An In-vitro Study of Electrodes Impedance in Deep Brain Stimulation

Haider A Mohammed Ali¹, Siham S Abdullah², Moneer Faraj³

¹College of Medicine, Al-Nahrain University
²Al-Nahrain University - Iraq
³College of Medicine, Baghdad

E-mail: haidermerjan@gmail.com, drsiihamsabah66@gmail.com, drmkfaraj@uob.edu.iq

Abstract. The success of Deep Brain Stimulation (DBS) therapy in movement disorders is highly reliant on the number of electric charges delivered to the brain through the implanted contact electrodes. A high electrode impedance will count the flow of these changes, affecting the clinical benefit of the treatment. DBS patients show impedance variation, and many of them lose therapeutic benefits after a while because of high impedance. The aim of study is to reveal the effect of long-term electric stimulation on the impedance of the electrical electrodes of DBS lead contacts in vitro. This study is conducted from March 2019 to November 2019 in the Department of Physiology and Medical Physics at the College of Medicine, Al-Nahrain University. The electric impedance of DBS electrodes is measured regularly for nine months in vitro. These measurements are conducted using two pairs of lead DBS electrodes: one inserted in normal saline impregnated with a carbidopa-levodopa pill and activated by a DBS electric pulses generator, and another pair as the control without stimulation. The recorded data shows an increase in the impedance of DBS electrodes over long-term electric stimulation and reversing the polarity of the stimulation may cause the impedance of the electrodes to decrease.

Keywords: Deep Brain Stimulation, electrodes impedance, impedance.

1. Introduction

Deep Brain Stimulation (DBS) is a surgical technique in which an implanted pulse generator delivers electric charges through the electrodes wire to stimulate deep nuclei in the brain and control many chronic neurological disorders [1-3]. This intervention technique became a prominent late-stage treatment option is now mainly used to control movement disorders, especially medical refractory Parkinson's disease (PD), dystonia, and essential tremor [4-6]. Also, it has been recently applied for neuropathic pain [7, 8], epilepsy [9, 10], Tourette's syndrome [7, 11, 12], obsessive-compulsive disorder [13, 14], and depression [15-17].

Considering the increased number of patients who had been given DBS, many factors may still limit the benefit of this remarkable therapy. Behind the professionalism of the surgical team, hardware complications of the DBS components are the biggest challenge hindering treatment success. The hardware complications of a DBS system may include the electric impedance of the electrodes which can affect the therapy.
1.1. Electricity principles and electronics
Clinical response works out by electrical charges that are injected into the neural tissue [18]. Physics of the electricity is fundamental to the impacts of the integrity of the DBS system since electricity is the fundamental of the mechanism of the action of the nervous system [19]. One of the parameters that DBS therapy success depends on, is the physical factors that they are electric stimulating voltage magnitude, charges current that delivered to the nervous system from the implantable pulse generator, pulse signal width, and the frequency of that pulse. See Figure 1.

![Figure 1. The electric parameters with the square wave in DBS [20].](image)

The electric potential that is provided by the implanted pulses generator (IPG) forces the electrons to move along the metal pathway through the extension wire to the lead wire that ends by four contact electrodes, which are fixed to the target point inside brain tissue.

1.2. Impedance types
Two types of impedance are measured in DBS:

1. Electrode impedance: It is used to evaluate the whole system integrity and refers to four electrodes impedance as well as the IPG case is the 5th electrode. The current is measured in a standard parameter that is configured in both bipolar and monopolar polarity [21]. The electrodes impedance in DBS is typically ranged from 500–1500 Ω for clinical therapy [22, 23].

2. Therapy impedance: This refers to impedance and current measurements of the active electrode(s) at the patient’s actual stimulation parameters to indicate a smaller volume of tissue activation that achieved the desired clinical effect while avoiding adverse side [24].

1.3. Impedance concept
Impedance is a physical term of resistance to the propagation of current in an alternating current (AC) system [21]. The effects and adverse effects of DBS result from the bulk of neural tissue activated, which is directly related to current density [25] that is introduced into the neural tissue which varies and greatly depends upon the electrode-tissue interface impedance [18]. Various factors can affect the impedance including material, voltage, cross-section geometry, length, and temperature [19]. The impedance of the electrodes in DBS may change and contribute to variations in clinical response to the electric stimulation [26].

1.4. Impedance in electrical circuits
The impedance could be defined as a complex resistance encountered when charges current flows through an electric circuit contained various capacitors, resistors, and inductors. This definition is applied to both direct current (DC) and alternating current (AC) [27]. In electric engineering, the simple electric circuit consists of three main components which they are inductor, capacitor, and
resistor but they differ in the way that connects consequently the equivalent impedance of the electric circuits differs as well. The impedance is a more common concept than either pure resistance, inductance, or capacitance, as they take phase differences between the input voltage and outputs current into account. Like resistance, the impedance is the ratio between applied voltage and current, explaining the ability of the electric circuit to resist the electrical current flow, represented by the "real impedance" named, but it also shows the ability of the electric circuit to store the electrical energy, reflected in the "imaginary impedance" term. In direct current circuit (DC), the current flow is constant and the reactance for inductive and capacitive are neglected and only the resistance (R) restricted the current flow, while in the alternating current circuit (AC) as in the case of DBS electronics circuit, the current flow is fluctuating as square waveform between zero and peak value periodically which determined by “amplitude” of voltage, that is the amplitude of stimulation, has a unit of volts (V). The frequency of stimulation is the rate of which the fluctuation changed per second and measured in hertz (Hz). Frequency is greatly influencing the value of impedance in the DBS circuit because the reactance is an effective factor changed by frequency.

1.5. Equivalent impedance in resistive, capacitive, and inductive circuits

The quantity in the AC electric circuit that is analogous to resistance in a DC circuit is the impedance (Z); like resistance, it is deliberated in ohms. Impedance is determined by all three electric circuit elements (L, C, and R); also, unlike DC resistance, impedance is a function of the frequency f of the AC generator. In general, impedance (Z) is included in three parts: the resistance (R), the reactance of the capacitor (XC), and the reactance of the inductor (XL). Reactance, which is measured in ohms, is the objection that a capacitor or inductor offers to the flow of AC; it is a function of frequency. The capacitor reactance is inversely proportionate to the capacitance and the frequency (XC = 1/2πfC). Thus, it is least at high frequencies, becomes progressively greater at lower frequencies, and is infinite at zero frequency (DC), because an ideal capacitor uses a perfect insulator between the capacitor plates that are not capable of carrying any direct current. The inductor reactance is directly proportional to the inductance and the frequency (XL = 2πfL). Thus, it is zero at zero frequency (DC) and increases progressively with increasing frequency. This happens because the effect of an inductor is to object changes in current, and the more rapidly the current changes, the greater the induced electromotive force opposing that change will be [29].

1.6. Electrode tissue impedance

Experimental measurements have shown that DBS electrodes impedance is largely dominated across the impedance of the neural tissue immediately adjacent to the electrode surface [30]. The impedance of the electrode/tissue interface (Z) represents the resistance encountered by the extracellular current injected at a certain frequency and is given by

\[ Z = R + jX \]  

(1)

where X represents the reactance of the equivalent electrical circuit.

The magnitude of the impedance is generally determined by the kinetics of the charge transfer processes at the electrode/electrolyte interface [31]. For clinical DBS electrodes, impedance can range approximately from 500 to 1500 Ω. From this, Ohm’s law (V = IR) can generally be used to calculate the potential (V) or current output (I) [18].
2. Materials and method

2.1. Materials
A DBS system consists of an electrodes lead wire, a neurostimulator (implanted pulses generator, IPG) which generates the electric pulses, and an extension wire connecting the electrodes lead wire to the neurostimulator, as shown in Figure 2.

![Figure 2. Deep brain stimulation components from Medtronic Inc. 1- Neurostimulator IPG. 2- Extension. 3- Electrodes lead wire terminated with four electrodes.](image)

The DBS lead wire is terminated with four electrode contacts. The names are 0, 1, 2, and 3 or 8, 9, 10, and 11, which are related either to the left or right side of the brain, respectively. The electric impedance of the four electrodes is measured by the N'Vision Clinician Programmer (Model 8840) which is a portable device offering a programming platform with an interactive touch screen for Medtronic's neurological implantable neurostimulator therapy devices as seen in Figure 3.

![Figure 3. The Model 8840 N'Vision Clinician Programmer (Medtronic Inc.).](image)

2.2. Methods
Two pairs of DBS lead wires were investigated in vitro: one pair was the control and kept in normal saline with no stimulation (one model 3389 lead wire denoted as "3389 control" and another model 3387 wire denoted as "3387 control"), and the second pair was activated by an implanted pulses generator (IPG) in normal saline with one carbidopa-levodopa pill (one model 3389 lead wire denoted as "3389 stims" and another model 3387 wire denoted as "3387 stims"), as shown in Figure 4.
Figure 4. Each DBS lead wire was inserted in normal saline in a test tube and sealed with wax at the base to prevent air entry or fluid leakage.

The data were collected by measuring the electrical impedance of the electrodes of the DBS lead wires up to eight months at every two months intervals. The stimulated pair (3389 stims and 3387 stims) of lead wires was activated for nine months. In the first eight months, the stimulation parameters were as follows: amplitude (Amp) = 2.7 Volts, pulse width (PW) = 90 µs, and rate = 180Hz for 3389 stim; and amplitude (Amp) = 1.9 Volts, pulse width (PW) = 90 µs, and rate = 180Hz for 3387 stims. In the 9th month, the stimulation voltage was doubled and reversed before the impedance measurement with the following parameters: amplitude (Amp) = 5.4 Volts for 3389 stims and amplitude (Amp) = 3.8 Volts for 3387 stims. The N'Vision device was used to measure the electric impedance for the same lead wire between electrodes 0, 1, 2, and 3, for each one of the four electrodes between electrode 0 and 1, electrode 0 and 2, electrode 0 and 3, electrode 1 and 2, electrode 1 and 3, and electrode 2 and 3. The parameters for the N'Vision programmer were fixed for all electrodes impedance measurements: amplitude (Amp) = 0.70 Volts, pulse width (PW) = 80 µs, and rate = 100Hz. The collected data were presented as electrodes impedance versus time plots created using Microsoft Excel 2013.

3. Results

The impedance measured during the nine-month stimulation period ranged from 295 to 3339 ohm. It was clear that there was an increase in the impedance from the first time of the lead wires inserted in normal saline to eight months post-insertion. Then, the impedance decreased after the stimulation voltage polarity doubled and reversed during the 9th month, indicating an unstable impedance as shown in Fig. 5 for 3389 stims and Fig. 6 for 3387 stims.

Figure 5. The impedance change of DBS lead wire for 3389 stims over nine months of stimulation. There was an increase in the impedance until the reverse of the stimulation polarity in the 9th month, and the impedance decreased to a previous value.
Figure 6. The impedance change of DBS lead wire for 3387 stims over nine months of stimulation. There was an increase in the impedance until the reverse of the stimulation polarity after eight months, and the impedance decreased to a previous value.

4. Discussion

The results suggest that impedance variability occurs, and stability over time may not take place in a patient undergoing DBS therapy. The changes in the impedance of the electrodes, especially with relation to time, affect the local field potentials along with the current amount for therapeutic stimulation delivered by DBS [32, 33]. Trials in animal models and human patients had documented fluctuations in the impedance of the electrodes through the first 30–100 days following implantation [30, 34–36]. This study shows that the variation in the DBS electrodes impedance is primarily related to the electrode-electrolytes interface as we found a dedicated impedance variability in-vitro with time during electric stimulation, as shown in Figure 5 and Figure 6.

4.1. Characteristics of electrode impedance in DBS

The measurements of the impedance of the electrodes ranged from 295 to 3339 Ω. The electrical impedance in the electrode–electrolytes system can be conceptualized as the potential ability to resist the flow of current. The electrical impedance of the electrodes–electrolytes interface operates in a non-linear manner under-stimulation parameter utilized in clinical practice [37]. This impedance is also highly influenced by electrical stimulation [30]. The cause of this variability is due to tissue characteristics and the electrode-tissue interface [18, 38]. According to clinical observation of symptoms in PD patients, the impedance may vary between 400 to 3000Ω; however, the variation was less at above 2000 Ω. The changes in electrical impedance properties were related to factors such as the accumulation of byproducts and encapsulation [39]. Encapsulation has been shown to alter the resistivity of the local environment. Prior research proposes that impedance may be influenced by chronic stimulation and activity of the electrodes [32, 40].

Our findings were corroborated by some studies that indicated an early increase in impedance postoperatively in dystonia patients [34, 40], but they differed from a study using the impedance values to evaluate the variability [41], where no obvious variation was found.

4.2. Electrochemical phenomena

When excess voltage and frequency were applied by the DBS programmer, electrode processes occurred. This may result in electrochemical phenomena, such as gas, e.g., hydrogen, emergence at the cathode (-), and evolution of oxygen at the anode (+). Redox reactions of organic molecules may take place, and potentially harmful materials, such as chlorine, metal ions, and toxic organics, may be produced in the electrodes and tissue. Excess electric stimulation may cause chemical components to
dissolve which will contribute to fast electrode corrosion and subsequent change of electrode impedance after a long period.

4.2.1. Capacitive reactions impedance. The transfer of electric charges at the electrode/electrolyte interface can be either non-faradaic capacitive or faradaic resistive charge transfer. The interface capacitance impedance of capacitive (non-faradic) charge transfer is accomplished when the capacitance of the electrode/electrolyte interface is charged or discharged by an electrical potential. This charge transfer leads to ionic rearrangements at the electrodes/tissue interface and flow of ionic currents close to the electrodes [42, 43]. Capacitive charge transfer is preferable since no chemical species are generated or consumed. However, capacitive charge transfer alone might not be enough to reach the current amplitudes required for neuronal activation. As such, faradaic charge transfer may occur at the interface of electrode-electrolyte to reach the neuronal activation thresholds [42, 44]. Porous capacitive electrodes or highly dielectric coatings can increase the charge injection capacity of the electrode [43].

4.2.2. Faradaic reactions. Faradic electrochemical reactions are related to the electrode surface when it is oxidized or reduced, impacting the electrodes impedance property. These interactions can be irreversible or reversible depending on the relative rates of electron transfer and kinetics of mass transfer [42, 45]. The impedance of faradaic reactions is related to the presence of collective transfer [28]. Although electron transfer does take place in the faradic results, chemical species confined to the DBS electrodes surface and noble metals or noble metal alloys are not consumed (pseudo-capacitive reactions) [44], like platinum which is considered as a noble metal. Irreversible reactions result in the obestrics of chemical species at the surface of the electrodes that dissolve and may diffuse into the tissue, precipitate around the electrode, or evolve into gas bubbles before a reversal can be achieved [43, 44]. Electrodes that are operating in the irreversible zone can cause tissue damage because irreversible reactions can modify the pH of the surrounding neural tissue and generate toxic products. The most common faradic irreversible response is water electrolysis, leading to the emergence of

\[ H_2(2H_2O + 2e^- \rightarrow H_2 + 2OH^-) \] at the cathode

and \[ O_2(2H_2O \rightarrow O_2 + 4H^+ + 4e^-) \] at the anode.

The formation of gas bubbles was observed by Wei, X. F. et al. in 2009. The electrodes surface in the DBS in vitro measurements was observed when the current amplitudes were above one mA. Water hydrolysis at the electrodes-tissue interface [37] was due to the initiation of faradaic reaction mechanisms. The increased current beyond the acting of water dipoles as a dielectric in the double-layer capacitance [47] was due to the high-frequency polarization voltage across the electrode surface, and the electrochemical reactants for the reactions are reversed on the surface of the electrode.

In another study done by Giemsa, J. et al. in 2005, the DBS electrodes lead behavior was characterized by employing microelectrodes in the experiments. They found unexpected properties for the behavior of the electrodes caused by a non-uniform distribution of the high current intensity along with the small surface areas of the active electrodes. The reactions resulted in gas bubbles that could be observed and related to the electrode size, indicating changes in the property of electrode-electrolyte via frequency-domain electrochemical techniques [48]. It was clear that the current density developed on the implanted electrodes surface during electrostimulation post-operation, causing drift of the electrode properties via electrochemical reactions at the electrode-electrolyte interface, which resulted in corrosion and erosion of the DBS lead wire electrodes [26]. The DBS electrodes were made of two different materials: platinum/iridium, which may form an electrochemical element. The adsorption of organic and non-organic species at the surface of the electrodes was another factor affecting the impedance, causing property changes of the metal–electrolyte interfaces.
Also, in this study, we examined DBS lead wires (model 3389 and 3387, Medtronic Inc.) in normal saline (0.9% NaCl) with one carbidopa-levodopa pill for nine months with electric stimulation. A thin layer formed on the surface of the connector between the lead wires and the extension wire, as we can see in Figure 7 and Figure 8, which may reduce the transport of ions of degradation products away from and to the surface and increase encapsulation surrounding the electrode over time. This observation is in line with our findings that long-term inundation caused changes in the electrode properties and impedance increased with surface corrosion. This finding is supported by a microscopic photo of our experimental lead wires, as shown in Figure 7.

**Figure 7.** The corrosion on the DBS system surface and necrosis before and after stimulation. (A) and (E) The surface of the DBS extension connector after four months of stimulation. (B) And (C) The terminal end of the DBS lead contact after three months of stimulation. (D) New DBS lead contact electrode. (F) Part of a new DBS extension connector.

**Figure 8.** The corrosion of the DBS system. (A) The picture shows the DBS extension connector after four months of stimulation in two parts with a brown color surface indicating electrochemical reaction. (B) A photo of the terminal end of DBS lead contacts showing the change in the surface color due to five months of electric stimulation.

Corrosion in the electrodes may result in the deposition of electrode metal in the brain. Metal ions are potential sources of protein denaturation and the generation of new antigenic determinants causing immune reactions [49], such as cytotoxicity caused by iron [50]. Additionally, the degradation of some organic compounds in the DBS target may result in the evolution of gases, such as oxygen, hydrogen,
and chlorine, representing non-physiological processes that can change the extracellular fluid properties. Similar changes cause neuronal tissue damage [51, 52].

The study results presented that the DBS electrodes impedance increased in the first eight months after stimulation of the electrodes. This result is in line with the clinical application under relevant electrostimulation. The electrical impedance of the electrodes decreased reversibly after one month when the stimulation voltage amplitude doubled and reversed. These changes in the electrical impedance of the electrodes–electrolytes interface could be due to the changes in the ionic contents near the electrodes [53]. The most obvious changes were the increase in the impedance of both the filament layer and the electrodes as well as the development of an encapsulation layer around the wires, as shown in Figure 9.

![Figure 9](image)

**Figure 9.** In-vitro encapsulation formation and the cleaning process. The DBS lead electrodes after six months of immersion in normal saline with one carbidopa-levodopa pill. The impedance measurements showed obvious changes. The development of the encapsulation layer probably suggests that the variation in the impedance measurements of a chronically implanted DBS electrode was due to the accumulation of organic or non-organic elements around the electrode contacts, forming a thin filament layer which may peel off after reversing the polarity of stimulation and doubling the stimulation voltage after one month.

### 4.3. **DBS electrodes materials**

To obtain an ultralow impedance, a platinum-iridium alloy coating was used which highly enhanced the DBS electrode by improving its electrical conductivity. The electrical inefficiency of platinum electrodes alone results in unnecessary power consumption and reduced battery lifetime. Increasing efficiency can extend implant life and/or reduce the battery size. Thus, today's DBS implants can benefit from more efficient electrode materials [56]. Iridium provides mechanical stiffness in platinum materials [57]. Pt-Ir alloys electrode also has minimal electrochemical impedance and a higher charge storage capacity in contrast to pure platinum used in biomedical applications [58, 59].

### 5. **Conclusions**

In this study, electric stimulation through DBS lead wires had to efface in accelerating the electrochemical reaction, which resulted in the electrical properties variation of the electrodes and increased the electric impedance for chronic stimulation. Reversing the polarity of stimulation may result in a cleaning process and thus decrease the impedance of the electrode.

**Conflict of Interest**

We have no conflicts of interest to disclose.
Acknowledgments
All the authors are grateful to the microscope lab team /Neuroscience Hospital and to Dr. Bahaa Salih Abdalnabi in CT-scan Department / Neurosurgical Hospital for their great efforts in supporting the implementation of this work.

References
[1] Krack P, Batir A, Van Blerecom N, Chabardes S, Fraix V, Ardouin C, Koudsie A, Limousin P D, Benazzouz A, LeBas J F, Benabid A L and Pollak P 2003 Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease N Engl J Med 349(20) 1925-34
[2] Fasano A, Daniele A, and Albanese A 2012 Treatment of motor and non-motor features of Parkinson's disease with deep brain stimulation The Lancet. Neurology 11(5) 429-42
[3] Herrington T M, Cheng J J and Eskandar E N 2016 Mechanisms of deep brain stimulation, J Neurophysiol 115(1) 19-38
[4] Ostrem J L and Starr P A 2008 Treatment of dystonia with deep brain stimulation, Neurotherapeutics 5(2) 320-30
[5] Marks J W 2015 Deep Brain Stimulation Management 2ed. Cambridge University Press Cambridge
[6] Bour L J, Contarino M F, Foncke E M J, de Bie R M A, van den Munchhof P, Speelman J D and Schuurman P R 2010 Long-term experience with intraoperative microrecording during DBS neurosurgery in STN and Gpi Acta Neurochir (Wien) 152(12) 2069-2077
[7] Perlmutter J S and Mink J W 2006 Deep brain stimulation Annu Rev Neurosci 29 229-57
[8] Kumar K, Toth C and Nath R K 1997 Deep Brain Stimulation for Intractable Pain: A 15-Year Experience Neurosurgery 40(4) 736-747
[9] Fisher R, Salanova V, Witt T, Worth R, Henry T, Gross R, Oommen K, Osorio I, Nazzaro J, Labar D, Kaplitt M, Sperling M, Sandok E, Neal J, Handforth A, Stern J, DeSalles A, Chung S, Shteter A, Bergen D, Bakay R, Henderson J, French J, Baltuch G, Rosenfeld W, Youkilis A, Marks W, Garcia P, Barbato N, Fountain N, Bazil C, Goodman R, McKhann G, Babu Krishnamurthy K, Papavassiliou S, Epstein C, Pollard J, Tonder L, Grebin J, Coffey R and Graves N 2010 Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy Epilepsia 51(5) 899-908
[10] Tekriwal and Baltuch G, Deep Brain Stimulation: Expanding Applications 2015 Neurol Med Chir Tokyo 55(12) 861-877
[11] Diederen N J, Kalteis K, Stamenkovic M, Pieri V and Alesch F 2005 Efficient intracellular pallidal stimulation in Gilles de la Tourette syndrome: A case report, Movement Disorders 20(11) 1496-1499
[12] Houeto J L, Karachi C, Mallet L, Pillon B, Yelnik J, Mesnage V, Welter M L, Navarro S, Pellisolo A, Damier P, Pidoux B, Dormont D, Cornu P and Agid Y 2005 Tourette's syndrome and deep brain stimulation J Neurol Neurosurg Psychiatry 76(7) 992-5
[13] Benabid A L, Pollak P, Gao D, Hoffmann D, Limousin P, Gay E, Benazzouz A and Payen I 1996 Chronic electrical stimulation of the ventralis internus nucleus of the thalamus as a treatment of movement disorders J Neurosurg 84(2) 203-14
[14] Gabrieis L, Cosyns P, Nuttin B, Demeulemeester H and Gymbels J 2003 Deep brain stimulation for treatment-refractory obsessive-compulsive disorder: psychopathological and neuropsychological outcome in three cases Acta Psychiatr Scand 107(4) 275-82
[15] Grubert C, Hurlemann R, Bewernick B H, Kayser S, Hadrysiewicz B, Axmacher N, Sturm V and Schlaepfer T E 2011 Neuropsychological safety of nucleus accumbens deep brain stimulation for major depression: effects of 12-month stimulation, World J Biol Psychiatry 12(7) 516-27
[16] Mayberg H S, Lozano A M, Voon V, McNeely H E, Seminowicz D, Hamani C, Schwalb J M and Kennedy S H 2005 Deep brain stimulation for treatment-resistant depression Neuron
45(5) 651-60

[17] Schlaepfer T E, Cohen M X, Frick C, Kosel M, Brodesser D, Axmacher N, Joe A Y, Kref M, Lenartz D and Sturm V 2008 Deep brain stimulation to reward circuitry alleviates anhedonia in refractory major depression Neuropsychopharmacology 33(2) 368-77

[18] Butson C R, Maks C B and McIntyre C C 2006 Sources and effects of electrode impedance during deep brain stimulation Clinical Neurophysiology 117(2) 447-454

[19] Montgomery E B 2016 Deep Brain Stimulation Programming Mechanisms Principles and Practice Principles of Electricity and Electronics Oxford University Press

[20] Zauber S E, Smith P A and Metman L V 2015 Fundamentals of deep brain stimulation programming, in: J W J Marks (Ed.) Deep Brain Stimulation Management Cambridge University Press Cambridge pp 64-76

[21] Farris S, Vitek J and Giroux M L 2008 Deep brain stimulation hardware complications: the role of electrode impedance and current measurements Mov Disord 23(5) 755-60

[22] Obeso J A, Olanow C W, Rodriguez-Oroz M C, Krack P, Kumar R and Lang A E 2001 Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease N Engl J Med 345(13) 956-63

[23] Volkmann J, Herzog J, Kopper F and Deuschl G 2002 Introduction to the programming of deep brain stimulators Mov Disord 17 Suppl 3 S181-7

[24] Deeb W, Patel A, Okun M S and Gunduz A 2017 Management of Elevated Therapeutic Impedances on Deep Brain Stimulation Leads Tremor Other Hyperkinet Mov (N Y) 7 493

[25] Bronstein J M, Tagliati M, McIntyre C, Chen R, Cheung T, Hargreaves E L, Israel Z, Moffitt M, Montgomery E B, Stypulkowski P, Shils J, Denison T, Vitek J, Volkmann J, Wertheimer J and Okun M S 2015 The Rationale Driving the Evolution of Deep Brain Stimulation to Constant-Current Devices Neuromodulation: Technology at the Neural Interface 18(2) 85-89

[26] Gimsa J, Habel B, Schreiber U, van Rienen U, Strauss U, 2005 Gimsa U Choosing electrodes for deep brain stimulation experiments--electrochemical considerations J Neurosci Methods 142(2) 251-65

[27] Lvovitch V F 2012 Fundamentals of Electrochemical Impedance Spectroscopy, Impedance Spectroscopy J Wiley & Sons pp. 1-21

[28] Lasia A 2014 Impedance of the Faradaic Reactions in the Presence of Mass Transfer, Electrochemical Impedance Spectroscopy and its Applications Springer New York, New York, NY pp. 85-125

[29] Daube J R and Rubin D I 2009 Clinical Neurophysiology Oxford University Press.

[30] Lempka SF, Miocinovic S, Johnson M D, Vitek J L and McIntyre C C 2009 In vivo impedance spectroscopy of deep brain stimulation electrodes J Neural Eng 6(4) 046001

[31] Wei X F and Grill W M 2009 Analysis of high-perimeter planar electrodes for efficient neural stimulation Front Neuroeng 2 15-15

[32] Abosch A, Lantin D, Onaran I, Eberly L, Spaniol M and Ince N F 2012 Long-term recordings of local field potentials from implanted deep brain stimulation electrodes Neurosurgery 71(4) 804-14

[33] Stypulkowski P H, Stanslaski S R, Denison T J and Giftakis J E 2013 Chronic evaluation of a clinical system for deep brain stimulation and recording of neural network activity Stereotact Funct Neurosurg 91(4) 220-32

[34] Rosa M, Marceglia S, Servello D, Foffani G, Rossi L, Sassi M, Mrakic-Sposta S, Zangaglia R, Pacchetti C, Porta M and Priori A 2010 Time dependent subthalamic local field potential changes after DBS surgery in Parkinson's disease Exp Neurol 222(2) 184-90

[35] Giannicola G, Rosa M, Servello D, Menghetti C, Carrabba G, Pacchetti C, Zangaglia R, Cogiamanian F, Scezlo E, Marceglia S, Rossi L and Priori A 2012 Subthalamic local field potentials after seven-year deep brain stimulation in Parkinson's disease Exp Neurol 237(2) 312-7

[36] Deuschl G, Herzog J, Kleiner-Fisman G, Kubu C, Lozano A M, Lyons K E, Rodriguez-Oroz M
C, Tamma F, Troster A I, Vitk J L, Volkmann J and Voon V 2006 Deep brain stimulation: postoperative issues Mov Disord 21 Suppl 14 S219-37
[37] Wei X F and Grill W M 2009 Impedance characteristics of deep brain stimulation electrodes in vitro and in vivo J Neural Eng 6(4) 046008
[38] Back C, Alesch F and Lammuller H 2003 Postoperative monitoring of the electrical properties of tissue electrodes in deep brain stimulation Neuromodulation 6(4) 248-53
[39] Grill W M and Thomas Mortimer J 1994 Electrical properties of implant encapsulation tissue Annals of Biomedical Engineering 22(1) 23-33
[40] Cheung T, Nuno M, Hoffman M, Katz M, Kilbane C, Alterman R and Tagliati M 2013 Longitudinal impedance variability in patients with chronically implanted DBS devices Brain Stimul 6(5) 746-51
[41] Sillay K A, Chen J C and Montgomery E B 2010 Long-term measurement of therapeutic electrode impedance in deep brain stimulation Neuromodulation 13(3) 195-200.
[42] Geddes L A 1997 Historical evolution of circuit models for the electrode-electrolyte interface Annals of Biomedical Engineering 25(1) 1.
[43] Cogan S F 2008 Neural Stimulation and Recording Electrodes Annual Review of Biomedical Engineering 10(1) 275-309
[44] Merrill D R, Bikson M and Jefferys J G R 2005 Electrical stimulation of excitable tissue: design of efficacious and safe protocols Journal of Neuroscience Methods 141(2) 171-198
[45] Bard A J and Faulkner L R 2000 Electrochemical Methods: Fundamentals and Applications 2nd Edition Wiley Textbooks.
[46] Rose T L and Robblee L S 1990 Electrical stimulation with Pt electrodes VIII Electrochemically safe charge injection limits with 0.2 ms pulses IEEE Trans Biomed Eng 37(11) 1118-20
[47] Bockris J O M and Conway B E 1958 Determination of the Faradaic Impedance at Solid Electrodes and the Electrodeposition of Copper The Journal of Chemical Physics 28(4) 707-716
[48] Schwan H P and Onaral B 1985 Linear and nonlinear properties of platinum electrode polarisation III: Equivalence of frequency- and time-domain behaviour Med Biol Eng Comput 23(1) 28-32
[49] Zitter H, Plenk H and Jr 1987 The electrochemical behavior of metallic implant materials as an indicator of their biocompatibility J Biomed Mater Res 21(7) 881-96
[50] Smythe J 1999 The neurotoxicity of glutamate, dopamine, iron and reactive oxygen species: functional interrelationships in health and disease: a review-discussion Neurotox Res 1(1) 27-39
[51] Cogan S F, Ludwig K A, Welle C G and Takmakov P 2016 Tissue damage thresholds during therapeutic electrical stimulation Journal of neural engineering 13(2) 021001-021001
[52] Günter C, Delbeke J and Ortiz-Catalan M 2019 Safety of long-term electrical peripheral nerve stimulation: review of the state of the art J Neuroeng Rehabil 16(1) 13-13
[53] Unterberg A W, Stover J, Kress B and Kiening K L 2004 Edema and brain trauma Neuroscience 129(4) 1021-9
[54] Keese C R, Wegener J, Walker S R and Giaever I 2004 Electrical wound-healing assay for cells in vitro Proc Natl Acad Sci USA 101(6) 1554-9
[55] Johnson M D, Otto K J and Kipke D R 2005 Repeated voltage biasing improves unit recordings by reducing resistive tissue impedances IEEE Trans Neural Syst Rehabil Eng 13(2) 160-5
[56] Petrossians A, Whalen J J and Weiland J D 2016 Improved electrode material for deep brain stimulation Conf Proc IEEE Eng Med Biol Soc 1798-1801
[57] Petrossians A, Whalen J, Weiland J and Mansfeld F 2011 Electrodeposition and Characterization of Thin-Film Platinum-Iridium Alloys for Biological Interfaces.
[58] Piersma B J and Greatbarch W 1987 Coupling Reactions at the Metal-Tissue Interface in Electrical Stimulation with Cardiac Pacemaker Electrodes Journal of The Electrochemical
Society 134(10) 2458-2464

[59] Agnew W F and McCreery D B 1990 Neural Prostheses: Fundamental Studies Prentice Hall.