again, we can look to the model to see if it will mimic this behavior. In the model, an open circuit delay will allow more time for the charge stored on the double layer capacitor to be discharged through C_2 and T_1 . The potential on C_{DL} will always be larger than or equal to that of C_2 during the stimulus pulse. Thus, during a delay, the current will naturally flow from C_{DL} onto C_2 . The extra charge on C_2 will be recovered in the slow recoverable portion. Thus, in the model, the slow recoverable charge will increase with increasing delay time. As the magnitude of potential across C_2 increases during the delay, the conductance of T_1 will concomitantly increase. The increased conductance of T_1 will allow more charge to pass through the resistor, and the amount of unrecoverable charge will also increase. Thus, an open circuit delay in the model will decrease the fast recoverable charge, and increase both the slow recoverable and unrecoverable charge. This was found experimentally.

There is one distinct exception to the experimental observations that the proposed model does not corroborate. This is the effect variations in pulse width have on charge recovery during large charge injections on gold. The relations discussed so far suggest that

time is an important factor in determining how the injected charge is recovered. The behaviors were all directly related to the duration of the stimulus pulse. Fast recoverable charge decreased, and slow recoverable and unrecoverable charge increased with increasing pulse width. During large magnitude charge injections on gold, though, charge recovery, as related to pulse duration, appears to be governed by a different parameter. At total charge magnitudes greater than $-75 \mu\text{C}/\text{cm}^2$, short pulse widths were found to create more unrecoverable charge than long pulse widths. This is the opposite to what has been discussed so far. Shorter pulse widths have higher current densities than long pulse widths for the same total charge. The level of unrecoverable charge then, correlates with the current density. Thus, more current passes into the unrecoverable process during shorter pulse widths. In electrochemistry, kinetics is defined as the dependence of current through an electrochemical process on potential. Thus, the amount of the unrecoverable charge on gold is kinetically determined. Since the unrecoverable process on gold is likely hydrogen evolution, as will be shown in the next chapter, the evolution of hydrogen on gold is primarily potential dependent rather than time dependent.

4.6 Summary

We have presented a simple three compartment model based on the three time components of charge measured during the potential clamp. Experimentally, we have found that the model could mimic the electrode behavior when the clamp potential was changed for a gold electrode in sulfuric acid. The lag in the potential of C_2 during stimulus pulses, also mimics the observed behavior. The shorter the pulse, the larger will be the apparent H_2 evolution potentials. Experimentally, we also observed that increasing pulse width, in general, decreases the fast recoverable charge, and increases both the slow and unrecoverable charge. This is the same behavior that would happen on the model when the

pulse width is increased. Similarly, increases in the delay decrease the fast recoverable charge, and increase the slow and unrecoverable charge experimentally. The model could also produce similar changes for changes in delay.

5. Processes Consuming Charge During Stimulation Pulses on Gold and Platinum Electrodes

5.1 Introduction

The electrochemical processes occurring on gold and platinum electrodes, during a typical neural stimulating pulse, are measured in this chapter. Also, the charge stored by each reaction is estimated. This requires combining the experimental data, collected using the P-C method and slow cyclic voltammetry, with other information. Slow cyclic voltammetry determines the potential at which reactions occur under low current conditions. We also need to have information about the reversibility and relative rates of these reactions. This can be found in the electrochemical literature. Thus, by combining, the cyclic voltammograms, the P-C data, and the kinetic information, we are able to determine which reactions are storing charge, and how much is stored in each reaction.

Knowing which processes store charge during a pulse, is the first step toward determining which processes are damaging. The electrochemical processes responsible for tissue damage are unknown. By quantifying the processes consuming charge, the potentially harmful one can then be identified. This can be done by maximizing the charge consumption of a single reaction in vivo, and looking for tissue damage. Correlations can be made between a reaction, and the level of tissue damage. This will indicate how damaging a reaction may be.

The one process we will not consider in this study is oxygen reduction. Reactions occurring in the absence of oxygen must be considered first, because reactions involving

oxygen reduction cannot be separated from other irreversible processes. Oxygen reduction is known to be irreversible on both gold and platinum. Hydrogen evolution can also create unrecovered products. If oxygen is included in the system, the unrecoverable charge measurement may include the charge associated with both oxygen reduction products and hydrogen gas. The only way to separate the two reactions is to first establish the charge levels of hydrogen evolution alone. Any charge increase above this level, in the presence of oxygen, can then be attributed to oxygen reduction. Determining the oxygen reduction charge levels will be left for future work.

5.2 Methods

The slow cyclic voltammetry experiments followed the same methods as detailed in chapter 3. The slow cyclic voltammetry was run before and after each individual P-C experiment to test for any changes in the surface. The standard voltammograms used in chapter 4 were also used in this chapter.

The P-C experiments performed in this chapter included all of the instrument modifications described in chapter 4. The pulse width was fixed at 100 μS , and the delay was set to 0 μS . The charge injection level was varied between $-12.5 \mu\text{C}/\text{cm}^2$ and $-175 \mu\text{C}/\text{cm}^2$, in increments of $-12.5 \mu\text{C}/\text{cm}^2$ for the gold electrodes. The $-175 \mu\text{C}/\text{cm}^2$ maximum charge was chosen because more than $20 \mu\text{C}/\text{cm}^2$ of unrecoverable charge was measured at this total charge level, and $175 \mu\text{C}/\text{cm}^2$ was the same total charge as used in the previous chapters. For platinum electrodes, the charge injection level was varied from $-12.5 \mu\text{C}/\text{cm}^2$ to $-300 \mu\text{C}/\text{cm}^2$, in increments of $-12.5 \mu\text{C}/\text{cm}^2$. The $300 \mu\text{C}/\text{cm}^2$ total charge was the maximum available with the instrumentation. The prestimulus electrode potential (clamp potential) was set at 0V SCE for the gold electrode. On platinum, the experiment was

repeated with clamp potentials of 0V SCE and -0.5V SCE. The clamp potential of -0.5V was used on platinum, because we wanted to be certain to include hydrogen evolution in our measurements. Clamping the electrode at the lower potential removed most of the hydrogen adsorption reaction, and thus assured that we could measure the hydrogen evolution process. The results shown are for a single electrode. The response of all three electrodes is shown by the 100 μ S curves in Appendix E.

5.3 Results

5.3.1 Cyclic Voltammograms

Examining the cyclic voltammogram, we can determine what reactions can occur over the potential range under study. A cyclic voltammogram for gold is given in Figure 5-1a. The H_2 evolution reaction is known to begin near -0.659V SCE at pH 7.0 (CRC Handbook of Chem and Physics). This was shown on the plot by the negative current beginning peak at -0.6V. The chloride adsorption reaction was marked by the very rounded peaks near -0.4V. Double layer charging is always present whenever the electrode changes potential. The only way to measure the double layer capacity is in the absence of any other reaction. We will assume a double layer capacity of 50 μ F/cm² that matches the virtual capacity on gold. The double layer charging current can be calculated from the equation $i=C(dV/dT)$, in which C is the double layer capacity, and dV/dT is the sweep rate. The double layer current for the gold cyclic voltammogram is $\pm 25 \mu$ A/cm² calculated using a 50 μ F/cm² double layer capacity and a 0.5 V/S sweep rate. Thus, double layer charging, hydrogen evolution, and chloride adsorption are the three reactions that can occur on gold.

The platinum cyclic voltammogram for sweeps starting at both 0V and -0.5V are shown in Figures 5-1b and 5-1c respectively. Looking first at an electrode swept from 0V,

Figure 5-1 - Cyclic voltammograms in 1M PBS, N₂ gas, 4mm area.

A) Gold from 0V at 500 mV/S, B) Platinum from 0V at 150 mV/S

C) Platinum from -0.5V at 150 mV/S

the very large negative peak at -0.65V represents the hydrogen evolution reaction. The two large current peaks at -0.4 and -0.5V are known to be the hydrogen adsorption reaction. Chloride adsorption can only be seen by comparing the cyclic voltammogram in the presence and absence of chloride. This has been done by Bagotzky et al (1970), and chloride adsorption is known to occur between the potentials of 0.15V and -0.6V SCE. As with gold, the double layer charging current occurs at all potentials. The double layer charging current can be determined using our double layer capacity ($47 \mu\text{F}/\text{cm}^2$ from virtual capacity at -0.5V) and the sweep rate (0.15V/S) as above, and is found to be $\pm 7.5 \mu\text{A}/\text{cm}^2$. The possible reactions occurring on a platinum electrode pulsed from 0V are hydrogen evolution, hydrogen adsorption, chloride adsorption, and double layer charging.

The cyclic voltammogram for a platinum electrode swept from -0.5V is shown in Figure 5-1c. Hydrogen adsorption still occurred between -0.5V and -0.6V. The negative current peak, beginning at -0.6V, was hydrogen evolution. The double layer current is assumed to be the same as for the electrode clamped at 0V. Chloride adsorption at potentials more negative than -0.5V was found to be less than 10% (Bagotzky et al, 1970), so the current associated with this process will be ignored. Thus, the possible reactions occurring during this sweep from -0.5V are hydrogen evolution, hydrogen adsorption, and double layer charging.

5.3.2 Pulse Clamp

Gold

Only two primary electrochemical processes appear to have occurred on the gold electrode during the stimulus pulse. This can be determined by examining the total charge curve in Figure 5-2a. The slope of this curve was nearly constant from zero to -110

Figure 5-2 - Gold, charge potential and percent total charge.
 1M PBS, Nitrogen gas, 100 μ S PW, 4mm area, $V_{\text{clamp}}=0\text{V SCE}$
 One of three electrodes. See Appendix E; 100 μ S pulses.

$\mu\text{C}/\text{cm}^2$ of total charge. A constant slope indicates that a single reaction dominated the electrode behavior over this level of charge. Beyond $-110 \mu\text{C}/\text{cm}^2$ of total charge, the slope became very shallow and constant. This indicates another process then dominated the electrode behavior at higher total charge densities.

Examining the curves for each time segment, shows the change of reactions more clearly. The slope of the fast recoverable curve had a virtual capacity of $51 \mu\text{F}/\text{cm}^2$. The slow recoverable curve was very steep, and only $17.5 \mu\text{C}/\text{cm}^2$ out of the $175 \mu\text{C}/\text{cm}^2$ of total charge went into slow reactions. The unrecoverable charge curve was initially very steep. The slope begins to change around -1.25V and becomes flat around -1.75V . Therefore, the unrecoverable process did not begin until the electrode potential was more negative than -1.25V SCE. The unrecoverable process consumed 70 of the $175 \mu\text{C}/\text{cm}^2$ of total charge at a potential of -1.75V .

The same observations result from analyzing the percent of total charge going into the fast recoverable, slow recoverable, and unrecoverable charge portions. These are shown in Figure 5-2b. Over 80% of the total charge went into fast recoverable processes, up to a total charge injection of about $-75 \mu\text{C}/\text{cm}^2$. For total charge magnitudes greater than this value, the fast recoverable percent decreased, and the unrecoverable percent increased. Beyond $-75 \mu\text{C}/\text{cm}^2$, the injected charge was consumed primarily by unrecoverable processes.

Notice the total charge-potential curve changes slope at $-110 \mu\text{C}/\text{cm}^2$, but the percent unrecoverable charge curve changes slope at $-75 \mu\text{C}/\text{cm}^2$. Since only one reaction was added, we would assume the two curves would change slope at the same total charge.

The difference is likely due to the fact that the total charge-potential curve includes all the processes simultaneously, while the unrecoverable charge curve only includes one process. Therefore, the latter is more sensitive to the total charge level at which potentially damaging products are generated.

Platinum

The response of a platinum electrode, pulsed from 0V SCE, is shown in Figure 5-3a. The delineation of changes in which reactions occurred, as indicated by the change in slope of the total charge curve, is not as clear as it was for gold. While there are some minor changes in slope of the curves, the most distinct change occurs near $-225 \mu\text{C}/\text{cm}^2$ of total charge. It appears the electrochemical processes may have changed at this level of total charge. As the processes are outlined in the discussion, it is not evident what the change is from these results. It could be the beginning of chloride desorption. It could be the change from weakly to strongly bound hydrogen adsorption. Different experiments will have to be done to make this determination.

The reactions can be seen more clearly by inspecting the curves of the measured charge segments. Examining the fast recoverable charge curve, we find the slope, between -12.5 and $-100 \mu\text{C}/\text{cm}^2$ of total charge, had a virtual capacity of $100 \mu\text{F}/\text{cm}^2$. This value exceeds the $50 \mu\text{F}/\text{cm}^2$ value assumed for double layer charging alone, so more than one process must have been included in the fast recoverable portion. The change in slope of the fast recoverable curve, around $-100 \mu\text{C}/\text{cm}^2$ of charge, may indicate the occurrence of a new reaction that is reversed within the $15 \mu\text{s}$ clamp time. The reaction could simply be the change from weakly bound hydrogen to strongly bound hydrogen. This will be discussed in much more detail in the discussion section. The change in slope may also

Figure 5-3 - Platinum, charge potential and percent total charge.

1M PBS, Nitrogen gas, 100 μ S PW, 4sq.mm., $V_{\text{clamp}}=0\text{V SCE}$

One of three electrodes. See Appendix E; 100 μ S pulses.

mean that the non double layer process was simply going faster at the more negative potentials, so more product was available to reverse. The slow recoverable curve had a similar shape to the fast recoverable charge curve. This could be because the reversal of one of the processes overlapped the fast recoverable and slow recoverable time division. If the process was not completely reversed in the 15 μ S clamp period, then some of the recovered charge would have showed up in the slow recoverable time segment. Practically no unrecoverable charge was detected on platinum electrodes pulsed from 0V over the total charge range of -12.5 to 300 μ C/cm².

The total charge was almost evenly split between the fast recoverable and slow recoverable portions in Figure 5-3b. Two slope changes occur in the fast and slow recoverable charge segments. The first was near -50 μ C/cm² of total charge. The second occurred when slightly more than -200 μ C/cm² of total charge had been injected. The first change in slope, near -50 μ C/cm² of total charge, was not clearly seen in the charge-potential diagram above. However, the change near -200 μ C/cm² of total charge was seen in the charge-potential plot. At total charge magnitudes less than -50 μ C/cm² the fast recoverable charge dominated, while at total charge magnitudes greater than -200 μ C/cm² the slow recoverable charge was slightly larger. The almost constant slope means the slow recoverable charge increased in exact proportion to the total charge. The fast recoverable charge accounted for roughly 50% of the charge, and no dramatic slope changes occurred on these curves. This reinforces the idea that only one other process, in addition to double layer charging, was storing the charge during stimulus pulses on platinum from 0V SCE. Virtually no unrecoverable charge was detected at any of the charge injection levels tested.

The charge-potential curves for platinum electrodes pulsed from -0.5V SCE are shown in Figure 5-4a. In this case, the slope of the total charge curve slowly decreases. The initial slope was much steeper than for a platinum electrode pulsed from 0V, and the final slope is more shallow. There are no distinct changes in slope to indicate at what charge or potential any changes in the reactions may have occurred.

The fast recoverable curve has the smaller virtual capacity of $47 \mu\text{F}/\text{cm}^2$ over the -12.5 to -300 $\mu\text{C}/\text{cm}^2$ total charge range. This can be compared to the $100 \mu\text{F}/\text{cm}^2$ for the platinum electrode pulsed from 0V. This smaller value is consistent with double layer charging being the only process that participated in the potential clamp. The slow recoverable curve has the same general shape as the total charge curve. This signifies that the electrode behavior was dominated by slow processes. The slow recoverable curve was also similar to the one for the electrode pulsed from 0V. This is interesting because it is unlikely the same process stored so much charge during pulses from both clamp potentials. Some unrecoverable charge was detected on this electrode, but not until potentials more negative than -1.0V SCE were reached. Even at a total charge of -300 $\mu\text{C}/\text{cm}^2$, the unrecoverable charge never constituted more than 20% of the total injected charge.

The charge percentage curves display even more information about how this electrode operated. They are shown in Figure 5-4b. At total charge magnitudes less than -100 $\mu\text{C}/\text{cm}^2$, the charge was split between the fast recoverable and slow recoverable processes. Increasing the magnitude of the total charge, decreased the fast recoverable portion and increased the slow recoverable portion. This is a similar behavior to what was found for a platinum electrode pulsed from 0V SCE. Unrecoverable charge was detected even at very low total charge levels, although the potential was quite negative of the

Figure 5-4 - Platinum, charge potential and percent total charge.
 1M PBS, Nitrogen gas, 100 μ S PW, 4sq.mm., $V_{\text{clamp}} = -0.5\text{V SCE}$
 One of three electrodes. See Appendix E; 100 μ S pulses.

hydrogen evolution potential determined by slow cyclic voltammetry. Apparently the potential changed very rapidly at low total charge levels. At total charge magnitudes exceeding $-100 \mu\text{C}/\text{cm}^2$, the percent of charge stored by the slow recoverable processes remained fairly constant at almost 60%. Also, the percentage consumed by unrecoverable processes increased as the percent stored by fast recoverable processes decreased. The detection of unrecoverable charge means that another process was added to the two detected so far.

The results from the experimentation are summarized in table 5-1. Also included in this table are the equations used for calculating the double layer current, the virtual capacity, and the charge stored by each reaction discussed below.

5.4 Discussion: Processes Consuming the Charge

The electrochemical processes that are storing the charge, and the amount of charge stored by each reaction can be estimated. The charge associated with each reactions in the cyclic voltammogram can be determined by integrating the current under each reaction peak. This gives a reasonable maximum value of the charge that can be stored by this process. From the P-C data, we know when a reaction will begin or end from changes in the slopes and from the relative amount of the fast recoverable, slow recoverable, and unrecoverable charge. With one other piece of information we can relate the reactions observed with the P-C method to those known from the cyclic voltammogram. The other information is the relative kinetics of the separate reactions. Kinetics determine the reaction rate as a function of electrode potential. Knowledge of the relative rates allows us to place the reactions identified with slow cyclic voltammetry in the fast recoverable, the slow recoverable, or the unrecoverable portions of the total charge. The kinetics of the reactions

Table 5-1 - Summary of data from pulse clamp experiments.

Gold							
Q Tot	Fast Recov	% FR	Slow Recov	% SR	Unrecov	% UR	Pot (V SCE)
-12.00	-10.40	86.67	-1.78	14.83	0.18	-1.50	-0.27
-54.00	-44.67	82.72	-9.53	17.65	0.20	-0.37	-1.01
-102.67	-81.00	78.90	-13.78	13.43	-7.88	7.68	-1.63
-152.00	-86.17	56.69	-15.03	9.89	-48.30	31.78	-1.73
-171.00	-86.50	50.58	-15.50	9.06	-66.50	38.89	-1.74
Platinum 0V							
Q Tot	Fast Recov	% FR	Slow Recov	% SR	Unrecov	% UR	Pot (V SCE)
-25.00	-14.40	57.60	-10.54	42.14	-0.07	0.26	-0.31
-99.33	-48.60	48.93	-49.77	50.10	-0.97	0.97	-0.62
-202.00	-98.83	48.93	-100.67	49.84	-2.50	1.24	-1.04
-298.00	-132.00	44.30	-163.46	54.85	-2.54	0.85	-1.17
Platinum -0.5V							
Q Tot	Fast Recov	% FR	Slow Recov	% SR	Unrecov	% UR	Pot (V SCE)
-25.13	-13.73	54.64	-11.16	44.42	-0.24	0.94	-0.73
-100.50	-41.33	41.13	-55.61	55.34	-3.55	3.54	-1.20
-201.67	-60.67	30.08	-114.43	56.74	-26.57	13.17	-1.42
-300.00	-64.00	21.33	-171.00	57.00	-65.00	21.67	-1.49

Double layer current = $Cdl(dV/dT)$; $Cdl = 50 \text{ uF/sq.cm.}$

Double layer capacity = Virtual capacity = dQ/dV OR 50 uF/sq.cm.

Gold = 50 uF/sq.cm. (same as virtual capacity)

Platinum = 47 uF/sq.cm. (from virtual capacity at -0.5V)

Chloride desorption charge =

Charge per monolayer * Percent coverage * Electrosorption valence.

Gold = -82.5 uC/sq.cm. (from CV; only used -17.5 during pulses)

Platinum = -0 to -56 uC/sq.cm. ($-382 \text{ uC/sq.cm.} * 80\% * 0.2$)

Hydrogen adsorption charge = $Q(\text{total}) - Q(\text{double layer}) - Q(\text{chloride desorption})$

Gold = hydrogen does not adsorb appreciably on gold.

Platinum = -188 to -244 uC/sq.cm. depending on chloride desorption.

Hydrogen evolution

Gold = $Q(\text{unrecoverable}) = -70 \text{ uC/sq.cm.}$

Platinum = $Q(\text{total}) - Q(\text{double layer}) = -178 \text{ uC/sq.cm.}$

OR = $3 * Q(\text{unrecoverable}) = -198 \text{ uC/sq.cm.}$

we are studying have all been determined. So by using information from the cyclic voltammogram, the charge-potential graphs, and the relative kinetics, we will calculate the charge stored by each reaction occurring during a pulse.

5.4.1 Double Layer

Double layer charging is a highly reversible non-Faradaic reaction occurring on both electrodes. Recall that double layer charging represents the separation of charge across the interface, and no charge transfer occurs with this process. This makes it an ideal candidate for charge injection during neural stimulation pulses. Double layer charging is an extremely fast process, and it is the fastest reaction under study. Therefore, the assumption is made throughout these studies that the double layer is always in equilibrium. The charge associated with the double layer process is then determined from the double layer capacity and the change in electrode potential.

For a gold electrode in 1M phosphate buffered saline, clamped at 0V SCE, a typical virtual capacity is $50 \mu\text{F}/\text{cm}^2$. Thus, the $50 \mu\text{F}/\text{cm}^2$ virtual capacity measurement makes it likely the process storing the fast recoverable charge is entirely double layer charging. If we use this value for the double layer capacity, and the electrode potential at the end of the pulse of -1.75V, we find that $-87.5 \mu\text{C}/\text{cm}^2$ of charge was stored by the double layer during a $-175 \mu\text{C}/\text{cm}^2$ total charge pulse on gold.

We found that when a platinum electrode was pulsed from 0V, the virtual capacity was over $100 \mu\text{F}/\text{cm}^2$. This value is much larger than the $50 \mu\text{F}/\text{cm}^2$ we have assumed to be the double layer capacity. Thus, the fast recoverable charge must not consist solely of double layer charge. However, when the electrode was pulsed from -0.5V, the virtual

capacity was $47 \mu\text{F}/\text{cm}^2$. This value is certainly consistent with the only fast recoverable process being double layer charging. If we use this value of $47 \mu\text{F}/\text{cm}^2$ as the double layer capacity on platinum, we can estimate the charge associated with the double layer for any change in electrode potential. The double layer process stored $-56 \mu\text{C}/\text{cm}^2$ of charge during a $-300 \mu\text{C}/\text{cm}^2$ total charge pulse on a platinum electrode clamped at 0V. The double layer charge was $-47 \mu\text{C}/\text{cm}^2$ on the same electrode pulsed from -0.5V.

5.4.2 Chloride Adsorption/Desorption

Since chloride is one of the electrolytes, chloride adsorption and desorption must also be considered. Using slow cyclic voltammetry, the reversible charge on a cathodically cleaned gold electrode swept between 0 and -0.6V SCE was found to be approximately $-92.5 \mu\text{C}/\text{cm}^2$. Assuming a double layer capacity of $50 \mu\text{F}/\text{cm}^2$, and a potential change from 0V to -0.6V, the double layer charging will store $-30 \mu\text{C}/\text{cm}^2$ of charge. This leaves $-62.5 \mu\text{C}/\text{cm}^2$ of charge available for other processes.

To calculate the charge that could be associated with chloride desorption we need to know the charge associated with a complete monolayer of chloride, and the percent of the surface actually covered by chloride. The charge associated with a monolayer of chloride depends on the number of atoms in the monolayer, and the amount of charge each atom shares with the metal. The amount of sharing can be from zero to one electron. Assume chloride shares 0.5 electrons for each adsorbed atom. The charge in a monolayer of atoms sharing a complete electron is, on platinum, roughly $-200 \mu\text{C}/(\text{real cm}^2)$.² The gold

² Based on the assumption of 1 adsorbed hydrogen atom per platinum atom, one gets approximately 2×10^{-9} moles of adsorbed hydrogen. Multiplying this number by the Faraday constant and using an electrosorption valence of 1, $193 \mu\text{C}/\text{cm}^2$ is required to plate a monolayer of hydrogen onto the surface.

atom is similar in size to a platinum atom, so the adsorption charge for gold and platinum should be very similar. So, if we assume a charge per monolayer of $-200 \mu\text{C}/(\text{real cm}^2)$, and an electron sharing of 50%, then $-100 \mu\text{C}/(\text{real cm}^2)$ of charge would be associated with a complete monolayer of chloride covering the surface. Chloride has been shown to cover between 20% and 50% of the surface of a gold electrode clamped near 0V SCE, depending on the method used (Yeager, 1983). Chloride completely desorbs when the electrode is clamped at potentials near -0.5V SCE (Yeager, 1983). Thus, chloride desorption could store -20 to -50 $\mu\text{C}/(\text{real cm}^2)$ of charge when changing the potential of a gold electrode from 0V to -0.5V SCE. Since electrode surfaces are not completely smooth we need to include the roughness factor. Assuming a roughness factor of 2, chloride desorption could store -40 to -100 $\mu\text{C}/\text{cm}^2$. Thus, the $-62.5 \mu\text{C}/\text{cm}^2$ of charge found in the cyclic voltammogram could be explained by the chloride adsorption/desorption process.

We can now estimate how much charge is stored by chloride desorption during a stimulus pulse. Comparing the slow cyclic voltammetry measurement with the charge measurements made using the P-C method, we find the consumption of charge by chloride desorption during a pulse was less than the maximum possible. When the double layer charge and the unrecoverable charge are subtracted from the injected charge only $-17.5 \mu\text{C}/\text{cm}^2$ of charge is left. Comparing this value with the $-62.5 \mu\text{C}/\text{cm}^2$ of available reversible charge indicates less than one third of the chloride likely desorbs. This conclusion is corroborated by the work of Hamelin & Bellier (1973). They found chloride desorption was slow enough to affect capacity measurements at frequencies of 12 Hz. This means chloride in her system was not desorbing during an effective pulse width of 42 mS. This pulse width is orders of magnitude larger than those used in our experiments. Thus,

chloride desorption does store some charge during a stimulus pulse on gold, but only about one third of the maximum available chloride desorption charge.

Chloride is known to adsorb strongly on platinum (Bagotzky et al, 1970). Bagotzky found that chloride covers 80% of the surface of a platinum electrode clamped at a potential of 0.7V versus the reversible hydrogen electrode, in 1M KCl, at pH 1. This translates to a potential of 0.04V SCE at a pH of 7.0. He also found that the kinetics of chloride adsorption and desorption were very slow. It took approximately 100 mS to remove half of the adsorbed Cl^- when stepping the potential down to the hydrogen evolution potential³. The amount of chloride desorbed was exponentially dependent on time. Even a pulse as long as 10 mS would desorb only one eighth of the adsorbed chloride under the conditions Bagotzky used. However, the potential during one of our pulses was much more negative than those used by Bagotzky. Therefore, more chloride likely desorbs than indicated by Bagotzky's results. The total charge available in Cl^- desorption can be estimated by assuming a coverage of 80%, a charge of $-350 \mu\text{C}/\text{cm}^2$ per monolayer (from the measured hydrogen adsorption below), and an electrosorption valence of 0.2 (Delahay, 1963). The resultant charge for Cl^- adsorption is then $-56 \mu\text{C}/\text{cm}^2$. No chloride desorption charge is included in the charge inventories of the pulses from -0.5V. This is because chloride covers less than 10% of the surface of at this potential (Bagotzky et al, 1970), so we will ignore the charge associated with this process. In summary, with the assumptions we made about adsorption valence, the total charge associated with chloride desorption is approximately $-52 \mu\text{C}/\text{cm}^2$ on gold and about $-56 \mu\text{C}/\text{cm}^2$ on platinum during pulses from

³ He stepped the potential from 0.5V versus the reversible hydrogen electrode down to 0V RHE. The electrolyte was 0.5M sulfuric and 0.1M KCl. While the pH and concentration are different for these experiments, they do show that chloride likely desorbs very slowly.

0V. Negligible charge is associated with chloride desorption during pulses from -0.5V. The charge contributed during a pulse is likely less than these values, because of the slow desorption kinetics. However, these calculations indicate the possible contribution of chloride desorption for both metals.

5.4.3 Hydrogen Adsorption

Hydrogen adsorption on gold is known to be extremely small. This can be seen in a cyclic voltammogram, in the absence of chloride, by the lack of current peaks between the oxide reduction peak at 0.7V and the hydrogen evolution peak at -0.3V (Appendix B). No processes other than double layer charging occurs between these two potentials. Therefore, hydrogen adsorption is not an important reaction on gold.

By contrast, hydrogen adsorption is a significant reversible process on platinum electrodes. The charge associated with hydrogen adsorption during a pulse from 0V can be measured on platinum using slow cyclic voltammetry. The charge associated with this reaction is determined by measuring the area under the peaks in the cyclic voltammogram associated with hydrogen adsorption. From the total area, the double layer charge and the chloride desorption charge must be subtracted. When we do this on three electrodes, we get an average value of $362 \mu\text{C}/\text{cm}^2$. Hydrogen adsorption on a clean platinum surface in H_2SO_4 has been established as being a fast reaction (Ludwig, 1968). The coverage, during a pulse from 0V SCE, can be calculated from the total charge minus the double layer charge minus the chloride desorption charge ($Q_{\text{TOT}} - Q_{\text{DL}} - Q_{\text{Cl(ADS)}}$), assuming no unrecoverable charge. The double layer charge we know from the electrode potential at the beginning and the end of the pulse. Experiments to determined the chloride desorption

charge have not been carried out. However, we know it lies somewhere between 0 and $-56 \mu\text{C}/\text{cm}^2$.

The hydrogen adsorption charge can be estimated by using the two extremes of chloride desorption. For a $-300 \mu\text{C}/\text{cm}^2$ pulse, assuming the chloride desorbs completely, the charge associated with hydrogen adsorption is calculated to be $-187 \mu\text{C}/\text{cm}^2$. This comes from the total injected charge ($-300 \mu\text{C}/\text{cm}^2$) minus the double layer charge ($47 \mu\text{F}/\text{cm}^2 * 1.2\text{V}$) minus the chloride desorption charge ($-56 \mu\text{C}/\text{cm}^2$). Since the total hydrogen adsorption measured with slow cyclic voltammetry was $-362 \mu\text{C}/\text{cm}^2$, a hydrogen adsorption charge of $-187 \mu\text{C}/\text{cm}^2$ represents a 52% coverage. If, on the other hand, no chloride desorbs, the hydrogen adsorption charge is calculated as the total charge ($-300 \mu\text{C}/\text{cm}^2$) minus the double layer charge ($47 \mu\text{F}/\text{cm}^2 * 1.2\text{V}$). The hydrogen adsorption charge then is $-244 \mu\text{C}/\text{cm}^2$. This represents a coverage of 67%. The actual hydrogen adsorption charge during a pulse is probably somewhere between -187 and $-244 \mu\text{C}/\text{cm}^2$. The slow Cl^- desorption kinetics make the larger number more likely.

5.4.4 Hydrogen Evolution

The evolution of H_2 on gold is an irreversible process due to the very slow kinetics of H_2 oxidation on gold. This is clearly shown by the P-C charge-potential curves (Figure 5-2). The fast recoverable (double layer) charge moves straight into unrecoverable charge (H_2 evolution) when the total injected charge exceeded -75 to $-100 \mu\text{C}/\text{cm}^2$. The $-70 \mu\text{C}/\text{cm}^2$ of unrecoverable charge measured on a gold electrode during a $-175 \mu\text{C}/\text{cm}^2$ pulse, we take to be the charge associated with the H_2 evolution during the pulse.

The hydrogen evolution reaction on platinum is a multistep process that results in the creation of H_2 gas. A likely mechanism for H_2 evolution on platinum is that molecular hydrogen adsorbs to the surface in one step, and two of these adsorbed hydrogens will combine to form H_2 in the second step. Since the adsorption step is very important for reversible charge injection on platinum electrodes, it has been considered separately in a previous section. In this section, when we refer to H_2 evolution, we are referring specifically to the recombination step in which H_2 is formed.

On platinum electrodes pulsed from 0V SCE, no unrecoverable charge was measured. We take this to mean that no H_2 evolution occurred during the pulses. This is surprising for three reasons. The adsorbed hydrogen covered at least 55% of the surface, and the electrode potential exceeded both the H_2 evolution potential determined by slow cyclic voltammetry and the potential found to create unrecoverable charge during pulses from -0.5V. There are two possible explanations for this finding.

First, the strongly bound hydrogen sites that are necessary for H_2 evolution to occur may be blocked by chloride during stimulus pulses. Ludwig (1968) found that strongly bound hydrogen must be present for the recombination of adsorbed hydrogen atoms to occur. Bagotzky et al (1970) showed that the strongly bound hydrogen sites will be blocked by adsorbed Cl^- . He also showed the kinetics of Cl^- desorption are quite slow. It is, therefore, possible that the recombination step does not occur during these pulses because the strongly bound hydrogen is not available. Even though the electrode potential reached -1.2V, we measured no unrecoverable charge implying that no gas evolution occurred when pulsed from the 0V clamp potential. However, from the -0.5V clamp potential, H_2 evolution began at a potential near -1.0V. Changing the clamp potential from 0V to -0.5V removed

most of the adsorbed Cl^- , and allowed the adsorption of strongly bound hydrogen. The availability of strongly bound hydrogen is the most likely reason for H_2 evolution to occur during pulses from the -0.5V clamp potential.

The second explanation is that a minimum coverage of hydrogen, greater than 50%, may be required before the recombination reaction will begin. To examine this prospect more completely, we need to consider the electrode behavior during pulses from the two different clamp potentials. Initially, the clamp potential is 0V , so no adsorbed hydrogen was present. During pulses, a minimum hydrogen coverage of 52% was achieved. Less than 1% unrecoverable charge was detected, and so no significant H_2 evolution occurred. At the -0.5V clamp potential, the hydrogen coverage was approximately 50%, as determined from the cyclic voltammogram. This was similar to the coverage that existed at the end of the $-300\text{ }\mu\text{C}/\text{cm}^2$ pulse from 0V as determined above. During pulses from the -0.5V clamp potential, unrecoverable charge was detected, implying H_2 gas began to evolve, at total charge injections less than $-50\text{ }\mu\text{C}/\text{cm}^2$. It is, therefore, possible that about 50% coverage is a threshold, below which H_2 evolution cannot occur.

Unrecoverable charge was only detected on electrodes pulsed from a clamp potential of -0.5V SCE. For this reason we will only quantify the evolved H_2 on electrodes clamped at the more negative potential. Measurement of H_2 evolution on platinum is complicated by the occurrence of hydrogen adsorption reaction. Also, the fact that H_2 can be oxidized during the clamp (as seen by the positive current peak adjacent the negative H_2 evolution peak on the cyclic voltammogram), means that the actual H_2 evolution was larger than the unrecoverable charge measurement. We will use two methods to determine the charge stored by the H_2 evolution reaction on the platinum electrodes. For the first approach, we

assume that all the reversible processes, as determined from the slow cyclic voltammetry plots, went to completion during the pulse. Examining the cyclic voltammogram we find approximately $-75 \mu\text{C}/\text{cm}^2$ of charge is available for hydrogen adsorption. The double layer stored roughly $-47 \mu\text{C}/\text{cm}^2$ of charge as the electrode potential moved from -0.5V to -1.5V . Very little chloride was adsorbed and the charge associated with this reaction will be ignored. Thus, the total available reversible charge is approximately $-122 \mu\text{C}/\text{cm}^2$. Injecting $-300 \mu\text{C}/\text{cm}^2$ of charge, and assuming $-122 \mu\text{C}/\text{cm}^2$ of charge went into the above reversible processes, means $-178 \mu\text{C}/\text{cm}^2$ of charge went into H_2 evolution.

The second approach involves the finding that two thirds of the evolved gas can be recovered given short pulse times and an unstirred solution (Delahay, 1963). Using this method, only one third of the evolved H_2 would actually be detected as unrecoverable charge. Thus, the 22% unrecoverable charge measured during a $-300 \mu\text{C}/\text{cm}^2$ total charge pulse represents one third of the evolved hydrogen. This means that 66% of the total charge or $-198 \mu\text{C}/\text{cm}^2$ actually went into gas evolution. Comparing this result, derived with the two thirds recovery rule, with the number found using slow cyclic voltammetry, we find the two charge amounts differ by only 10%. Thus, the charge consumed by H_2 evolution during a $-300 \mu\text{C}/\text{cm}^2$ pulse probably falls somewhere between -178 and $-198 \mu\text{C}/\text{cm}^2$.

5.4.5 Summary

For a gold electrode, we can summarize the processes consuming charge during a $-175 \mu\text{C}/\text{cm}^2$ stimulus pulse. A graphical summary can be seen in figure 5-5. From the cyclic voltammogram, it is known that double layer charging, H_2 evolution, and chloride adsorption all occur within the potential range tested. Assuming a double layer capacity of $50 \mu\text{F}/\text{cm}^2$, the double layer stored $-87.5 \mu\text{C}/\text{cm}^2$ of charge. The measured unrecoverable

Figure 5-5 - Summary of charge going into various reactions.
Gold, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

charge was $-70 \mu\text{C}/\text{cm}^2$ of charge. This was assumed to be completely H_2 evolution because of the irreversible nature of H_2 evolution on gold. Only $-17.5 \mu\text{C}/\text{cm}^2$ of the injected charge remained. From the cyclic voltammogram, we found that $-62.5 \mu\text{C}/\text{cm}^2$ of reversible charge was available between 0V and -0.6V, excluding the double layer charge. Thus, only $-17.5 \mu\text{C}/\text{cm}^2$ out of the $-62.5 \mu\text{C}/\text{cm}^2$ of available charge was used during the pulse. The most likely slow process consuming this small amount of charge is chloride desorption/adsorption. Thus, it appears the chloride desorption/adsorption process is too slow to store the maximum available charge on gold electrodes during typical neurostimulation pulses. So, during a $-175 \mu\text{C}/\text{cm}^2$ total charge pulse, we deduced that double layer charging stored $-87.5 \mu\text{C}/\text{cm}^2$ of charge, chloride desorption stored $-17.5 \mu\text{C}/\text{cm}^2$ of charge, and $-70 \mu\text{C}/\text{cm}^2$ of charge went into H_2 evolution.

The determination of the processes participating during a $-300 \mu\text{C}/\text{cm}^2$ total charge pulse on a platinum electrode, clamped at 0V SCE, can also be summarized. Figure 5-6 shows the results if we assume that chloride completely desorbs, while figure 5-7 shows the results if we assume that no chloride desorbs. Based on the cyclic voltammogram, there are four processes that are possible during a pulse. They are double layer charging, H_2 evolution, chloride adsorption, and hydrogen adsorption. Assuming a double layer capacity of $47 \mu\text{F}/\text{cm}^2$, the double layer charging process stored $-56 \mu\text{C}/\text{cm}^2$ of charge. We found very little, if any, H_2 evolution occurred during any pulse from 0V SCE, as demonstrated by the lack of detected unrecoverable charge. If we assume all the chloride desorbed during a pulse, then $-56 \mu\text{C}/\text{cm}^2$ of charge went into this process. The remaining $-188 \mu\text{C}/\text{cm}^2$ of the charge went into hydrogen adsorption. From the cyclic voltammogram we know the total hydrogen adsorption charge available is $-362 \mu\text{C}/\text{cm}^2$. Therefore, the hydrogen adsorption reaction would be 52% complete. At the other extreme, we can assume no

Figure 5-6 - Summary of reaction charge storage on platinum from 0V. Platinum, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure 5-7 - Summary of reaction charge storage on platinum from 0V. Platinum, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

chloride desorbed. In this case, the only two processes consuming charge were double layer charging and hydrogen adsorption, and we find that $-244 \mu\text{C}/\text{cm}^2$ of charge was stored by hydrogen adsorption. With no chloride desorption the hydrogen adsorption reaction would be 67% complete. So, during a $-300 \mu\text{C}/\text{cm}^2$ total charge pulse on a platinum electrode clamped at a potential of 0V, we estimate that double layer charging stored $-54 \mu\text{C}/\text{cm}^2$ of charge, chloride adsorption stored between 0 and $-56 \mu\text{C}/\text{cm}^2$ of charge, hydrogen adsorption stored between -188 and $-244 \mu\text{C}/\text{cm}^2$ of charge, and no H_2 evolution occurred.

Lastly, we can summarize the participation of reactions on platinum electrodes pulsed from -0.5V. The summary is shown graphically in figure 5-8. During a $-300 \mu\text{C}/\text{cm}^2$ pulse, the fast recoverable charge was $-47 \mu\text{C}/\text{cm}^2$. We assumed this charge to be double layer charge. The charge consumed by H_2 evolution was found to be somewhere between -178 and $-198 \mu\text{C}/\text{cm}^2$. The upper limit was calculated using the unrecoverable charge and the two thirds recovery rule. The lower limit was established by assuming all the reversible charge determined by the P-C and cyclic voltammogram is stored during the pulse. The amount of charge in the hydrogen adsorption reaction depends on the H_2 evolution assumptions. The hydrogen adsorption reaction stored $-53 \mu\text{C}/\text{cm}^2$ of charge assuming the upper limit of H_2 evolution, and $-75 \mu\text{C}/\text{cm}^2$ of charge assuming the lower limit of H_2 evolution determined above. From -0.5V very little chloride was adsorbed, and this reaction is neglected. Thus, about $-47 \mu\text{C}/\text{cm}^2$ of charge went into the double layer, -53 to $-75 \mu\text{C}/\text{cm}^2$ of charge into hydrogen adsorption, and -178 to $-198 \mu\text{C}/\text{cm}^2$ of charge into H_2 evolution.

Figure 5-8 - Summary of reaction charge storage on platinum from -0.5V. Platinum, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

6. Discussion of Results and Conclusion

6.1 Electrochemical Processes

The P-C technique was developed to study the electrode behavior on time scale consistent with typical stimulus pulses. The instrumentation and technique have been shown to measure accurately the injected and recovered charge during a typical stimulus pulse. Further, the technique has been used to study the behavior of different electrode materials, stimulus parameters, and charge injection levels. The electrochemical behavior of the electrode during a stimulus pulse has been examined for the first time. We found that kinetic considerations are clearly important. The H_2 evolution potential becomes much more negative during a stimulus pulse than would be predicted by slow cyclic voltammetry. Because the potential is more negative, the double layer process can store much more recoverable charge during a neural stimulus pulse. On gold, we also can measure exactly how much hydrogen was evolved, and at what charge injection level the process began.

On platinum, the safe charge injection limit exceeded the $-300 \mu C/cm^2$ instrumentation charge limit for pulses from 0V. This correlates with Brummer's finding that the hydrogen adsorption reaction could store up to $350 \mu C/cm^2$. However, our measurement was made under conditions that matched typical neural stimulation. The $300 \mu C/cm^2$ level is much larger than the $74 \mu C/cm^2$ limit predicted by Robblee. We matched her finding, but showed that much more charge can safely be injected beyond this charge level. It would appear that her method give a conservative estimate of the safe charge limit.

We know that many processes likely occur simultaneously, and on platinum, they cannot be aligned with the P-C charge segments as they were for gold. Hydrogen adsorption and hydrogen reoxidation both occur in the slow recoverable charge segment. It was also not possible to separate directly chloride desorption from hydrogen adsorption. However, it was possible to deduce a range of charge stored by each of these processes. This makes the P-C technique extremely useful, even in more complex systems.

Using the information gained by this study we can consider how it might be used in the design of a prosthesis system. The electrode and stimulation waveforms are two critical parts of this system. We can look at what shape the ideal waveform might take under various conditions. We will also consider what are important factors in electrode design.

6.2 Neural Prosthesis Design Considerations

6.2.1 The Ideal Stimulus Pulse

The ideal pulse shape is constrained by physiological and electrical factors. The pulse width compromise at 100 μ S is a combination between using the least charge (result of a physiological constraint), and using a reasonable current (electrical constraint). Electronically, a controlled current waveform is simple to generate, and will have the most stable stimulation threshold over time. These constraints have made the 100 μ S controlled current waveform the accepted standard, and no other stimulation paradigm has proven more effective.

The total injected charge is the one parameter that is electrochemically constrained. The injected charge is determined from the stimulus current amplitude and the pulse

duration. Assuming that an electrode product is responsible for tissue damage, then a safe stimulus pulse should generate no unrecoverable charge as determined by the P-C method. The total charge parameters should be chosen so that the injected charge will not exceed the safe charge injection limit. For gold, the charge is limited to $-80 \mu\text{C}/\text{cm}^2$, for SS316, the number is greater than $-150 \mu\text{C}/\text{cm}^2$, and for platinum the value is at least $-300 \mu\text{C}/\text{cm}^2$.

6.2.2 The Ideal Reversal Pulse Shape

The optimal reversal waveform depends entirely on the processes that occurred during the stimulus pulse. The reversal pulse will be discussed in the context of the electrochemical processes that occurred during the stimulus pulse. Because the reversal waveforms are affected by the charge level, the discussion is divided into three charge injection categories.

Small Charge Injections (less than $-50 \mu\text{C}/\text{cm}^2$)

When less than $-50 \mu\text{C}/\text{cm}^2$ of charge is injected, the charge goes into fast recoverable processes for the metals considered. On gold, the primary process occurring during stimulation is believed to be double layer charging. On platinum, in addition to double layer charging, hydrogen adsorption is found to occur. Oxide reduction and double layer charging are the primary reactions storing charge on SS316. No unrecoverable charge was detected on any of the three materials below $-50 \mu\text{C}/\text{cm}^2$ of total charge. Therefore, no products were created, and we believe no tissue damage should be observed.

The reversal pulses should be fast and charge matched to the stimulus pulse for charge injections below $-50 \mu\text{C}/\text{cm}^2$. This is because most of the injected charge was found to be rapidly reversible. The ideal reversal pulse would be a large current spike that

returned the electrode potential to its prestimulus value very quickly. The charge should be returned quickly because at the $-50 \mu\text{C}/\text{cm}^2$ charge level, the electrode potential is more negative than the H_2 evolution potential as determined by slow cyclic voltammetry. Thus, long delays or slow reversal could result in H_2 evolution.

Medium charge injections (-50 to $-150 \mu\text{C}/\text{cm}^2$)

Increasing the injected charge to the -50 to $-150 \mu\text{C}/\text{cm}^2$ range begins to separate the materials based on their electrochemical behavior. Gold is now believed to have two main processes that store the charge. Double layer charging was found to store all the charge up to about $-80 \mu\text{C}/\text{cm}^2$ of total charge. Beyond that value all of the charge goes into H_2 evolution. The point at which double layer charging stops and H_2 evolution begins is very distinct. During pulses from 0V , the major process occurring on platinum is hydrogen adsorption, while on SS316 the major process is likely oxide reduction. The reversal of hydrogen adsorption apparently becomes slower as the total charge increases. However, the reversal of oxide reduction apparently does not slow with increased total charge. Less than 1% of injected charge was found in the unrecoverable charge segment on both platinum and SS316 during pulses from 0V in the -50 to $-150 \mu\text{C}/\text{cm}^2$ of total charge range. Thus, no hydrogen was assumed to evolve from either metal.

The optimum reversal pulse shape is different for each material in this charge injection range. With up to $-80 \mu\text{C}/\text{cm}^2$ of total charge, gold has double layer charging as the main process. Thus, the reversal pulse should be of short duration and charge matched with the stimulus pulse. The presence of unrecoverable charge beyond $-80 \mu\text{C}/\text{cm}^2$ of injected charge, means that the reversal charge should no longer match the injected charge. The reversal pulse should be kept at $-80 \mu\text{C}/\text{cm}^2$ of charge, regardless of the amount of

injected charge. The electrode potential will be driven positive by the excess reversing charge.

On platinum, a much larger portion of the injected charge was returned during the clamp as slow recoverable charge. This means that the reversal pulse should also be slowed down to accommodate the reversal processes. Failing to do this will drive the electrode more anodically during the reversal phase. The more positive potential stems from trying to drive charge into the reversal processes faster than they can accept the charge. The result is the electrode moves more positive, and electrode corrosion may result. The anodic drift will occur even though all of the charge is recoverable, because the reversal rate is not as fast as the forward rate and cannot return the charge as fast. The way to avoid this problem is to slow down the reversal pulse so it matches the rate the processes can be reversed.

SS316 did not exhibit nearly as much slow recoverable charge as platinum. Most of the injected charge on SS316 was stored in fast processes, so the reversal pulse can rapidly return the charge fast. Therefore, the ideal reversal pulse will be a large current spike that contains all the injected charge.

Large charge injections (-150 to -300 $\mu\text{C}/\text{cm}^2$)

The gold electrode was not tested over this charge range. Since -150 $\mu\text{C}/\text{cm}^2$ of total charge already exceeded its safe charge injection limit by -70 $\mu\text{C}/\text{cm}^2$, so no new information would have been gained by testing gold over this large total charge range. The platinum electrode was found to accommodate up to -300 $\mu\text{C}/\text{cm}^2$ of injected charge with the reversible processes. During a -300 $\mu\text{C}/\text{cm}^2$ total charge pulse on platinum, double layer

charging only stored about one sixth of the charge. The percent of the total charge in stored in double layer charging decreased with increasing charge. At the $-300 \mu\text{C}/\text{cm}^2$ total charge level, the hydrogen adsorption process was somewhere between 50 and 70% complete. Chloride desorption likely participated, and the value was less than $-56 \mu\text{C}/\text{cm}^2$ of charge. Chloride may be blocking the strongly adsorbed hydrogen sites, and impeding H_2 evolution. More than half the injected charge was returned in the slow recoverable process that was likely some of the hydrogen adsorption. Thus, the reversal pulse must also be slowed accordingly. An initial current spike is necessary to return the electrode potential to its prestimulus value. In this case though only half the injected charge should be placed in this current spike because only half the charge was returned in the fast recoverable charge segment. The rest should be spread out in an exponentially decaying current.

We can now begin to build a picture of how these electrodes operate. On gold, the charge goes into the very fast double layer charging process up to the $-80 \mu\text{C}/\text{cm}^2$ level at which H_2 begins to evolve. Once H_2 begins to evolve, all the charge is assumed to go into this irreversible process. The slow recoverable charge constitutes less than 20% of the total charge on gold. An schematic picture of how this happens is shown in Figure 6-1. Platinum, by contrast, has a very slow transition between the fast, slow, and unrecoverable processes. This has been determined by considering the pulses from both the 0V and -0.5V clamp potentials. A schematic is also shown in Figure 6-1. As the injected charge level increases, the charge recovered in the fast recoverable portion slowly decreases from over 60% to less than 20%. The slow recoverable portion increases to 60%. While we could not detect unrecoverable charge during pulses from 0V on platinum, the pulses from -0.5V showed a slow transition between slow recoverable charge and unrecoverable charge. Thus, we could expect the transition during pulses from 0V would also be slow.

Figure 6-1 - Platinum and gold current pulses showing how the charge injection likely changes with increasing charge.

6.2.3 Methods to Maximize Safe Charge Injection

The key to safe charge injection is maximizing the recoverable charge. The technique for accomplishing this is somewhat material dependent. For gold, the best way is to have no delay and use very fast reversal pulses. A delay must be used in a neural prosthesis to avoid quenching the developing action potential with the reversal pulse, but removing the delay does maximize the recoverable charge. Reversible charge injection cannot exceed $-80 \mu\text{C}/\text{cm}^2$ of charge. On platinum, as with gold, the maximum charge recovery occurs with no delay. At low charge injections, the reversal pulse can be tens of microseconds, because the stimulus processes can be reversed very rapidly. At higher levels the charge reversal, the pulses must include the exponentially decaying current to accommodate the more slowly reversing processes at the higher stimulus charge levels.

6.2.4 Methods to Maximize Tissue Damage

Knowing how to maximize the tissue damage would help to understand the behavior of electrodes during stimulation. Assuming unrecoverable charge is damaging, long delays will increase the levels of damage at any total charge level. Unrecovered charge can also be generated on gold by exceeding the $-80 \mu\text{C}/\text{cm}^2$ reversible charge injection limit. Hydrogen evolution is assumed to be the irreversible process occurring beyond this point. The straight forward generation of H_2 on gold is actually quite useful for tissue damage studies. It is possible to generate a known amount of hydrogen with this metal.

The best way to create unrecoverable charge on platinum is to force the interpulse potential close to the H_2 evolution potential, as determined by slow cyclic voltammetry. This would reduce the hydrogen adsorption reaction that consumes most of the charge

injected from more positive potentials. Long delays are important in maximizing the unrecoverable charge on platinum, because H_2 can be reoxidized on this metal. Time must be provided for the evolved H_2 to diffuse away. A delay of 1000 μS more than doubled the amount of unrecoverable charge in this study.

6.2.5 The Electrolyte in the Body

Many other compounds exist in the extracellular fluid that were not used in the electrolyte for this study. Certain compounds such as hemoglobin need not be considered as an electrolyte, because if the blood vessels are compromised to the extent that hemoglobin escapes, other complications will make the prosthesis unusable. However, there are proteins and glucose in the extracellular fluid that can be studied. Electrochemically, the proteins could be reduced during the stimulus pulse. This could have two effects. First, the electrode potential may not move as negative during the pulse. The proteins would store some of the charge that would otherwise go into the processes measured in this study. This would be beneficial because a more positive electrode potential would create fewer electrochemical products. However, one of the products would be the reduced protein. The reduced protein may stimulate the inflammatory response, or it may oxidize some other compound that may reside on a cell membrane.

This could result in tissue damage. Glucose could have similar effects. The electrochemical effects could be tested with the P-C method by adding these compound individually to the electrolyte. The effect of the reduced species on the adjacent tissue, though, would have to be tested in vivo.

6.2.6 The Ideal Electrode Material

A good electrode material must meet many criteria, only some of which are related to electrochemistry. Because of this, different materials are used for different applications that maximize the factor important for that application. From the electrochemical standpoint, there are three key considerations. First, the ideal electrode material must be able to store and return as much charge as possible. With smaller electrodes, materials with charge capacities in the millicoulomb per square centimeter range must be found. None of the materials tested in this study meets this criteria. Gold, as has been shown, has very little charge capacity. Platinum has this attribute to some extent with its hydrogen adsorption reaction. This reaction is limited, though, to around $-350 \mu\text{C}/\text{cm}^2$. Thus, including double layer charge and chloride desorption charge, the safe charge limit with platinum is probably around $-500 \mu\text{C}/\text{cm}^2$.

The second consideration is that the process must be fast enough to store the injected charge during the $100 \mu\text{S}$ pulse. The process does not have to reverse rapidly, because the reversal pulse can be slowed. The double layer process is more than fast enough to store charge during a typical stimulus pulse on all the materials in this study. Platinum also fulfills this requirement with the hydrogen adsorption reaction that participate to a great extent in the $100 \mu\text{S}$ pulse. The problem with both metals is their relatively small safe charge injection limit. Higher safe limits can be achieved by roughening the electrode to increase the surface area, but the small pores cannot participate during stimulus pulses. Thus, the increased capacity is not effective during the stimulus pulse.

Lastly, the ideal electrode material would also be immune to corrosion in a chloride containing media. Corrosion of the electrode must be avoided at all costs. Gold corrodes

very rapidly; SS316 and platinum both corrode but more slowly. Therefore, none of these materials meet this requirement.

Any electrode material must be workable so it can be made into the many shapes required for the different prosthesis applications. While this is not an electrochemical consideration, it can determine the applications in which the material can be used. It is unlikely that any one material will have all the mechanical properties required for the many different applications. Therefore, a material that could be permanently plated or sputtered onto a substrate may be the best. This way, a strong material such as stainless steel intramuscular electrode could be coated with and have the surface properties of a different material. Similarly, a very stiff intracortical electrode could be made by using a different substrate.

6.2.7 The Ideal Electrode Shape

While this study did not directly address the issue of electrode shape, electrochemical parameters contribute to a good shape. The electrode shape of most prostheses is based on the mechanical requirements of the application. Intramuscular electrodes are usually barbed, and nerve cuff electrodes are usually cylindrical bands, etc. Electrochemical considerations rarely play a role in electrode design.

The charge injection levels are safest when the current is uniformly distributed over the electrode surface. Nonuniform regimes will undoubtedly cause higher levels of toxic products for the same injected charge. This is because at certain areas the current will be much higher and the effective charge density will greatly exceed the average charge density. Certain shapes such as spheres, recessed disks, or rounded disks can provide a

uniform current distribution over the electrode surface. Other shapes, such as the barbed tip, or the flat disk electrode do not provide uniform current distribution. For a flat disk electrode, about 60% of the current is directed through an outer annulus of 20% of the area (Rubinstein 1987). This means the electrode can safely inject less than 33% of the safe charge limit found with electrochemical studies. A disc electrode can be sunk into the surrounding insulating material. A hole that is only $1/3$ as deep as the radius of the electrode creates a current distribution that varies less than 5% over the radius of the electrode (Rubinstein 1987; Ksienski, 1990). This is very close to uniform for practical purposes, and would result in significantly larger safe charge injection. Since factors other than electrochemical concerns must be considered in electrode design, uniform current distribution will not always be achieved. However, it should be included in the design criteria.

6.3 Conclusions

With the P-C method we have increased the understanding about how neural stimulating electrodes operate. The findings are: 1) the electrode potential during a stimulus pulse on gold, platinum, and SS316 electrodes can significantly exceed the slow cyclic voltammetry H_2 evolution potential, 2) the primary charge storage reactions are different for the three different materials, 3) the safe charge injection limits and optimum reversal waveform can be resolved, 4) a 3 element electrical analog model can mimic most observed electrode behaviors, and 5) the charge stored in each of the reactions occurring during the stimulus pulse can be deduced from the P-C data. These findings are listed in the following paragraphs.

The first finding is that gold, platinum, and SS316 electrodes exhibit some similar behaviors during neural stimulus pulses. The primary common attribute is that during typical stimulus pulses no unrecoverable charge was detected, even though the electrode potential exceeded the slow cyclic voltammetry hydrogen evolution potential by hundreds of millivolts. We conclude the lack of unrecoverable charge means that H_2 was not evolved. Therefore, the reaction potentials determined by slow cyclic voltammetry do not necessarily reflect the potentials at which the reaction will occur during stimulus pulses. Kinetics must be considered for an accurate portrayal of electrode behavior under stimulation conditions.

The primary difference between the electrode materials was the relative charge found in the three time segments during the reversal pulse. By analyzing these differences, it was found that only two main processes appeared to be involved in charge transfer on gold electrodes during a pulse. One was quite fast (likely double layer charging), while the other was irreversible (likely H_2 evolution). Platinum and SS316 each displayed an additional reversible reaction that could store much more charge than gold. On SS316, the additional process was very rapid in both the forward and reverse direction. The process was likely oxide reduction. On platinum, the process could go forward quite rapidly, but the reversal could take many milliseconds to complete. The process was likely hydrogen adsorption.

The third finding was deriving the stimulus waveforms that would minimize tissue damage and electrode corrosion. The safe charge injection limits can be estimated using the unrecoverable charge measurement. It was found that in all cases the safe charge injection limit was greater than that calculated by limiting the potential during the pulse to the slow cyclic voltammetry H_2 evolution potential. The safe limit was the smallest for gold at about

-150 $\mu\text{C}/\text{cm}^2$. The limit was in excess of -150 $\mu\text{C}/\text{cm}^2$ for SS316 and -300 $\mu\text{C}/\text{cm}^2$ for platinum. While these measurements are for single pulses under uniform current conditions, they are based on the direct measurement of unreversed products. Lower limits may result from rapid pulsing and non uniform current.

The P-C results show the optimum reversal pulse shape is a large current spike followed by an exponentially decaying current timed to match the rate of the reversal processes. The large current spike should return the electrode potential to its prestimulus value most rapidly. We can examine the model to illustrate the reason for this pulse shape. When a constant current pulse is applied to the model most of the charge goes onto C_{DL} , and some goes onto C_2 . When the pulse is over, the charge on the double layer capacitor will move onto C_2 , and possibly through T_2 , as long as the potential of C_{DL} exceeds the potential of C_2 . Thus, returning the double layer potential to its prestimulus value will prevent any additional charge from moving into other processes. Once the electrode potential has been returned to its prestimulus value, the charge must be returned at a rate consistent with the processes being reversed. Returning the charge too fast will result in a positive drift of the electrode potential and possible corrosion under conditions of balanced charge injection.

The fourth conclusion we can draw from this work is that a 3 element model will imitate most of the observed electrode behavior. The model describes the electrode behavior, and is not mechanistic in nature. It was found by varying the clamp potential on gold electrodes in sulfuric acid we deduced, that the slow recoverable component behaved like the linear capacitor, C_2 , in the model. The presence of this element in the model duplicates the observation that the double layer potential exceeds the reaction potential

during stimulating pulses. It was also found that the expected behavior of the 3 element model matched the electrode behavior during the pulse width and delay experiments in phosphate buffered saline. This was true for both gold and platinum electrodes. In general, the fast recoverable charge decreased, the slow recoverable charge increased, and the unrecoverable charge increased with increasing pulse width and delay. This may mean that tissue damage is more likely with longer pulse widths and delays.

The fifth result was to deduce the amount of charge that was stored in each of the reactions that occurred during the stimulus pulse. This was done for gold and platinum in phosphate buffered saline. We showed that the majority of the recoverable charge on gold went into double layer charging, while the majority of the recoverable charge on platinum goes into hydrogen adsorption. Specifically, on gold during a $-175 \mu\text{C}/\text{cm}^2$ total charge pulse, $-87.5 \mu\text{C}/\text{cm}^2$ of charge went into the double layer, $-17.5 \mu\text{C}/\text{cm}^2$ of charge went into chloride desorption, and $-70 \mu\text{C}/\text{cm}^2$ of charge went into H_2 evolution. On a platinum electrode pulsed with $-300 \mu\text{C}/\text{cm}^2$ of charge from 0V, $-56 \mu\text{C}/\text{cm}^2$ of charge went into the double layer, between 0 and $-56 \mu\text{C}/\text{cm}^2$ of charge went into chloride desorption, -188 to $-244 \mu\text{C}/\text{cm}^2$ of charge went into hydrogen adsorption, and no charge went into H_2 evolution. During a $-300 \mu\text{C}/\text{cm}^2$ pulse on platinum from -0.5V SCE , $-47 \mu\text{C}/\text{cm}^2$ of charge went into the double layer, -55 to $-75 \mu\text{C}/\text{cm}^2$ of charge went into hydrogen adsorption, and -178 to $-198 \mu\text{C}/\text{cm}^2$ of charge went into hydrogen evolution. Of the hydrogen that was evolved almost two thirds of it was reoxidized during the 20 mS reversing potential clamp.

We have shown that the electrochemistry during typical neurostimulation pulses can be analyzed with the P-C method. We have also shown the value of this method in deriving safe charge injection limits, reversal pulse shape, and the charge stored by the

reactions occurring during the stimulus pulse. The P-C method can be used to study many other aspects of stimulating electrode behavior some of which are discussed in the following section.

6.4 Future Work

6.4.1 Instrument and Cell

To study the safe charge injection limits of platinum electrodes stimulated from 0V SCE, it will be necessary to increase the stimulator charge measuring capabilities. We expect that the limit should be somewhere around $-500 \mu\text{C}/\text{cm}^2$, so the present charge measuring capacity would need to be doubled. We cannot simply reduce the electrode size to accomplish this goal. Reducing the electrode size will increase the access resistance and likely destabilize the instrument. Doubling the charge measuring capability would involve increasing the capacity of the circuit that measures the charge.

The study of micro electrode operation would also be interesting. Micro electrodes do not have the IR correction and compensation problems of their macro counterparts. The instrumentation would have to be altered so that very small currents and charges could be measured. This would involve completely rebuilding the output stage of the instrument. It has been found that micro electrodes can inject up to $-800 \mu\text{C}/\text{cm}^2$ of total charge with no observed tissue damage (Bullara et al, 1983). Fewer products may be created on these electrodes, or they may be operating more reversibly than their macro counterparts. Thus, it may help the understanding of electrode behavior to study charge injection on micro electrodes.

6.4.2 Other

The effect of nonuniform current distribution on the amount of unrecoverable charge would be interesting to study. The safe charge injection limits should decrease with non uniform current, because unrecoverable products will be created in the areas of high current density long before the average safe charge injection limit is reached. Many electrodes used in neural prostheses do not have uniform current distribution. Is unknown how large the effect of non uniform current distribution is, especially in the more complex shapes such as the barbed intramuscular electrode. Studying the safe charge injection limits of electrodes similar to those used in the body could indicate just how much more charge could be injected if uniform current distribution were used. Safe charge injection limits for the actual stimulating electrodes could also be determined.

The possibility that adsorbed chloride may impede H_2 evolution during short stimulation pulses on platinum is very intriguing. Studying the effect of the chloride ion concentration on the evolution of H_2 during stimulation pulses may aid in the understanding of how platinum stimulating electrodes operate in the body. It may also aid the understanding of the H_2 evolution process on platinum. The effect of ions with different inhibition properties on the amount of strongly bound hydrogen could be studied.

Oxygen radicals created by the reduction of oxygen have become a popular mechanism for the observed damage. Radicals are known to be destructive to tissue, and oxygen is likely reduced during a stimulus pulse. Adding oxygen to the system would be another logical step toward understanding the processes occurring during pulses in the body. With the baseline of electrode behavior in the absence of oxygen established with this study, we can now observe the contributions of oxygen by comparing the current results

with those in the presence of oxygen. Further, if a three electrode cell could be implanted in the body, the electrode could be clamped at a potential more positive than H_2 evolution but more negative than oxygen reduction. If tissue damage is observed under these circumstances, then oxygen radicals may be involved in stimulation induced tissue damage.

The electrolyte composition could be varied to test whether some of the compounds that exist in extracellular fluid can store charge during a stimulus pulse. The two important compounds are glucose and albumin. These compounds can be prevalent in extracellular fluid. The P-C method could be used to test whether these compounds can be reduced during a stimulus pulse, and further, whether they are reoxidized during the reversal pulse. While moving the P-C technique into the body is important, testing the more prevalent compounds in vitro would help to understand the more complex behavior that will likely occur in the body.

The P-C technique could also be used to study the response of different materials to typical neural stimulus pulses. Studying SS316 more completely, would help the intramuscular field. The study of iridium oxide would also be interesting. It has been found that while this material can store very large quantities of charge during slow cyclic voltammetry, the capacity decreases significantly during stimulation pulses. However, this material has not been subjected to the charge measurements possible with the P-C technique. It may be that it can use the very large charge capacities during the stimulus pulse, but the potentials may be very negative. Only by studying iridium oxide with the P-C method can we be certain of its actual safe charge injection limits. It will also tell us how to design the best reversing pulse for this material. Other materials that may be helpful are the conducting polymers, titanium, and the valve metals such as tantalum.

A future goal is to implement this technique inside the body. Doing this would allow direct measurement of the unrecovered charge in vivo. The measured unrecoverable charge could be compared with the observed tissue damage for a direct test of relation between unreversed electrochemical products and tissue damage. It would also permit the manipulation of processes more accurately. Controlling the prestimulus and post stimulus potentials could be used to directly manipulated the processes occurring on the electrode. Fulfilling this goal would be the first direct measurement of presence of unreversed electrochemical products during stimulation in vivo.

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Appendix A: Instrument Schematic

1 P0
 2 P2
 3 P4
 4 P6
 5 PH 2
 6 IPI/MULTIPLE PULSE
 7 START
 8 GND
 9 +5
 10 REST/CLAMP
 11 PH 1
 12 PH 3
 13 P5
 14 P7
 15 P1
 16 P3

Ext Trigger Directly From Board

NAME: OSCILLATOR CIRCUIT
 DATE: MARCH 14, 1988

NAME: PULSE WIDTH GENERATOR #1
DATE: MARCH 14, 1988

NAME: PULSE WIDTH GENERATOR #4
DATE: MARCH 14, 1988

NAME: POTENTIAL MONITOR
DATE: MARCH 14, 1988

NAME: CHARGE MONITOR
DATE: MARCH 14, 1988

Title	CURRENT BUFFER
Size	Document Number
REV	A
Date:	April 25, 1990
Sheet	of

**Appendix B: Typical Cyclic Voltammograms for
Gold, Platinum, and Stainless Steel**

Figure B-1

- A) - Gold in 0.05M H_2SO_4 . Area=4mm; N_2 atmosphere; 20 mV/S
- B) - Platinum in 0.15M H_2SO_4 . Area=4mm; N_2 atmosphere; 100 mV/S
- C) - stainless steel in 0.15M H_2SO_4 . Area=4mm; N_2 atmosphere; 100 mV/S

Figure B-2

- A) -Gold in 0.3M phosphate buffered saline. Area=4mm; N₂ atmosphere; 50 mV/S
- B) - Platinum in 0.3M phosphate buffered saline. Area=4mm; N₂ atmosphere; 30 mV/S
- C) - stainless steel in 0.3M . Area=4mm; N₂ atmosphere; 30 mV/S

Figure B-3 shows sweeps from 0.5V SCE to hydrogen evolution potential.

Figure B-3

- A) - Gold in 0.3M phosphate buffered saline. Area=4mm; N_2 atmosphere; 50 mV/S
- B) - Platinum in 0.3M phosphate buffered saline. Area=4mm; N_2 atmosphere; 50 mV/S
- C) - Stainless steel in 0.3M phosphate buffered saline. Area=4mm; N_2 atmosphere; 50 mV/S

Figure B-4A

Gold in 1.0M phosphate buffered saline. Before electrochemical cleaning.

Only sonicated in EtOH. Area=4mm. N_2 atmosphere, 500 mV/S

Figure B-4B

Gold in 1.0M phosphate buffered saline. After cleaning by evolving H_2 .

Area=4mm; N_2 atmosphere; 500 mV/S.

A and B differ in the potential range swept.

Figure B-4C

Platinum in 1.0M phosphate buffered saline. Before cleaning. Only sonicated in EtOH.

Area=4mm; N₂ atmosphere; 150 mV/S

Figure B-4D

Upper: Platinum in 1.0M phosphate buffered saline after cleaning by evolving H_2 .

Upper and lower are the same electrode swept through different potential ranges.

Area=4mm; N_2 atmosphere; 150 mV/S

Figure B-5A

Gold standard cyclic voltammogram in 1.0M phosphate buffered saline.

Sweep rate 500 mV/S, N₂ atmosphere, 4mm area.

B)

C)

Figure B-5B

Platinum standard cyclic voltammogram in 1.0M phosphate buffered saline.

Sweep rate: 150 mV/S, N₂ atmosphere, 4mm area.

Upper: from 0V clamp potential; Lower: from -0.5V clamp potential.

Appendix C: Typical Potential versus Time plots

Figure C-I - Potential pulse for gold.
0.05M sulfuric acid, N₂ gas, 4mm area

Figure C-2 - Potential pulse for gold, platinum, and SS316.

0.3M phophate buffered saline, N2 gas, 4 mm area

Figure C-3 - Potential pulses for gold and platinum.
1.0M phosphate buffered saline, N₂ gas, 4 mm area

Appendix D: A Typical Experiment

Preparations

The importance of meticulous methods cannot be overstressed in electrochemistry. Minor alterations in methods or cleanliness can change the results. Inconsistency in either of these two can create a variability which makes interpreting the results very difficult. With this in mind, what follows is the description of a typical experiment in the hope future workers will more easily repeat the results given a proper description.

The first step involves washing all glassware in 50% sulfuric acid, 50% nitric acid solution. The cell and any ancillary containers are cleaned for every experiment. The reference electrode apparatus is cleaned periodically (every six months or so). Don't put the Pd in the acid bath as it will dissolve! Solution containers are cleaned when new solution is made. Water containers cleaned about once a year because contaminants are introduced very slowly. After acid dipping, all glassware is rinsed with ultrapure water.

Electrode manufacture.

The first step in making electrodes is to cut the round glass bottoms. Slide cover plates make an ideal product for this application. Simply mark a small circle on the cover slip with a diamond tip glass cutter. The glass surrounding the circle can be broken off with tweezers. The glass plates are then washed in EtOH and wiped dry with a Kimwipe.

Four centimeters of electrode wire for each electrode is then cut from the roll and sonicated in EtOH for 1 to 2 minutes. A small amount (about .25 ml/disk) of the ultraviolet

curing polyimide is then placed on the glass disks and spread over the surface with a glass rod. The glass disks are then placed in a jig that allows the electrode wires to be placed vertically onto the disks and held there. The jig must allow for light from the ultraviolet source to hit the polyimide on the disks. Once the electrodes are placed vertically onto the polyimide coated disks, the polyimide is cured by shining the 275W sunlamp onto the apparatus for 10 minutes. The polyimide is very wavelength specific and you must use the wavelength used in the sunlamps. (EPROM erasing lights do not work).

Reference Electrode Preparations

The reference electrode is charged by passing a negative DC current between the small gold electrode in the reference electrode apparatus and the Pd wire (Pd wire is the cathode). The current should be approximately 1 mA per cm^2 of Pd wire area. The charging time is approximately one hour. The charging electrolyte should not contain chloride as the small gold "counter" electrode in the reference compartment will corrode and plate onto the Pd electrode. The charging electrolyte used for this study was 0.1M sulfuric acid. When the charging is complete the acid is washed from the reference electrode apparatus with the electrolyte to be used for the experiment. Be sure to remove all the acid as it can diffuse back into the working solution during the experiment.

While the reference electrode is being charged, bubble the gas through the electrolyte reservoir to purge any undesirable atmospheric gases (such as oxygen). This is generally done for an hour prior to the experiment.

Electrode cleaning

There are two levels of electrode cleaning performed for these experiments. The first level consists of sonicating the electrode in EtOH for one minute. This removes most gross impurities. Further cleaning is accomplished by pulsing the electrode past HEP_{pc} (150 to 200 $\mu C/cm^2$ for gold) at 1 Hz for one minute. This pushes the electrode potential well below that required to evolve hydrogen during a 100 μS pulse, and gives a double layer capacity of 40-50 $\mu F/cm^2$ in phosphate buffered saline. platinum and stainless steel do not show this cathodic cleaning ability, but are cleaned the same way to maintain experimental consistency.

The electrode is placed in the cell prior to filling it with electrolyte. The cover is replaced on the cell and it is then filled with electrolyte. The solution is moved from the reservoir by closing the outlet to the outside and forcing solution through the glass tubes into the cell. Excess solution is drawn up through the reference electrode compartment until the desired fluid height is reached. The height is determined once on a new cell using a ruler to get 5 mm of fluid over the disk. A mark is then made on the cell (with a diamond tip glass cutter) at the base of the meniscus. In the future, the solution is removed until the meniscus lines up with the mark on the cell. The reservoir outlet to the air remains plugged so the gas now passes over the solution into the cell.

Experimental Procedure

At this point the electrode is connected to the instrument and is ready to be "clamped" at the resting potential as determined by the experimenter. Points to remember are:

- 1) Make sure the calomel/palladium reference electrode switch is in the palladium reference electrode position.

- 2) Move the speed to its slowest position.
- 3) Dial both IR correction and IR compensation dials to zero.
- 4) Move current resolution switch to the 100 mA/V position.
- 5) Move current amplifier (100x + LPF) switch to x1.
- 6) Now move "clamp" switch to the potential control position.

Failing to do any one of these steps will result in the instrument not clamping the electrode properly, and the electrode surface will be changed irreparably.

Once the electrode is clamped, the IR correction and compensation must be set. This is done by pulsing the electrode continuously (usually at 1 Hz) with sufficient current to flatten the end of the pulse potential using about 30 μ S pulse width and 100 μ S delay. The oscilloscope should be set to a small time per division such as 2 or 5 μ S/div. The entire wave won't fit on the screen, but by pre and post triggering the scope the pulse/delay transition can be seen. The IR correction should be increased until the end of the stimulus pulse aligns with the potential when the current becomes 0. To do this move the current waveform down until it overlaps the potential waveform as shown in Figure D-1. Any electronic artifacts during the switching time (1-2 μ S) should be ignored. The best way to learn the proper procedure is to use a high precision resistor in an electronic load. Check the result you get using the above procedure with the known resistance in the load (it is best to actually measure the resistance with an ohm meter). A check on how well the IR correction is set is to look at the beginning of the stimulus pulse. The potential should project back to the resting potential right at the point when the current turns on. Move the current curve over the potential curve to see when this occurs.

The clamp time interval must be set properly to avoid introducing errors into the result. It is important to understand that in a system such as the one used for these studies no clear physical distinction exists between fast and slow recoverable reactions. A perfect instrument could clamp fast enough to only incorporate DL charge during the clamp. However, the current instrument is not perfect, and some cross over non DL (Faradaic) charge will be found in the charge acquired during the clamp. Some error will, therefore, always exist. Keeping a constant clamp time will keep the error in terms of percent of SR charge incorporated in the FR measurement fairly constant. It is toward the end of maintaining consistency of this error that the constant clamp time (usually 15 μ S) is imposed.

Setting the clamp speed is done by placing the first cursor on the potential waveform at the end of the pulse (Figure D-1), and separating the scope cursors by the desired interval (usually 15 μ S). The speed and compensation should be set such that the second cursor sits at the point the potential just reaches the resting potential. In general, a slight overshoot of the potential is desirable. When ringing is required to achieve the desired clamp speed keep it to ± 50 mV around the clamp potential. Constant clamp speed should be maintained throughout the experiment. It can and does change, and must be corrected periodically.

Figure D-1 - Waveforms for setting IR correction.
Gold, 1.0M PBS, 4mm area, N2 gas.

Appendix E: Data From Pulse Width and Delay Experiments

Figure E-1 - Charge potential curves for changes in pulse width.
Gold, #1, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.
A) Total charge, B) Fast recoverable charge.

Figure E-1 - Charge potential curves for changes in pulse width.
 Gold, #1, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.
 C) Slow recoverable charge, D) Unrecoverable charge.

Figure E-1 - Percent total charge curves for changes in pulse width. Gold, #1, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas. E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.

Figure E-1 - Charge potential curves for changes in pulse width.

A) Total charge, B) Fast recoverable charge.

Gold, #2, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-1 - Charge potential curves for changes in pulse width.

C) Slow recoverable charge, D) Unrecoverable charge.

Gold, #2, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-1 - Percent total charge curves for changes in pulse width.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Gold, #2, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-1 - Charge potential curves for changes in pulse width.

A) Total charge, B) Fast recoverable charge.

Gold, #3, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-1 - Charge potential curves for changes in pulse width.

C) Slow recoverable charge, D) Unrecoverable charge.

Gold, #3, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-1 - Percent total charge curves for changes in pulse width.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Gold, #3, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Gold, #1, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Gold, #1, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Gold, #1, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Gold, #2, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Gold, #2, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Gold, #2, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Gold, #3, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Gold, #3, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-2 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Gold, #3, 1.0M phosphate buffered saline, 4mm area, Nitrogen gas.

Figure E-3 - Charge potential curves for changes in pulse width.

A) Total charge, B) Fast recoverable charge.

Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-3 - Charge potential curves for changes in pulse width.
 C) Slow recoverable charge, D) Unrecoverable charge.
 Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: 0V SCE.

Figure E-3 - Percent total charge curves for changes in pulse width.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N2 gas.
 Clamp potential: 0V SCE.

Figure E-3 - Charge potential curves for changes in pulse width.

A) Total charge, B) Fast recoverable charge.

Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE

Figure E-3 - Charge potential curves for changes in pulse width.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE

Figure E-3 - Percent total charge curves for changes in pulse width.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N2 gas.
 Clamp potential: 0V SCE

Figure E-3 - Charge potential curves for changes in pulse width.

A) Total charge, B) Fast recoverable charge.

Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-3 - Charge potential curves for changes in pulse width.
C) Slow recoverable charge, D) Unrecoverable charge.
Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N2 gas.
Clamp potential: 0V SCE.

Figure E-3 - Percent total charge curves for changes in pulse width.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: 0V SCE.

Figure E-4 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-4 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-4 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: 0V SCE.

Figure E-4 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-4 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-4 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: 0V SCE.

Figure E-4 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-4 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: 0V SCE.

Figure E-4 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N2 gas.
 Clamp potential: 0V SCE.

Figure E-5 - Charge potential curves for changes in pulse width.

A) Total charge, B) Fast recoverable charge.

Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-5 - Charge potential curves for changes in pulse width.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-5 - Percent total charge curves for changes in pulse width.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: -0.5V SCE.

Figure E-5 - Charge potential curves for changes in pulse width.
A) Total charge, B) Fast recoverable charge.
Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
Clamp potential: -0.5V SCE.

Figure E-5 - Charge potential curves for changes in pulse width.
 C) Slow recoverable charge, D) Unrecoverable charge.
 Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: -0.5V SCE.

Figure E-5 - Percent total charge curves for changes in pulse width.
E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
Clamp potential: -0.5V SCE.

Figure E-5 - Charge potential curves for changes in pulse width.
 A) Total charge, B) Fast recoverable charge.
 Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N2 gas.
 Clamp potential: -0.5V SCE.

Figure E-5 - Charge potential curves for changes in pulse width.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-5 - Percent total charge curves for changes in pulse width.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N2 gas.
 Clamp potential: -0.5V SCE.

Figure E-6 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-6 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-6 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #1, 1.0M phosphate buffered saline, 4mm area, N2 gas.
 Clamp potential: -0.5V SCE.

Figure E-6 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-6 - Charge potential curves for changes in delay.

C) Slow recoverable charge, D) Unrecoverable charge.

Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-6 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #2, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: -0.5V SCE.

Figure E-6 - Charge potential curves for changes in delay.

A) Total charge, B) Fast recoverable charge.

Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-6 - Charge potential curves for changes in delay.

C) Slow Recoverable, D) Unrecoverable charge.

Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.

Clamp potential: -0.5V SCE.

Figure E-6 - Percent total charge curves for changes in delay.
 E) Fast recoverable, F) Slow recoverable, G) Unrecoverable charge.
 Platinum, #3, 1.0M phosphate buffered saline, 4mm area, N₂ gas.
 Clamp potential: -0.5V SCE.