ABSTRACT

Model
Parameter Identification of the
Oscillatory Potential in the Electroretinogram

by
Sung Hoon Jang

A mathematical model of the oscillatory potential which may be a useful clinical tool to diagnose the progression of diabetic retinopathy. The model has been investigated by compressing from oscillatory potential into three parameters which contain most of the information for the oscillatory potential data.

About thirty subjects including both normal and diabetic subjects were investigated in this study. Comparing normal and diabetic subjects, we found amplitude parameter was most important factor to classify subjects by normal and diabetic.

Since modeling of the oscillatory potential and the estimation of the model parameters were our final goal, we haven't proposed to the underlying physiological meanings.

MODEL

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APPROVAL PAGE

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CHAPTER 1

INTRODUCTION

Vision involves a complex sequence of events involving sensory cells, Photochemical processes, which produce signals in the retinal neurons, in optic nerve fibers, and in the various centers of brain. Finally, a discriminative response occurs.

The electroretinogram (ERG) and visual evoked response (VER) have become very important in the study of the visual system. The ERG, usually recorded from the human retina, is a potential that represents a summation of electrical activity of millions of retinal cells in the retina upon a sudden change of illumination. It is detectable from many locations on or at the surrounding skin of the eye. Therefore, the specific contribution of retinal cells to this response is only beginning to be understood.

According to Granit (1947) [1] , in 1877 Dewar and McKendrick first reported that electrical potentials could be recorded from an animal eye by attaching an electrode to the skin. As long ago as 1907, Bruecke and Garten showed the separation of ERGs into a-, b-, and c-waves [cited in Hartline [4]] . Kahn and Lowenstein (1924) [3] attempted the first clinical use of the ERG. Although they attempted to use the ERG as part of the clinical examination, their method was too difficult to be used in a clinical setting. Later, human ERGs were successfully recorded by Hartline (1925) [4] with a string galvanometer. The analysis of ERGs was advanced by Granit (1933) [5] , who introduced an amplifier into circuit and was able to record ERGs both from the center and from the periphery of eyes. The separate waves so recorded supported his analysis.

In 1953, Cobb and Morton [6], by using a strong light stimulus of short duration (gas-discharge lamp), were able to report that the human ERG includes multiple smaller wavelets which are superimposed on the positive b-wave. Bornschein and Goodman [7] in 1957 pointed out that two negative wavelets, a1 and a2, separating the a-wave into two peaks, were followed by several positive ripples in the ascending limb of the b-wave in the human ERG. They stated these wavelets were an additional type of oscillatory response. Yonemura [8] in 1962 stated that the a1 and a2 wavelets are followed by four smaller ripples which are superimposed on the initial part of the b-wave, which are therefore, part of the oscillatory potential.

The origin of the oscillatory potential has been the subject of many hypotheses. The nature of the oscillations is still obscure. Nevertheless, the oscillatory potentials seem to reflect neuronal activity in the bipolar cells and an interaction the rod and cone mechanism in the inner part of the retina. The interplexiform cells can also participate in the generation of the oscillatory potential in feedback circuits of the primate retina [9] .

The oscillatory potential is generated in the inner layer of the retina and may show the condition of the inner layer of the retina. Thus it is being increasingly considered in the diagnosis of patients with severe cases of glaucoma, obstruction of the central artery of the retina and diabetic retinopathy. These findings have been confirmed in the experimental work of Yonemura [8] who has shown that oscillatory potential disappeared or decreased greatly in these diseases while the a- and b-waves of the flash ERG were normal or larger than normal in their amplitudes. Specifically, Yonemura found specifically that the ERG of simple atrophy of the optic nerve presented no significant difference from the normal one. The oscillatory potential disappeared usually or sometimes in the obstruction of the central artery of the retina, advanced glaucoma, siderotic degeneration of the retina and diffuse uveitis. The oscillatory potential disappeared or greatly diminished even in almost all the cases with slight diabetes, although the ERG a- and b-waves were not necessarily reduced in these cases. This finding seems significant in diabetic retinopathy, where the oscillatory potential disappeared or greatly reduced. The oscillatory potential thus has practical value to make early diagnosis between diabetic and angiosclerotic retinopathies [8] .

Diabetic retinopathy is a disease of the retina associated with diabetes mellitus, many of whose symptoms are associated with the inner layer of the retina. These symptoms include small, punctate hemorrhages and numerous, smaller, round, red spots (microaneurysms) . In this same area are hard, sharply defined, white or yellowish, soapy or waxy exudates which may be isolated coalesced into larger masses in a circinate manner around the macula. The disease is frequently found in association with arteriosclerotic and hypertensive retinal changes [12] , also in the inner layer.

Since measurement of the function of the inner layer is important, this thesis will deal with modeling of the ERG and oscillatory potential and the estimation of the model parameters. These model parameters will be compared with implicit times and amplitudes extracted from the record which are the more typical measures of the

oscillatory potential. A mathematical model representing the oscillatory potential as a set of parameters can help analyze the oscillatory potential responses and produce more consistent results. Each parameter value of the model is obtained after fitting the oscillatory potential data to the oscillatory potential model by using parameter identification techniques. The information contained in the oscillatory potential data can then be compressed into a set of three parameters which define the oscillatory potential.

Similar work has been done previously on the parameter identification of the oscillatory potential by Huizhong Pan [13] . Our intention is to continue his initial idea by improving a model that produces a better fit of the oscillatory potential response and may have some physiological meaning. In this study, a system model has been constructed functionally and anatomically based on the visual system.

CHAPTER 2

THE HUMAN RETINA

The human retina is a complexly constructed piece of neural tissue consisting of millions of neurons arranged within a layered architecture. The whole retina is a thin sheet of tissue lining the back of the eye and composed of these millions of highly organized neurons and circuits and a complement of glial cells to provide architectural stability and the physiological environment for the functioning of neurons. Very sensitive photoreceptors are capable of responding to individual photons of light.

2.1 The Organization of The Human Retina

The structure of retina is shown in Figure 2.1. According to Polyak (1941) [14], there are two main layers of cell nuclei. One is the outer nuclear layer (ONL), which contains the cell bodies of the photoreceptors, and the other is the inner nuclear layer (INL), which contains the bodies of the bipolar and ganglion cells.

The outer synaptic layer (OSL) lies between the outer and inner nuclear layers, which has synaptic interactions of photoreceptors, horizontal cells, and bipolar neurons. Between the inner nuclear layer and the ganglion cell layer is the inner synaptic layer (ISL) , which has synaptic interactions involving bipolar neurons, amacrine cells, and ganglion cells.

The glial cells of Mueller fully occupy the face (inner surface) of the retina on the vitreous chamber and fill the spaces between the bipolar cells. Between the glial cells of Mueller and the ganglion cells lies the layer of optic fibers (OFL) . The optic fiber layer consists of the axons of the ganglion cells which form pathways on the inner surface of the retina and form the optic nerve.
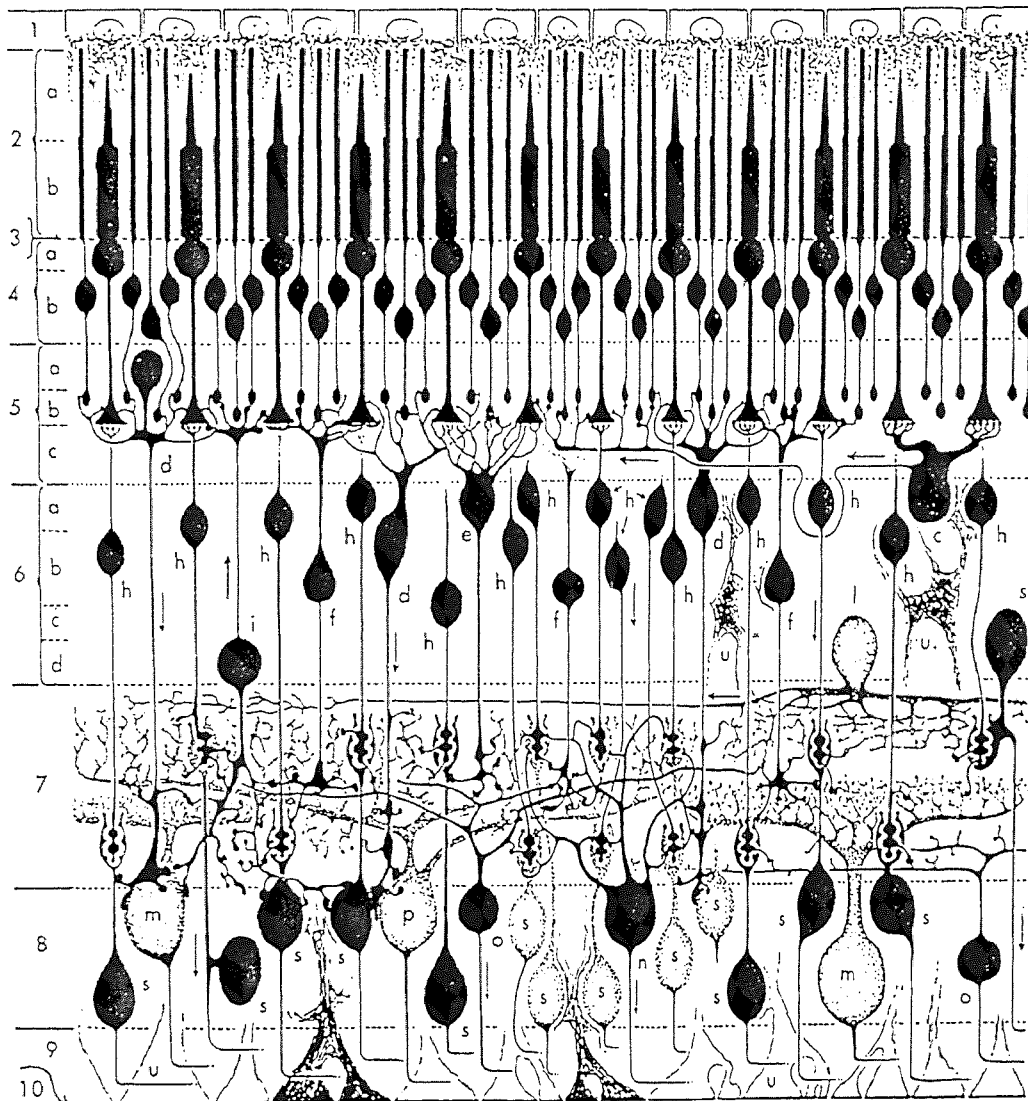
Figure 2.1 The structure of retina as revealed by method of Golgi. Layers and zones are indicated as follows: 1, pigmented epithelium; 2a, outer segments of photoreceptors ; 2b, inner segments of photoreceptors; 3, external limiting membrane; 4a, b, photoreceptor nuclei; 5a, photoreceptor axons; 5b, photoreceptor terminals; 5a, b, c, outer synaptic layer; 6a, b, c, d, outer nuclear layer; 7, inner synaptic layer; 8, ganglion cell somata; 9, optic fiber layer; 10, inner limiting membrane. Nerve cells are indicated as follows; c, horizontal neuron; d, e, f, h, i, various types of bipolar neurons; l, amacrine neurons; m, n, o, p, s, various ganglion cells; u, glia cells of Muller. (From Polyak (1941) [14]) .

2.2 Photoreceptors in Visual System

Most of our knowledge about the meaning of signals are generated in rods and cones and transmitted along the pathway to the optic nerve dates from about 1970, and the pace of advances has increased rapidly. Much of this progress is due to the use of intracellular microelectrodes to record directly from retinal cells.

The job of the photoreceptor cell in the retina is to catch light and pass a message to the next stage at the OPL. There are 120 million rods and six million cones in the normal human retina which converge to the approximately one million optic nerve fibers. The photoreceptors of the visual system are each highly sensitive to a specific type of energy. The retina contains two types of photoreceptor cells (rods and cones) concerned with transduction from light to electrochemical form. The cones, which are specialized for color vision, are more sensitive to detail, and are found toward the center of the retina, while the rods are in the periphery. Bipolar cells (see Figure 2.1.) act as relay stations between the light receptors and the optic nerve fibers.

As shown in Figure 2.3, the rods and cones respond differently to increases in light intensity. Inward current on the surface of the cell produce negative voltage changes. As the light becomes brighter, there is an increase of the amplitude of the response in a cone. Figure 2.3 shows the changes of the current in the outer segment membrane of a single rod. Increased light intensity increases the amplitude as well as the duration of the cone response. Increasing the intensity of a light flash suppresses increasing amounts of the inward dark current. When the light is fully bright, all of the dark current is suppressed. Rushton [10] found a relation between log threshold and pigment concentration of the rods and the cones after an exposure to bright light and also showed the time constant of cone pigment regeneration was demonstrated to be more rapid than that of the rod pigment.

According to Moses [11] , there are two types of ganglion cells in the human retina, one being diffuse and the other being distinct, the latter one being called midget ganglion cell because of its small size. The midget ganglion cell affects a synaptic contact with a single cone bipolar cell and is often related to a single cone. The diffuse ganglion cells have relatively long and numerous dendrites with mutual overlapping of the territories of adjacent cells. Some midget ganglion cells may be in synaptic contact with bipolar cells of the diffuse type.
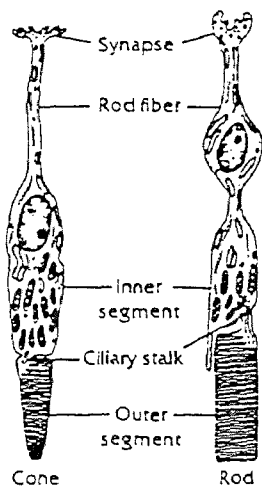
Figure 2.2 Diagram of a cone and a rod
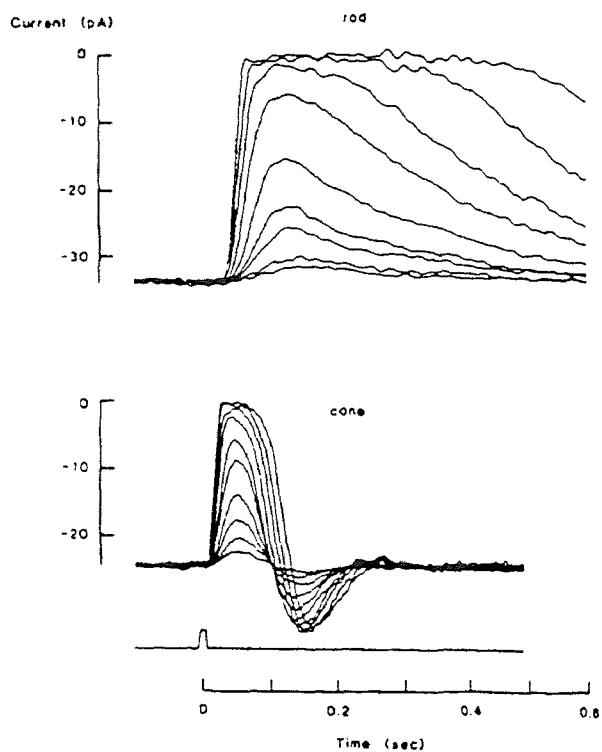
Figure 2.3 Reduction in circulating current through a rod and a cone that is produced by light flashes. The flash intensity is increased by a factor of about 2, ranging between 2.9 and 900 photoisomerizations in the rod and between 190 and 36000 in the cone. Timing of the flash is shown below. (From Baylor DA: Invest Ophthalmol Vis Sci 1987; 28: 34-49) .

2.3 The Electroretinogram

The electroretinogram (ERG) is an electrical potential obtained from a contact lens electrode with a ground at the ear (test procedure is described in Chapter 5) . The ERG comprises components from many retinal sources. Figure 2.4 shows a typical ERG from a normal adult. Granit [1] has described an analysis of the ERG into three major components, a-wave, b-wave, and c-wave. Figure 2.5 (a) , (b) , and (c) depict a-, b-, and c-wave components.

Cobb and Morton [6] described a further component of the ERG as a series of wavelets which occur during the ascending b-wave. These wavelets can be characterized as a further component shown in Figure 2.5 (d) . These components are combined in 2.5 (e) into a wave representing an ERG.

25.00 uv/div

1 0S

10 ms/div
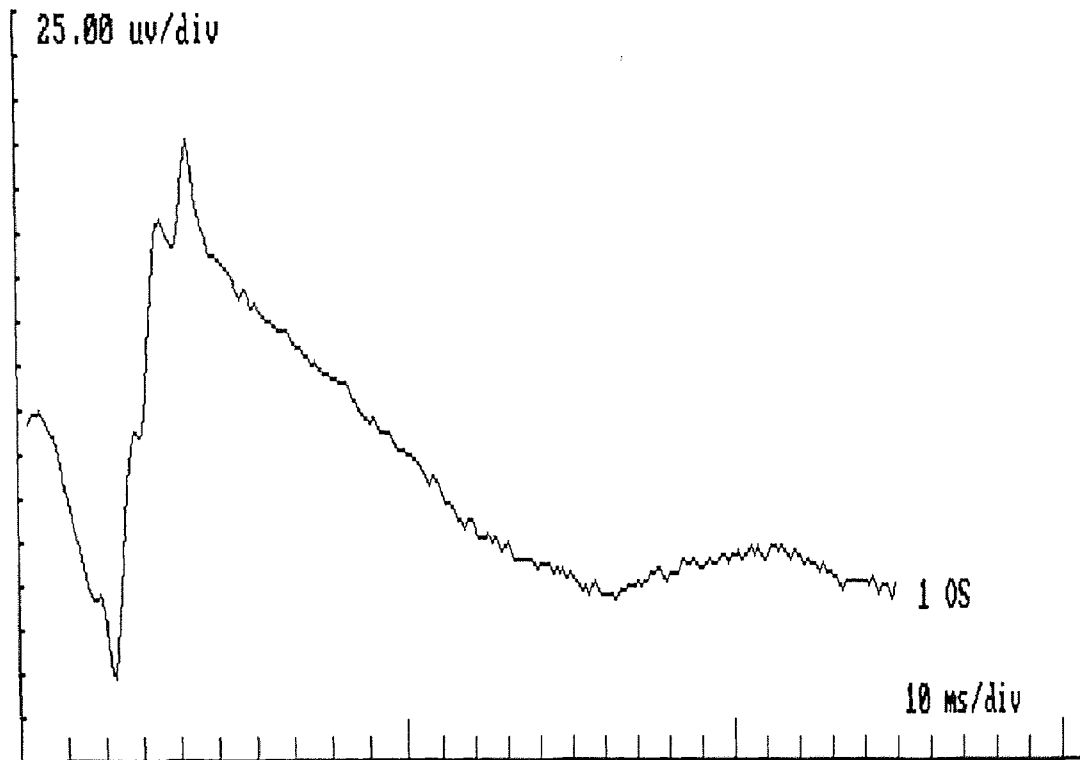
Figure 2.4 Typical dark-adapted ERG of normal adult (digitized signal at 1 khz sampling rate, unfiltered) .

(a) a-wave

(b) b-wave

(c) c-wave

(d) oscillatory potential
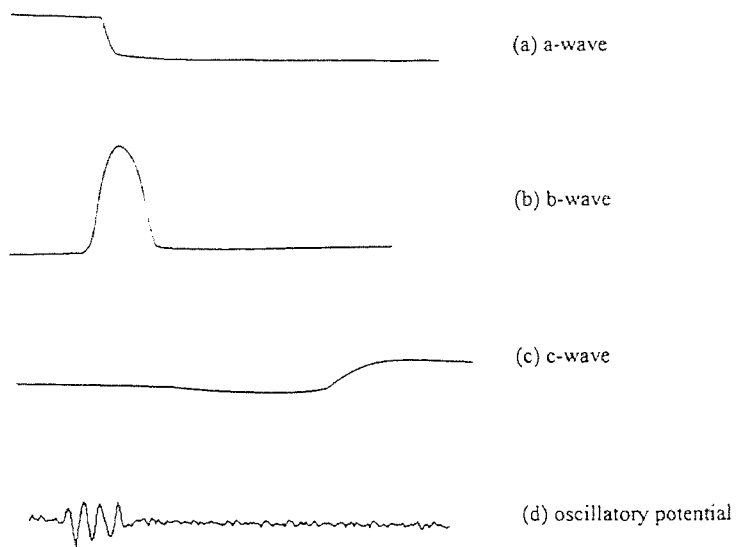
Figure 2.5 Breakdown of ERG major components.

25.00 uv/div

1 OS

2 OS

10 ms/div
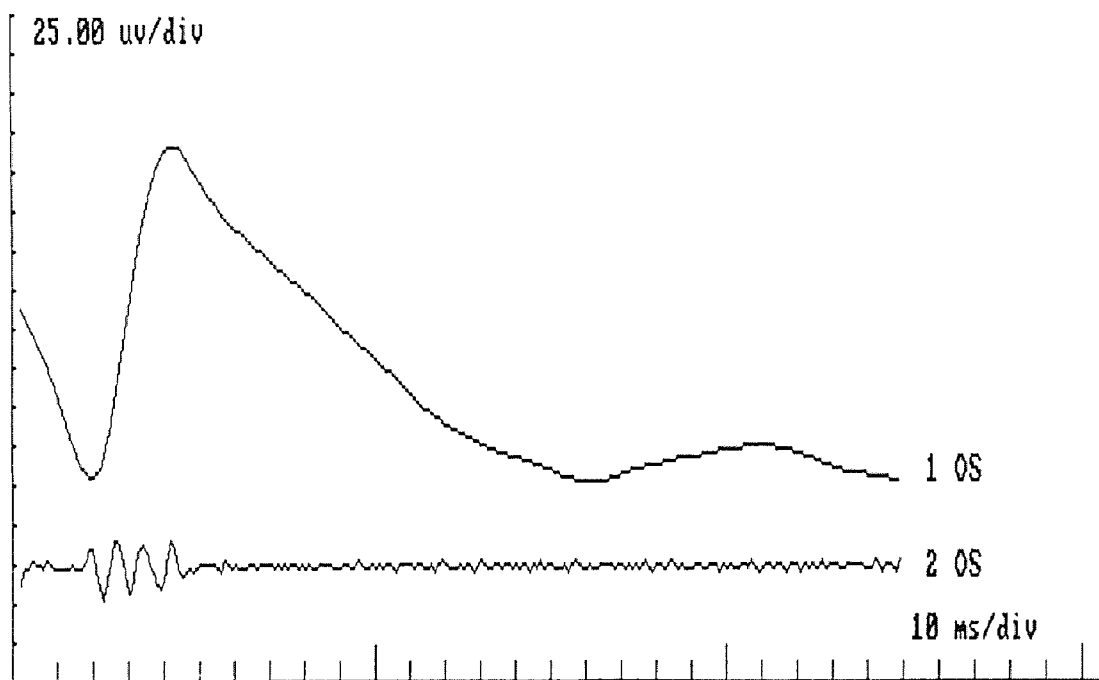
Figure 2.6 Separation of ERG of Figure 2.4 into smoothed ERG and oscillatory potential. Top: Low-pass filtered (< 70 Hz) ERG (a-, b-, and c-wave components) . Bottom: High-pass filtered (> 70 Hz) ERG (oscillatory potential) .

Typically, clinical ERG analyses have considered only the low-frequency components, representing mainly the a-, b-, and c-wave components. An example of such a waveform is the upper trace of Figure 2.6, which shows the ERG of Figure 2.4 after low-pass filtering at 70 Hz. The lower trace of Figure 2.6 shows the oscillatory potential obtained from high- pass filtering of the same ERG.

Figure 2.7 presents a frequency power density function from the ERG in Figure 2.4. Most power is concentrated in the lower frequency components below 60 Hz. However, a small additional component appears between frequencies of approximately 110 to 150 Hz. This appears to match the range of the oscillatory potential, which should be isolated by high-pass filtering (> 70 Hz) . This was verified by observation of transients obtained with (high-pass) filter cutoff frequencies such as 60 and 80 Hz. In the present work, bilateral (Butterworth) filtering was used, causing no delay (see chapter 5) .
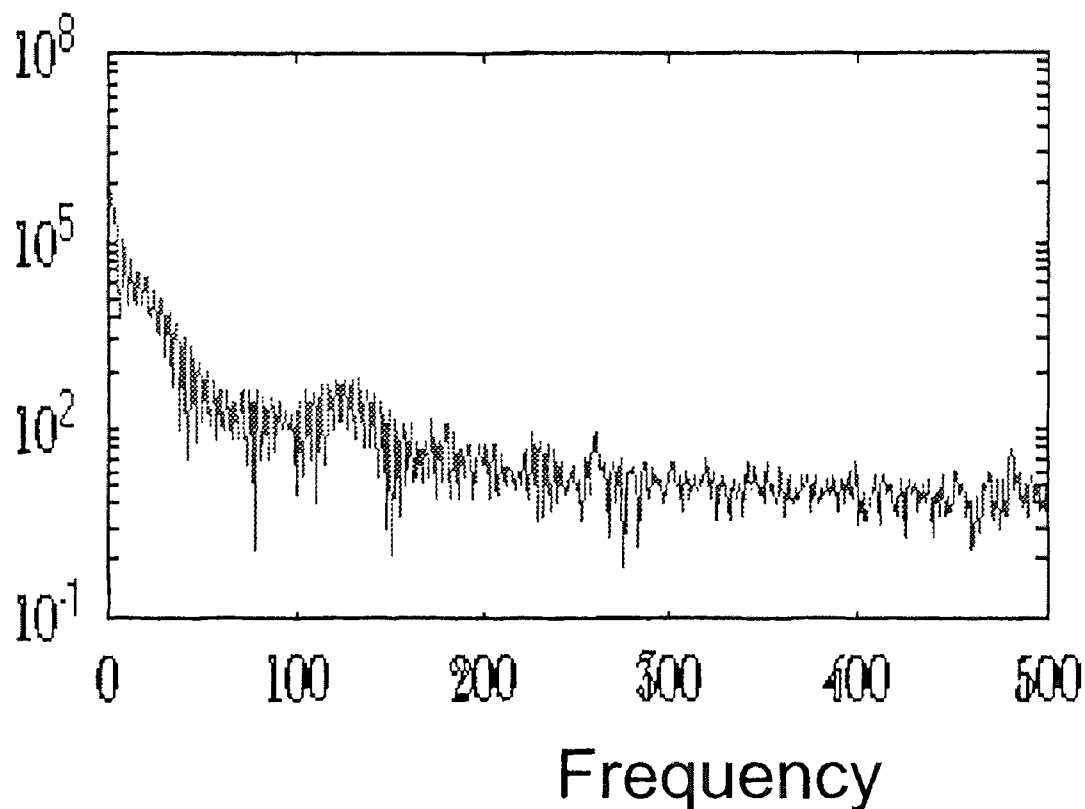
Figure 2.7 Power density spectrum of dark-adapted ERG response to single white flash.

CHAPTER 3

PRESENTLY USED (CLASSICAL) METHODS FOR ANALYSIS OF THE OSCILLATORY POTENTIAL

Presently established methods for analysis of the oscillatory potential are based on a classification of the oscillatory potential in terms of individual wavelets, called "op1, op2, ... op5". [15] [16] . This is illustrated in Figure 3.1 and 3.2 for two slightly different definitions of these wavelets, to be referred to here as *Method A* and *Method B* respectively. Both *Method A* and *Method B* are based on the bandpass-filtered ERG, obtained by white flash in a Ganzfeld stimulator under scotopic conditions, using contact lens electrodes.

The purpose of the present work is to advance a different approach, namely the modeling of the oscillatory potential so that it can be expressed in terms of the values of its model parameters. The moldeling approach will be discussed in Chapter 4 and 5. However, in order to obtain a comparison between the modeling and the classical approaches, data processing was developed for both. In the present chapter, the processing for classical methods A and B will be discussed.

In *Method A* (Figure 3.1) , which has been referred to as "calliper-square measurement of the oscillatory potential amplitudes" [15] , added heights of the wavelets peaks are measured as follow. X- and y-coordinates of the individual oscillatory potential troughs and peaks are determined by moving a cursor on the screen. A maximum of five oscillatory potential nodes is considered. A computer program has been written to calculate the amplitudes of the individual nodes by connecting the coordinates to adjacent troughs and computing the distance from each oscillatory potential peak to the line as shown in Figure 3.1. For a more detail, see the computer program in Appendix C, which evaluates both *Method A* and *B*.

In *Method B* (Figure 3.2) , the amplitude of oscillatory potential is measured as the voltage difference between the trough to peak of each wavelet by moving a cursor on the screen. The sum of the amplitudes of individual wavelets is then calculated. The computer program (Appendix C) includes calculation of the individual wavelet amplitudes by subtracting each trough from each peak. Also, the summed oscillatory potential amplitude is calculated by adding the individual oscillatory potential amplitudes.
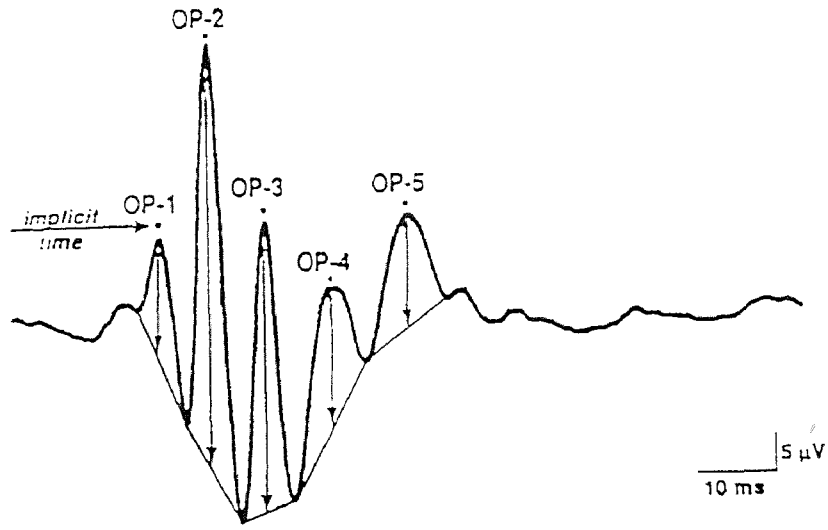
Figure 3.1 *Method A* for measuring oscillatory potential amplitudes. The summed amplitudes of oscillations represent the voltage of oscillatory potential. The oscillatory peaks are named of op1, op2, op3, op4, and op5 [15] .
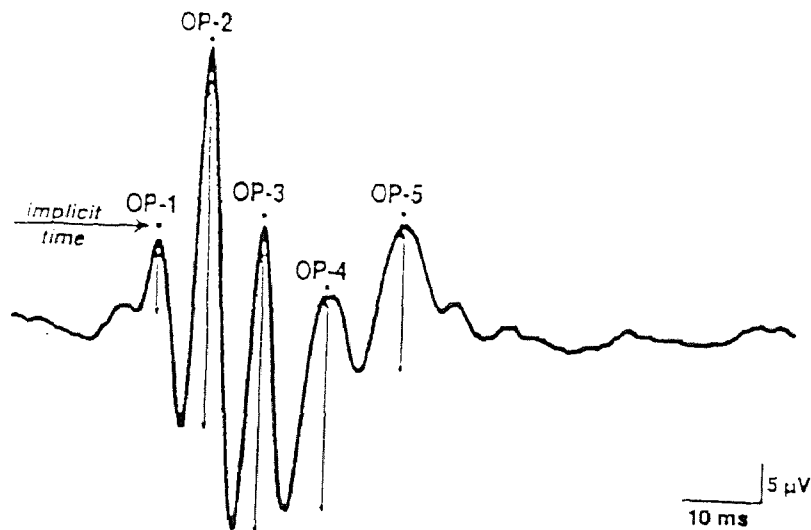
Figure 3.2 *Method B* for measuring oscillatory potential amplitudes. The oscillatory peaks are named of op1, op2 op3, op4, and op5 [16] .

Data obtained from one normal and diabetic subject each are shown in Tables 1 and 2 respectively. Data for four more normal eyes and four more diabetic eyes each are presented in Chapter 6, for comparison with the data obtained from modeling method.

Table 3.1 Table of Measurement for the Amplitude and Peak Time of Oscillatory Potential Component in the Normal Subject.

| | AMPLITUDES (μV) | | The peak |
	Method A	Method B	times (msec)
OP1	38.723	24.733	19
OP2	57.273	62.164	27
OP3	51.108	48.874	34
OP4	43.462	50.389	42
OP5	12.258	15.428	53
SUM	202.825	201.590	
AVERAGE	40.565	40.318	

Table 3.2 Table of Measurement for the Amplitude and Peak Time of Oscillatory Potential Component in the Diabetic Subject.

	AMPLITUDES (µV)		The peak
	Method A	Method B	times (msec)
OP1	4.295	7.671	13
OP2	24.467	15.474	18
OP3	34.316	40.870	26
OP4	15.558	17.009	36
OP5	16.448	15.794	45
SUM	95.055	96.730	
AVERAGE	**19.011**	**19.346**	

CHAPTER 4

MODELING OF THE OSCILLATORY POTENTIAL

4.1. A Model for the ERG

A model representing this ERG response as a-wave and b-wave has recently been introduced by Juan Castro [17] in the following form.

$$ERG(t) = E_a(t) + E_b(t) \qquad (4.1a)$$

Where

a-wave:
$$E_a(t) = k_1 \cdot \left(1 - e^{-\left(\alpha_1 \left(\frac{t}{T} \cdot e^{\left(1-\frac{t}{T}\right)} \right)^5 \right)} \right) \qquad (4.1b)$$

b-wave:
$$E_b(t) = k_2 \cdot t^3 \cdot e^{-(3\cdot\alpha_1\cdot t)} \cdot \sin(\omega \cdot t) \qquad (4.1c)$$

*   t: time in seconds.
*   T: time of the peak response in seconds.
* k_1: parameter related to the amplitude of the a-wave.
* k_2: parameter related to the amplitude of the b-wave.

This model is illustrated in Figure 4.1.
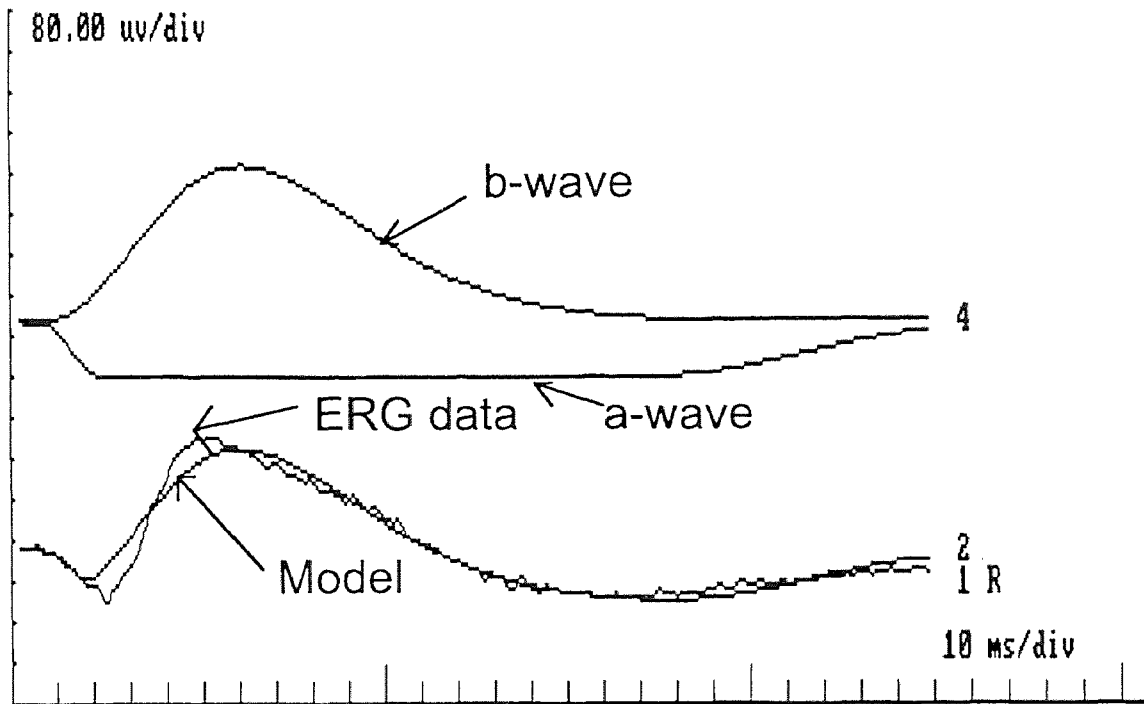
Figure 4.1 Typical ERG from a normal subject and its model response using equations (4.1) [17] .

4.2 Models for the Oscillatory Potential

Models which can represent the shape of the oscillatory potential have been introduced, as follows [13] :

$$OP_1(t) = k_1 \cdot t^n \cdot e^{-A_1 \cdot t} \cdot \sin(2 \cdot \pi \cdot f_1 \cdot t + D_1) \tag{4.2}$$

For the model shown in Figure 4.2, the set of parameters is

$$\{k_1, \quad n, \quad A_1, \quad f_1, \quad D_1\} =$$

$$\{0.00447 \frac{\mu v}{(m\sec)^n}, \quad 4, \quad 0.1537 \frac{1}{m\sec}, \quad 118.8 Hertz, \quad 0.01267 rad\}$$

$$OP_2(t) = k_2 \cdot t^n \cdot e^{-A_2 \cdot t} \cdot \sin(\omega \cdot t) \cdot \sin(2 \cdot \pi \cdot f_2 \cdot t + D_2) \qquad (4.3)$$

For the model shown in Figure 4.3, the set of parameters is

$$\{k_2, \quad n, \quad A_2, \quad \omega, \quad f_2, \quad D_2\} =$$

$$\{0.03913 \frac{\mu v}{(m\sec)^n}, \quad 3, \quad 0.126 \frac{1}{m\sec}, \quad 0.034 \frac{rad}{m\sec}, \quad 118.8 Hertz, \quad 0.011 rad\}$$

Where k_1 and k_2 are related to the amplitude of the oscillatory potential, and n is the order of the function. All parameters were obtained by curve fitting using a simplex algorithm. The program has been adapted to the models used in this work.

Model OP_2 (t) was considered as the product of a b-wave model, generalized from equation (4.1c) to $b(t) = k_2 \cdot t^n \cdot e^{-A_2 \cdot t} \cdot \sin(\omega \cdot t)$, and a term $\sin(2 \cdot \pi \cdot f_2 \cdot t + D_2)$ representing the high-frequency oscillation [13] .

Since ω_o is sufficiently small in equation 4.3, we can consider $\sin(\omega_o \cdot t) \cong \omega_o \cdot t$. When substituting $\sin(\omega_o \cdot t) \cong \omega_o \cdot t$ into equation 4.3, gives

$$OP_2(t) \cong k_2 \cdot \omega \cdot t^{n+1} \cdot e^{-A_2 \cdot t} \cdot \sin(2 \cdot \pi \cdot f_2 \cdot t + D_2)$$

Multiplying and dividing the above expression by A_2^{n+1}, we can define OP_3 (t) as the approximated OP_2 (t) as:

$$OP_3(t) = \frac{k_2 \cdot \omega}{A_2^{n+1}} \cdot (k_2 \cdot t)^{n+1} \cdot e^{-A_2 \cdot t} \cdot \sin(2 \cdot \pi \cdot f_2 \cdot t + D_2)$$

With $k_o = k_2 \cdot \omega / (A_2^{n+1})$, $A_o = A_2$, $f_o = f_2$, $D_o = D_2$ and renaming n+1 → n, the following expression had been obtained [18] :

$$OP_3(t) \cong k_o \cdot (A_o \cdot t)^n \cdot e^{-A_o \cdot t} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t + D_o)$$

(4.4)
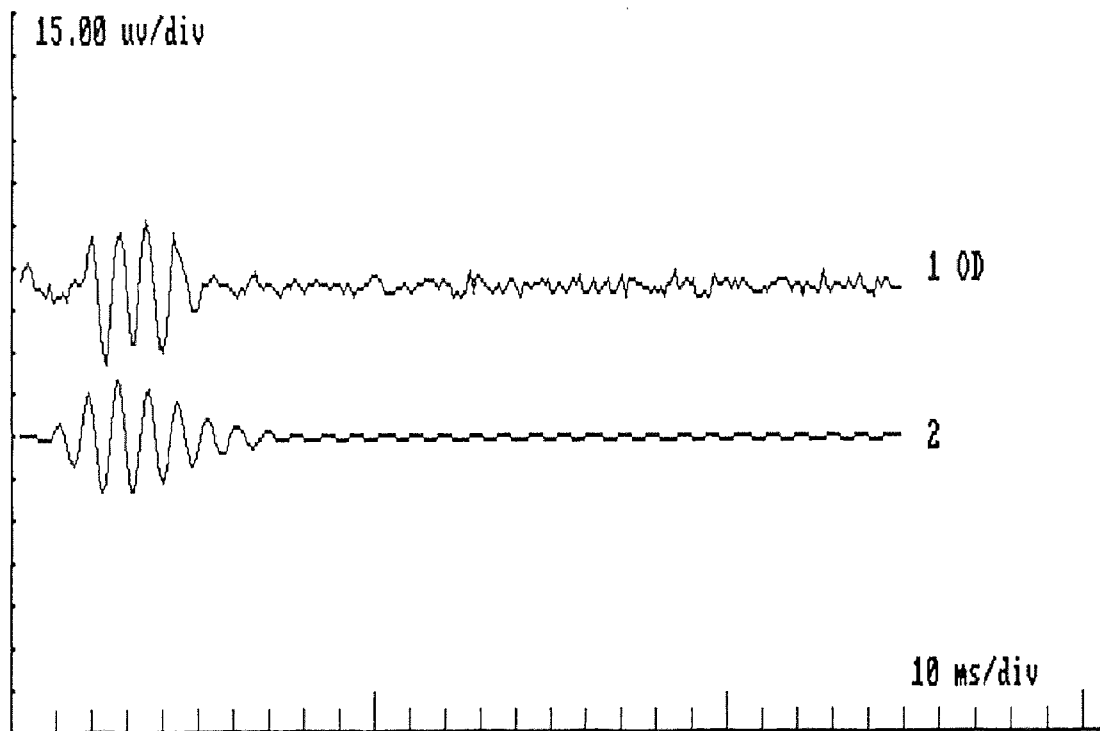
Figure 4.2 Oscillatory potential of the model OP_1 (t) .
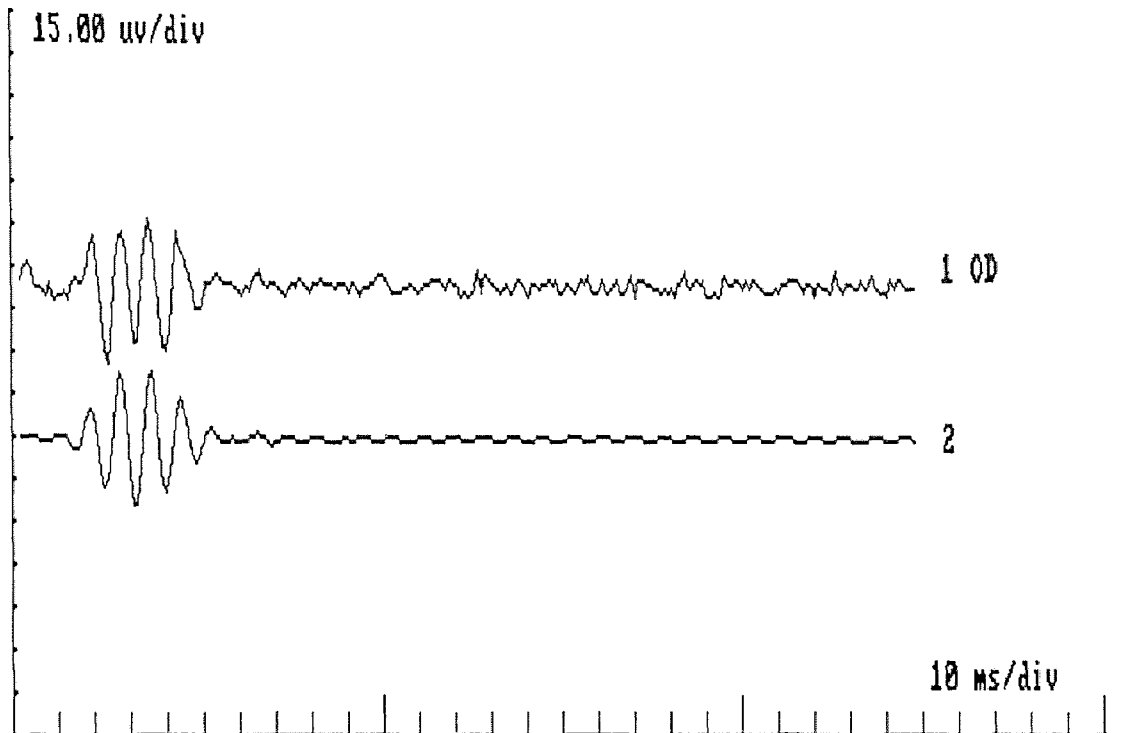
Figure 4.3 Oscillatory potential of the model OP_2 (t) .

Parameter identification (least-square fitting) , was performed initially for all five parameters in OP_3 (t) . It was found then that

(a) Phase-angle D_o is almost randomly distributed, and

(b) The value of n is close to 7.

Therefore, the following three-parameter model is used

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t) \qquad (4.5)$$

The model is shown in Figure 4.4 and the set of parameters (for the same ERG data in this chapter) is

$$\{k_o, \quad A_o, \quad f_o\} = \quad \{0.04726\mu v, \quad 0.2327\frac{1}{m\sec}, \quad 108.8 Hertz\}$$

Since all figures look similar, model OP_1 (t), OP_2 (t) , and OP (t) should be compared by both error standard deviation (ERR STD) and estimated error function (EEF) . The methods are shown as:

$$ERR \quad STD = \sqrt{\frac{\sum\limits_{i=1}^{n}(X_i - u)^2}{n-1}} \tag{4.13}$$

$$EEF = \frac{ERR \quad STD}{\sqrt{n-m}} \tag{4.14}$$

Where X is the error between data and model response at time-instant i, n = 280 is the number of samples used in each response, u is the average value of the error X, and m is the number of the parameters. Tables 4.1 and 4.2 represent the results. In these tables, we can see model OP (t) fits the oscillatory potential slightly better than model OP_1 (t) and OP_2 (t) .
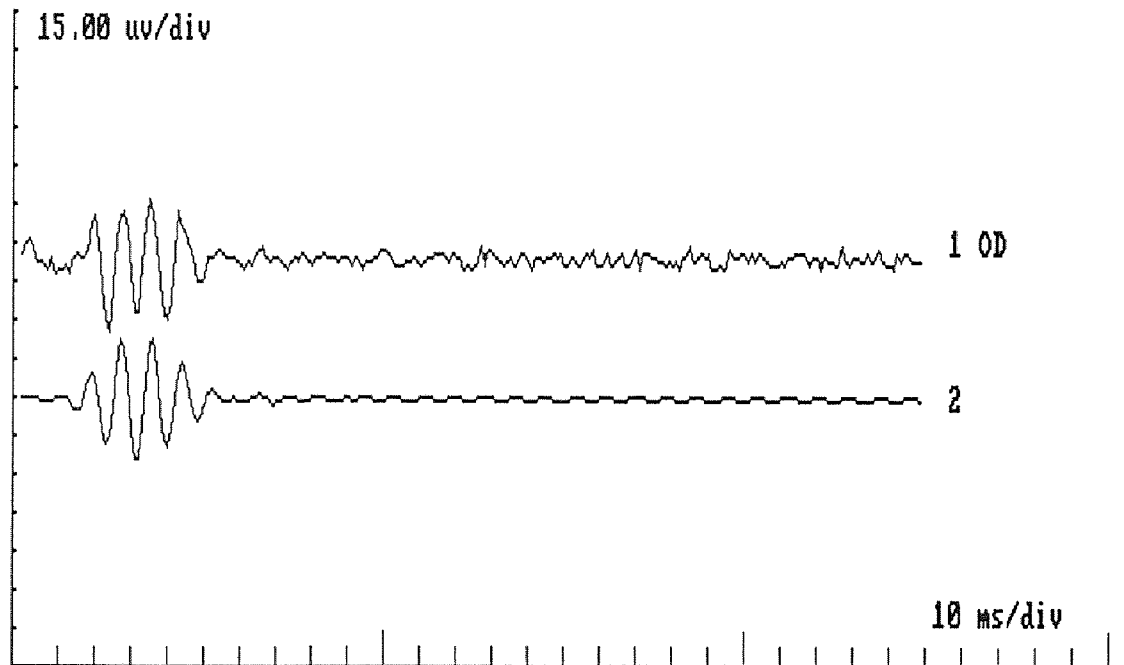
Figure 4.4 Oscillatory potential of the model OP (t) .

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Table 4.1 Comparison of ERR STD for the Oscillatory Potential with Different Models;
Normal Subjects (N) and Diabetic Subjects (D) .

Model Subject	$OP_1(t)$ ERR STD	$OP_2(t)$ ERR STD	OP (t) ERR STD
1.(N)	2.81479	2.51780	2.40447
2.(N)	3.21723	4.92403	3.11097
3.(N)	2.31614	2.00953	1.90950
4.(N)	3.01813	2.95984	2.85764
5.(N)	4.98553	4.86053	4.63994
6.(N)	3.71240	3.22751	2.84758
AVERAGE (Normal)	**3.34404**	**3.41654**	**2.96168**
1.(D)	8.28257	8.29908	8.24304
2.(D)	9.73782	9.82694	9.56148
3.(D)	9.68943	9.62793	9.16609
4.(D)	6.72071	6.76052	6.49454
AVERAGE (Diabetic)	**8.60763**	**8.62862**	**8.36629**

Table 4.2 Comparison of EEF for the Oscillatory Potential with Different Models; Normal Subjects (N) and Diabetic Subjects (D) .

Model Subject	$OP_1 (t)$ EEF	$OP_2 (t)$ EEF	OP (t) EEF
1.(N)	0.17946	0.16447	0.15017
2.(N)	0.20512	0.26458	0.19875
3.(N)	0.14767	0.12838	0.12031
4.(N)	0.19243	0.18910	0.18521
5.(N)	0.31124	0.31053	0.29643
6.(N)	0.23669	0.20620	0.18193
AVERAGE (Normal)	**0.21210**	**0.21054**	**0.18880**
1.(D)	0.52808	0.53021	0.52663
2.(D)	0.62086	0.62782	0.61086
3.(D)	0.61778	0.61511	0.58560
4.(D)	0.42850	0.43191	0.41492
AVERAGE (Diabetic)	**0.54881**	**0.55126**	**0.53450**

CHAPTER 5

TEST PROTOCOL

The ERG protocol and technical specifications should follow an international standard that describes a set of basic responses that should be recorded wherever and whenever an ERG is performed. Since ERGs obtained in this manner are comparable in waveform and amplitude, use of those clinical and research data can be shared and evaluated by the same criteria anywhere and anytime.

5.1 System for ERG Testing

A system developed in the Electrophysiology Laboratory of Eye Institute of New Jersey was used to facilitate the recording of ERGs and to generate sufficient data for this study. This MFTS3 is constructed with an XT computer, a Metrobyte DASH-16 data acquisition board and a GRASS 8-10 multichannel recording amplifier. The also includes a LKC Ganzfeld unit, LKC pattern monitor, and Nicolet pattern monitor, as stimulating devices [17].

The MFTS3 program, stored on the XT computer, is written in C language except for a small portion that reads the data acquisition board, which was written in assembly language. This program directs user providing by instructions and help. The system is very flexible allowing the use of any variety of protocols for testing.

Once data is recorded on the system it can be digitally filtered into three categories (low-pass, high-pass, and band-pass) , displayed on a screen, and stored on disk or used for generation of reports. This is not only useful for eliminating high frequency or 60 Hz noise but also for viewing certain bands of frequencies which provide some clinical information.

The arrangement for the MFTS3 testing system is presented in Figure 5.1. As presented in Figure 5.1, the patient's electrodes are connected to an electrode connection box which routes the signals to the LKC system and MFTS3 system. The jacks in the

electrode connection box contain the same labels as the push buttons in the push-button electrode selector panel of the GRASS recorder must be set to the position in which the electrodes are connected to in the electrode connection box. It is necessary to make sure that position (+) and negative (-) poles are selected properly in the GRASS machine. The jacks for channels labeled ch2, ch3, and ch4 on the GRASS amplifier are used for right eye, left eye, and neutral in the MFTS3 system. The output of these 3 channels from the GRASS amplifier is permanently connected to the A/D conversion inputs (ch1, ch2, and ch3 respectively) of the DASH connection box by a one conductor shielded wire.

Trigger signals are used to indicate to the data acquisition board when a stimulus occurs. Since there are three stimulating devices, three triggers are used to detect to occurrence of each stimulus. The triggers are connected from the trigger outputs of stimulating devices to the DASH connection box. One conductor shielded wires are used. The shields of the pin labeled GND in the DASH connection box and the conductors connect to the pins labeled IP0, IP1, and IP2.
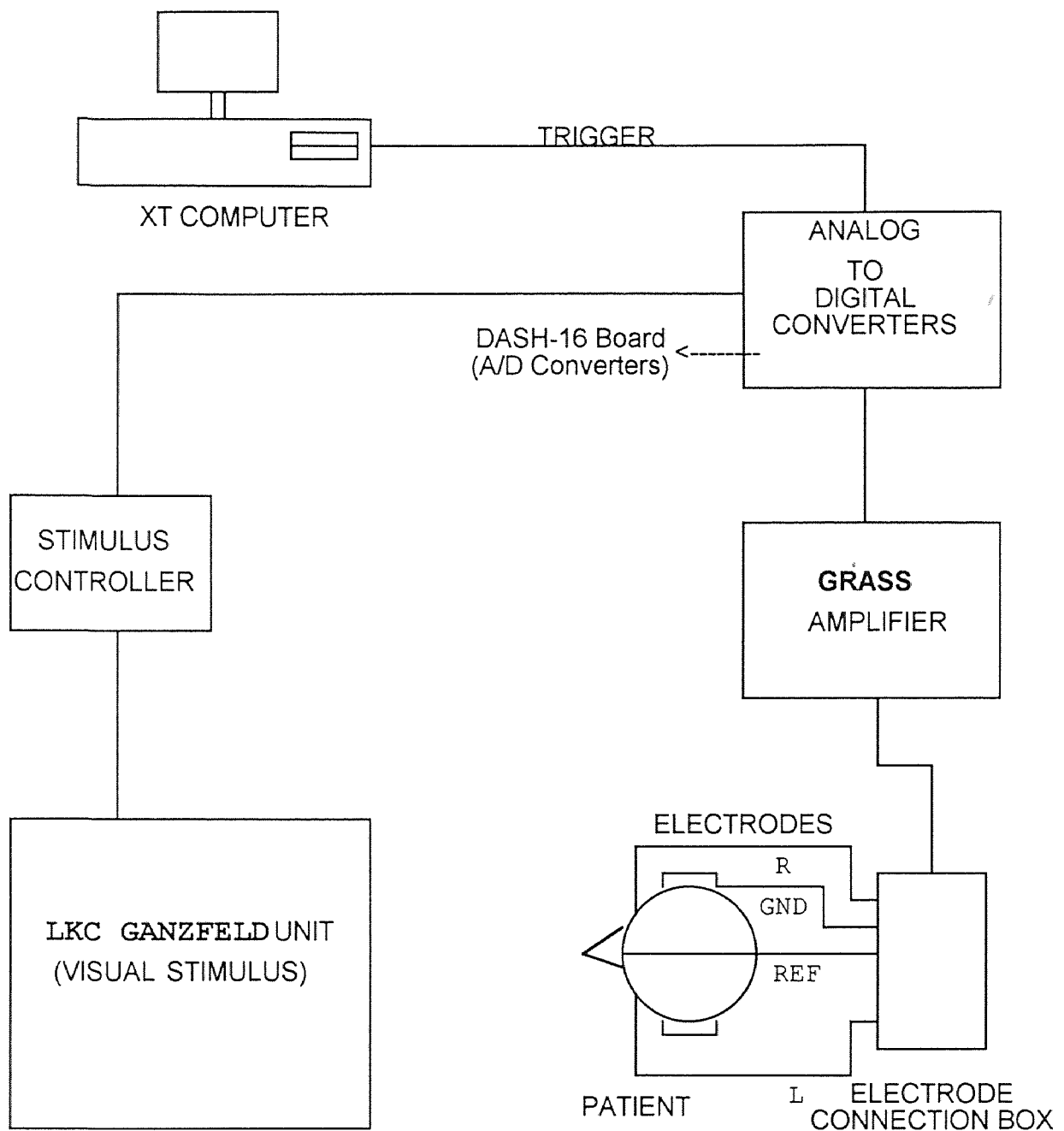
Figure 5.1 Major components of the ERG testing system.

5.2 Methods and Materials

The Multi-Function Test System version 3.0 (MFTS3) program is used for obtaining the ERG responses. Once data is recorded on a disk by the program, it can be digitally filtered, displayed on a screen, stored on disk or used for generation of reports. To obtain ERG response, the following steps are required to perform a test using the MFTS3 system.

1. Calibrate the MFTS3 system.

2. Select the test of type to perform.

3. Enter the patient general information.

4. Turn on the LKC system and initialize it for the test.

5. Dilate the patient's pupils.

6. Dark adapt the patient for 30 minutes.

7. Anesthetize patient's cornea.

8. Connect skin electrodes and ERG jet electrodes to the patient and system.

9. Adjust the filter settings in the Grass recorder and select the push buttons in the Push-button Electrode Selector Panel.

10. Follow the instructions on the MFTS3 system to perform the test.

The patient's pupils were fully dilated with a mydriatic (1% Mydriacyl and 2 1/2% Neo-Synephrine hydrochloride) in order to obtain good recordings. After a 30 minute dark adaptation period, 0.5% Proparacain hydrochloride was used to anesthetize the corneas in order to minimize the discomfort produced by the ERG jet electrodes. ERG jet electrodes were placed on the surface of the corneas, served as the active electrodes. A skin electrode for both eyes on the alcohol-cleansed forehead with electrode cream, served as the reference electrode. A second skin electrode was applied to the alcohol-cleansed earlobe to act as the electrical ground. Both eyes were tested simultaneously.

5.3 Method of Recording ERG Test

The MFTS3 program can be used for the recording of an ERG test. To perform the test, type "mfts3" at the DOS (c:>) prompt and hit [ENTER] :

c:> mfts3 [ENTER]

This will present the main menu of program :

[T] : TEST

[R] : REPORT

[C] : CALIBRATION

[Q] : QUIT

The options of the main menu can be selected by either typing the letter or using up and down cursor arrows and pressing [ENTER] .

A test can be performed after calibrating the system. If test was selected, the system will ask information about patient, such as : name, address, birth date, etc. After the general information about the patient has been gathered, the type of test to be performed can be selected. The user is presented with the following options :

[E] SINGLE FLASH RECORDING (ERG)

[V] AVERAGE RECORDING ERG or VER

[O] ELECTRO-OCULOGRAM

[U] USER DEFINED TEST

[Q] QUIT

Select [E] to perform the ERG test typing by the letter.

If Single Flash Recording (ERG) is chosen, the LKC Ganzfeld unit will be used as a stimulating device. The Single Flash Recording (ERG) option on the MFTS3 system will present a new menu prompting the user for the type of protocol to be used.

[0] Standard ERG Protocol

[1] Massof Protocol

[2] User Defined Protocol

Select [0] to perform the standard ERG test entering by the number.

The standard ERG protocol is a short ERG test that allows the user to run through five different stimulus :

10 dB Scotopic, Single Flash, Blue Filter

0 dB Scotopic, Single Flash, Red Filter

0 dB Scotopic, Single Flash, White Filter

0 dB Photopic, Single Flash, White Filter

0 dB Photopic, 30 Hz Flicker, White Filter

Once the protocol is selected the ERG-display screen is presented. The lower part of the screen contains the following menu :

F1: Record F2: Baseline F3: Store F4: Previous F5: Next F6: Quit F7: Time Range

Use the function keys F1-F7 to select the desired action.

After data has been gathered and stored on disk the MFTS3 system can be used to created a printed report or to view the data.

CHAPTER 6

RESULTS

In chapter 3, the classification of the oscillatory potential into individual wavelet was discussed. Their definition in terms of trough to peak difference is shown in Figure 3.1 and 3.2. For four normal and four diabetic subjects, the individual wavelet amplitudes, as well as their summed and average values, are shown in Table 6.1 and 6.2 respectively. The average amplitude for the four diabetic patients in Table 6.2 is 72.00 % lower than that for the four normal subjects of Table 6.1, where average amplitude for the normal subjects is $(44.774 \pm 3.199 \ \mu V)$ and that for the diabetic subjects is $(12.536 \pm 3.009 \ \mu V)$.

Figures 6.1 and 6.2 show ERGs and oscillatory potentials obtained with bilateral (12th order Butterworth) band-pass filter of 70 to 500 Hz, for a normal and diabetic subject respectively.

25.00 uv/div

1 OS

2 OS

10 ms/div
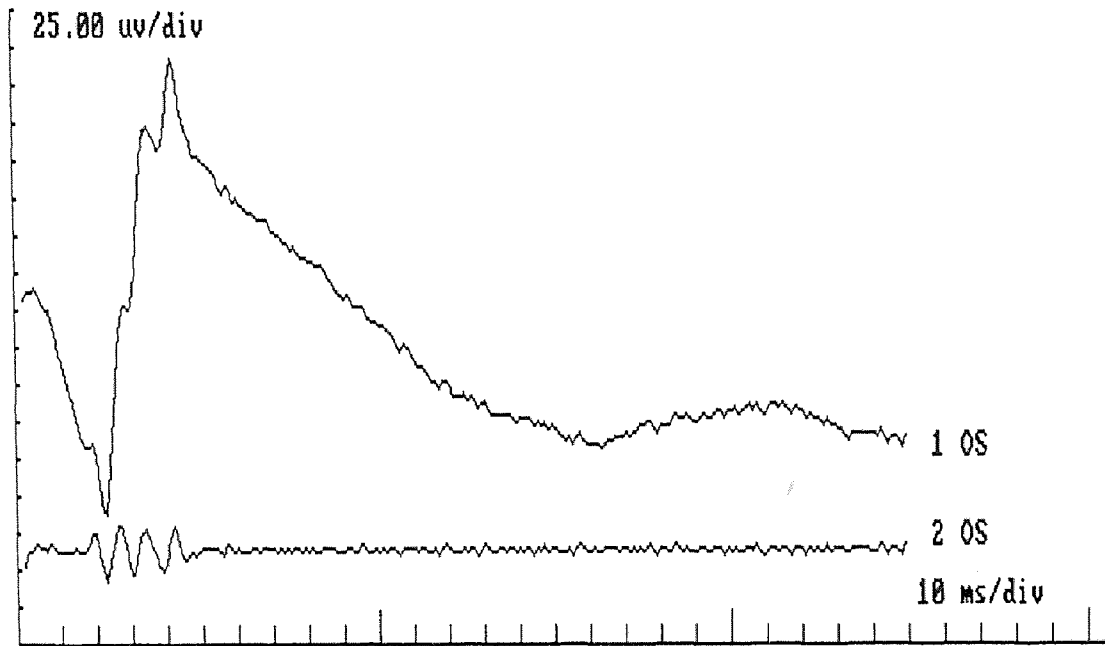
Figure 6.1 ERG and oscillatory potential waveforms from a normal subject.

Table 6.1 Table of Measurement for the Amplitude of Each Oscillatory Potential Component in the Normal Subjects.

Subject wavelet	1.(N) (μV)	2.(N) (μV)	3.(N) (μV)	4.(N) (μV)	Average (μV)	STD
OP1	6.746	6.773	1.461	7.373	5.588	2.767
OP2	48.221	57.347	49.653	70.762	56.496	10.321
OP3	46.024	90.316	69.709	95.829	75.470	22.621
OP4	65.476	46.474	59.817	31.163	50.733	15.286
OP5	36.457	22.476	46.891	34.510	35.084	17.337
TOTAL	202.924	220.386	227.531	241.637	223.120	16.101
AVERAGE	40.585	44.677	45.506	48.327	44.774	3.199

```
25.00 uv/div
                                              1 OS




                                              2 OS


                                    10 ms/div
```
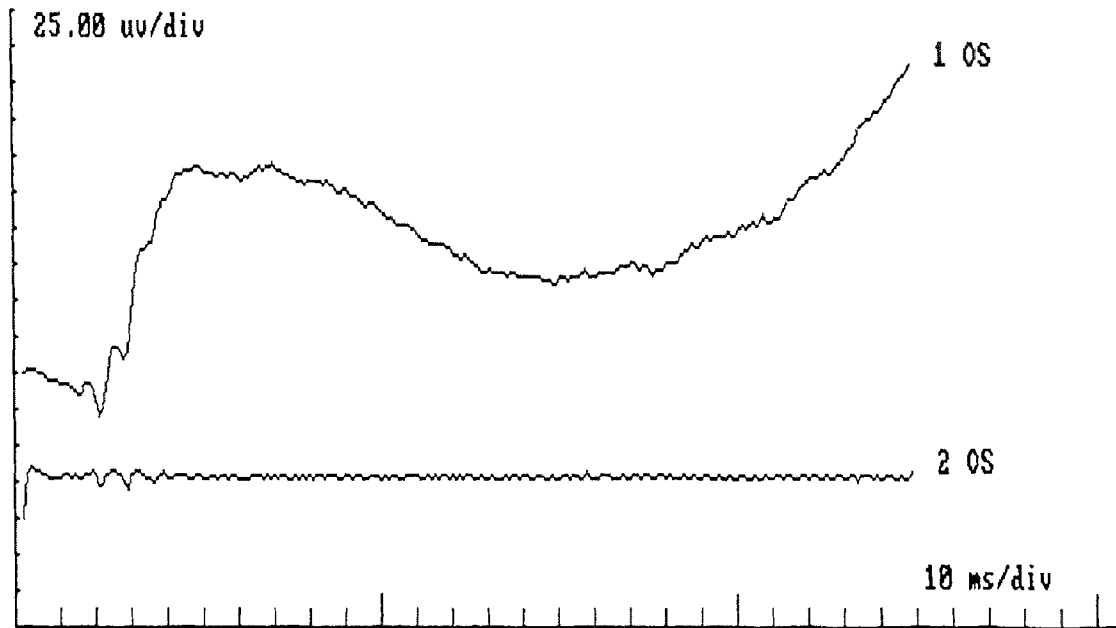
Figure 6.2 ERG and oscillatory potential waveforms from a diabetic subject.

Table 6.2 Table of Measurement for the Amplitude of each Oscillatory Potential Component in the Diabetic Subjects.

Subject wavelet	1.(D) (μV)	2.(D) (μV)	3.(D) (μV)	4.(D) (μV)	Average (μV)	STD
OP1	17.299	9.789	6.925	3.438	9.363	5.894
OP2	1.873	19.406	20.325	13.340	13.736	8.494
OP3	9.855	11.781	24.638	17.304	15.895	6.629
OP4	10.046	16.920	16.790	8.948	13.176	4.472
OP5	8.732	22.307	1.249	9.742	10.508	8.670
TOTAL	47.805	80.203	69.937	52.772	62.679	15.046
AVERAGE	**9.561**	**16.040**	**13.987**	**10.554**	**12.536**	**3.009**

Table 6.3 Parameters of the Oscillatory Potential Model for the Normal Subjects.

Parameter Data	k_o (μv)	A_o (1/msc)	f_o (Hertz)
ODB-1	0.05956	0.45195	133.53
OSB-1	0.06646	0.25599	126.05
ODB-2	0.05857	0.26309	128.05
OSB-2	0.05962	0.24472	127.42
ODB-3	0.04280	0.22134	121.16
OSB-3	0.04525	0.23568	121.21
OSB-4	0.04310	0.21015	120.76
OSB-4	0.04113	0.24240	119.87
ODB-5	0.05220	0.18994	119.05
OSB-5	0.05102	0.21473	123.27
ODB-6	0.05425	0.19532	119.39
OSB-6	0.05888	0.22689	119.48
ODB-7	0.04110	0.20227	119.82
OSB-7	0.05956	0.22305	122.99
AVERAGE	0.05239	0.24125	114.82
STD (par)	0.00842	0.06445	9.878

Table 6.4 Parameters of the Oscillatory Potential Model for the Diabetic Subjects.

Parameter Data	k_o (μv)	A_o (1/msc)	f_o (Hertz)
ODB-1	0.00024	0.32794	83.02
OSB-1	-0.00949	0.26879	80.67
ODB-2	0.00491	0.21046	127.51
OSB-2	0.01174	0.21736	127.18
ODB-3	0.01500	0.40468	112.44
OSB-3	0.03957	0.41580	118.73
ODB-4	0.00179	0.21719	97.78
OSB-4	0.00712	0.82184	87.90
ODB-5	0.01167	0.22041	98.67
OSB-5	0.00932	0.24986	114.63
AVERAGE	0.00919	0.33543	104.853
STD (par)	0.01281	0.18751	17.622

The parameters for each waveform are identified and summarized on Tables 6.3 and 6.4 and shown in Appendix A and B. The methods of ERR STD (OP) and EEF (OP) were described in chapter 4. The method for estimation of STD (parameter) is shown as :

$$STD\ (parameter)\ =\ \sqrt{\frac{1}{n-1}\sum_{i=1}^{n}(p_i - \mu_p)^2} \qquad (6.1)$$

where n = 14 eyes tested for normals and n = 10 eyes tested for diabetics, p_i is the value of parameter p and μ_p is average value of parameter p ($p = k_o$, A_o, f_o).

The average values of the oscillatory potential parameters from normal and diabetic subjects are presented in Table 6.5. Comparing the parameter k_o, which is mostly related to the oscillatory potential amplitudes and slightly related to the peak times of the oscillatory potential for the normal and diabetic subjects, we clearly see how the parameter k_o value for the normal subjects (0.05239 ± 0.00842 µv) is significantly greater than that for the diabetic subjects (0.00919 ± 0.01281 µv) . This is a significant evidence that the oscillatory potential is lacking or greatly reduced in diabetic retinopathy.

Table 6.5 Average of the Oscillatory Potential Parameters from Normal and Diabetic Subjects.

	PARAMETER		
	k_o (µv)	A_o (1/msec)	f_o (Hertz)
Normal	0.05239 ± 0.00842	0.24125 ± 0.06445	114.489 ± 9.878
Diabetic	0.00919 ± 0.01281	0.33543 ± 0.18751	104.853 ± 17.622

Comparing another important parameter, A_o, which is related to the peak times of the oscillatory potential, parameter A_o value of diabetic subjects (0.33543 ± 0.18751 1/msec) is much greater than that for the normal subjects (0.24125 ± 0.06445 1/msec) . It means that wavelets for the diabetic subjects have earlier peak times than that for the normal subjects with reduced their amplitudes.

Parameter f_o is related to the frequency of the oscillatory potential. Since this parameter represents no significant difference between normal (114.489 ± 9.878 Hertz) and diabetic subjects (104.853 ± 17.622 Hertz) , this factor doesn't seem to be a important parameter to consider.

CHAPTER 7

CONCLUSIONS

A new mathematical model of the oscillatory potential has been investigated in the present study by compressing information from oscillatory potential into three parameters. These parameters contain most of the information contained in the oscillatory potential raw data.

After determination of the model parameters, we have found that parameters k_o and A_o of the oscillatory potential model may be significant parameters to predict the states of the diabetic retinopathy. The use of this mathematical model may be a useful clinical tool to diagnose the progression of diabetic retinopathy.

Though the model parameters contain most of the information contained in the oscillatory potential, no relation has found to the underlying physiology. This is subject to future investigation.

APPENDIX A

OSCILLATORY POTENTIAL RESPONSES AND THEIR

MODEL REPRESENTATION FROM NORMAL SUBJECTS

This appendix includes oscillatory potential responses
and their parameter identification from normal subjects.
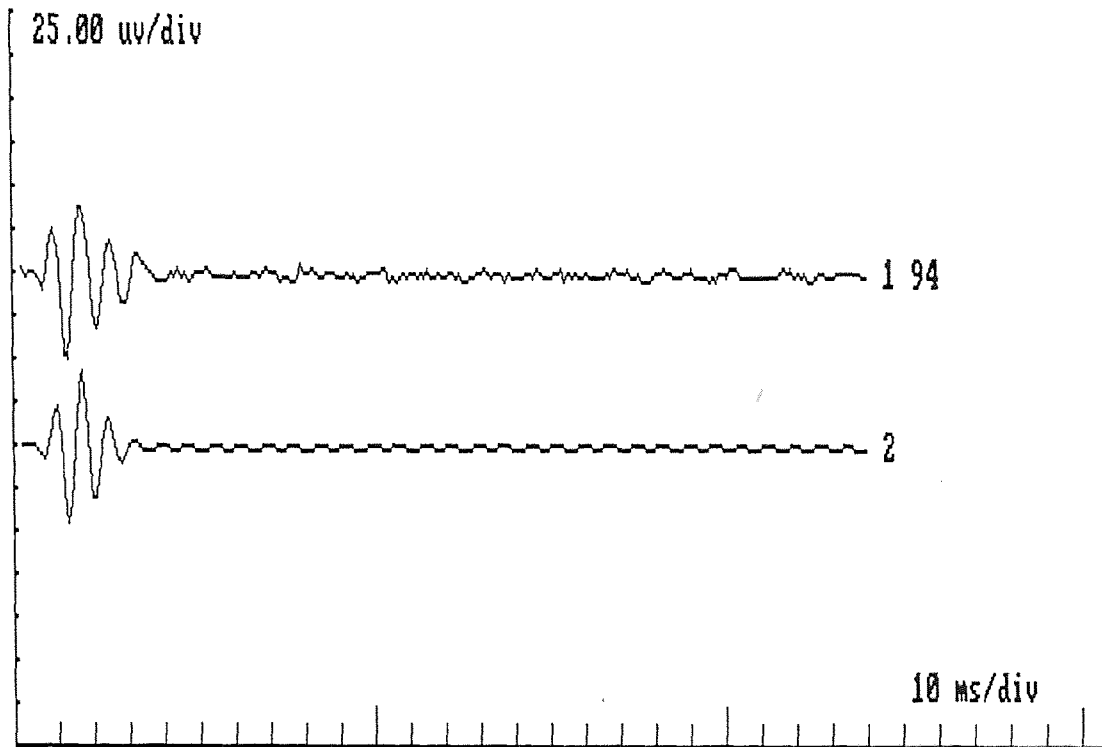
25.00 uv/div

1 94

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 db Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.05956 μv
(2) ------------ A_o =   0.45195   1/msec
(3) ------------ f_o =   133.53   Hertz

PATIENT : ODB-1   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

25.00 uv/div

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 db Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
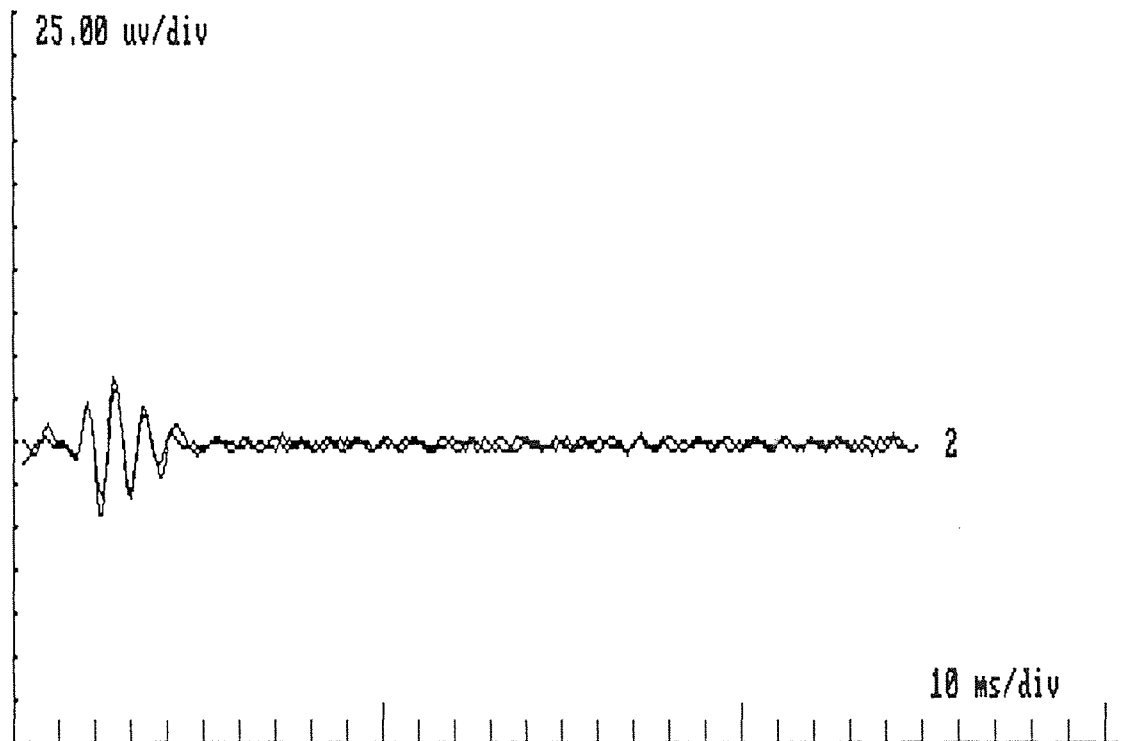
(1) ------------ k_o =   0.06646 μv

(2) ------------ A_o =   0.25599   1/msec

(3) ------------ f_o =   126.71   Hertz

PATIENT : OSB-1   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

20.00 uv/div

1 OS

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 db Scotopic Single Flash White   FREQUENCY :   EYE : R

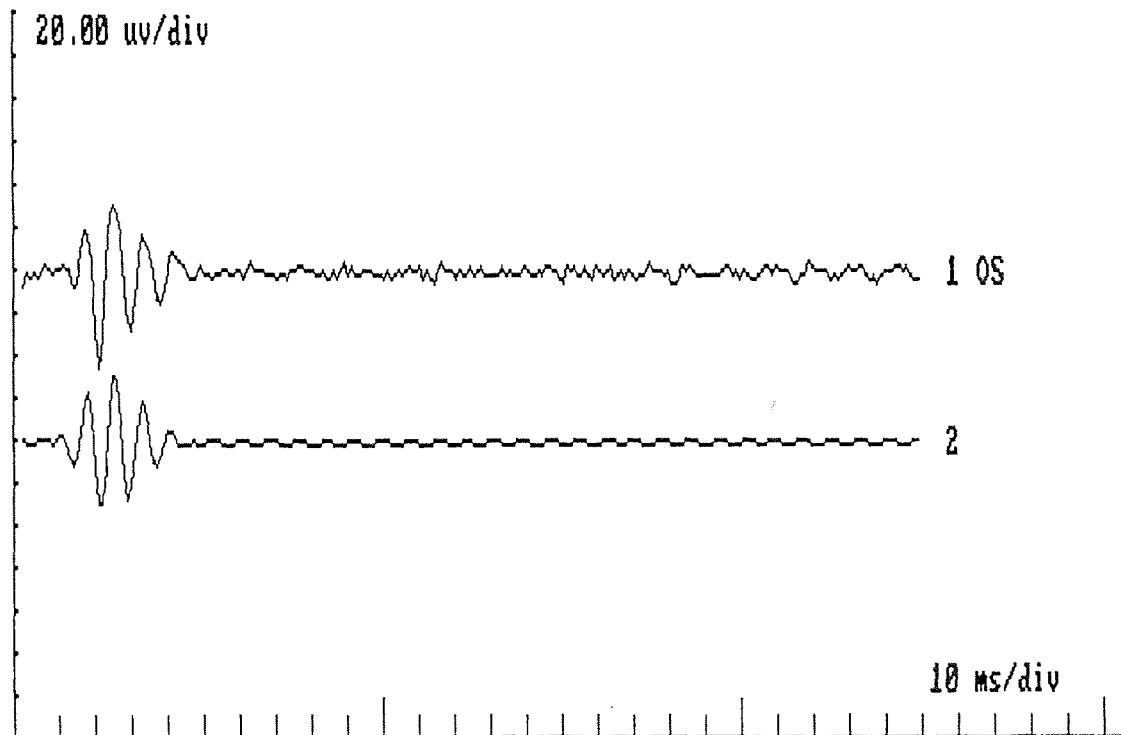FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.05857 μv

(2) ------------ A_o =   0.26309   msec

(3) ------------ f_o =   128.05   Hertz

PATIENT : ODB-2   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

20.00 uv/div

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single Flash White   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass :   70 Hz   Low Pass :   500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
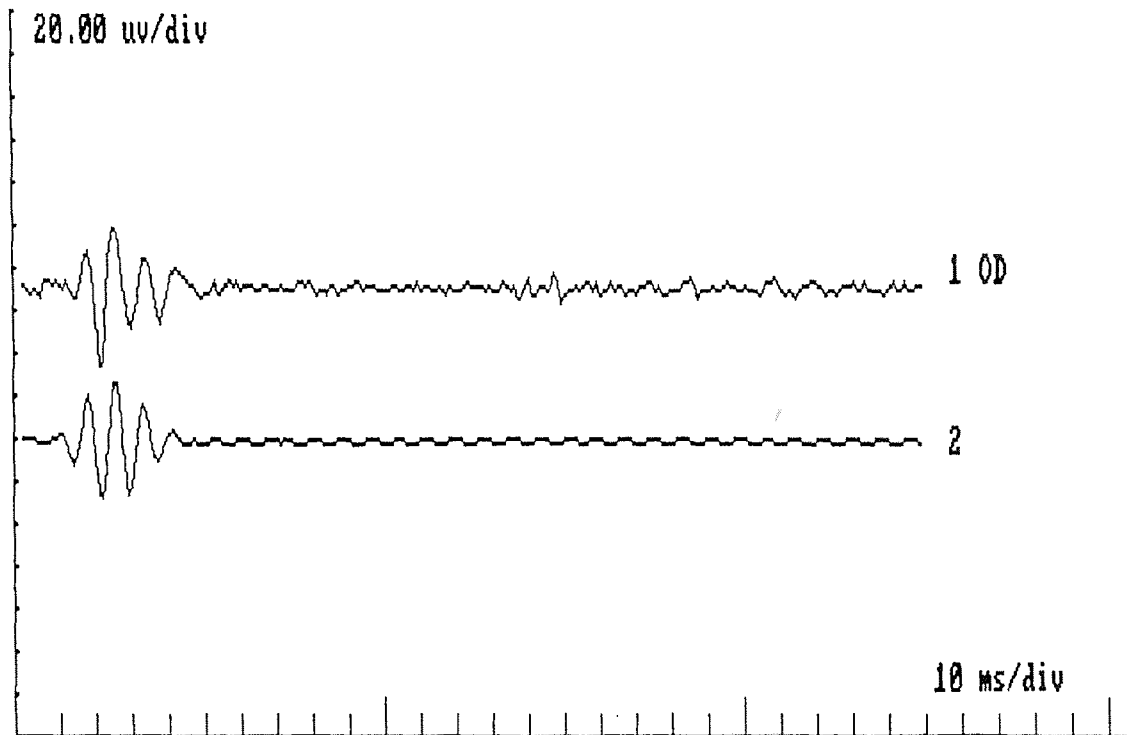
(1) ------------ k_o =   0.05962 μv
(2) ------------ A_o =   0.24472   1/msec
(3) ------------ f_o =   127.42   Hertz

PATIENT : OSB-2   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

15.00 uv/div

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.04280 μv
(2) ------------ A_o =   0.22134   1/msec
(3) ----------- f_o =   121.16   Hertz

PATIENT : ODB-3   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

20.00 uv/div

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz
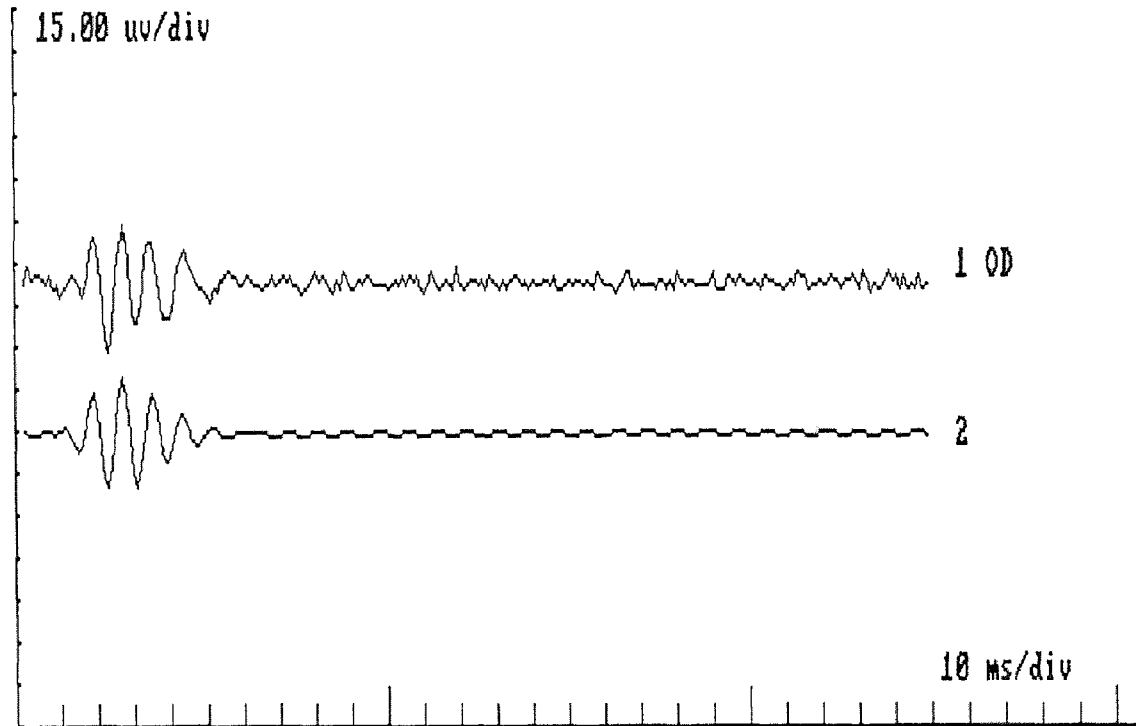
2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.04525 μv
(2) ------------ A_o =   0.23568   1/msec
(3) ------------ f_o =   121.21   Hertz

PATIENT : OSB-3   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

15.00 uv/div

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz
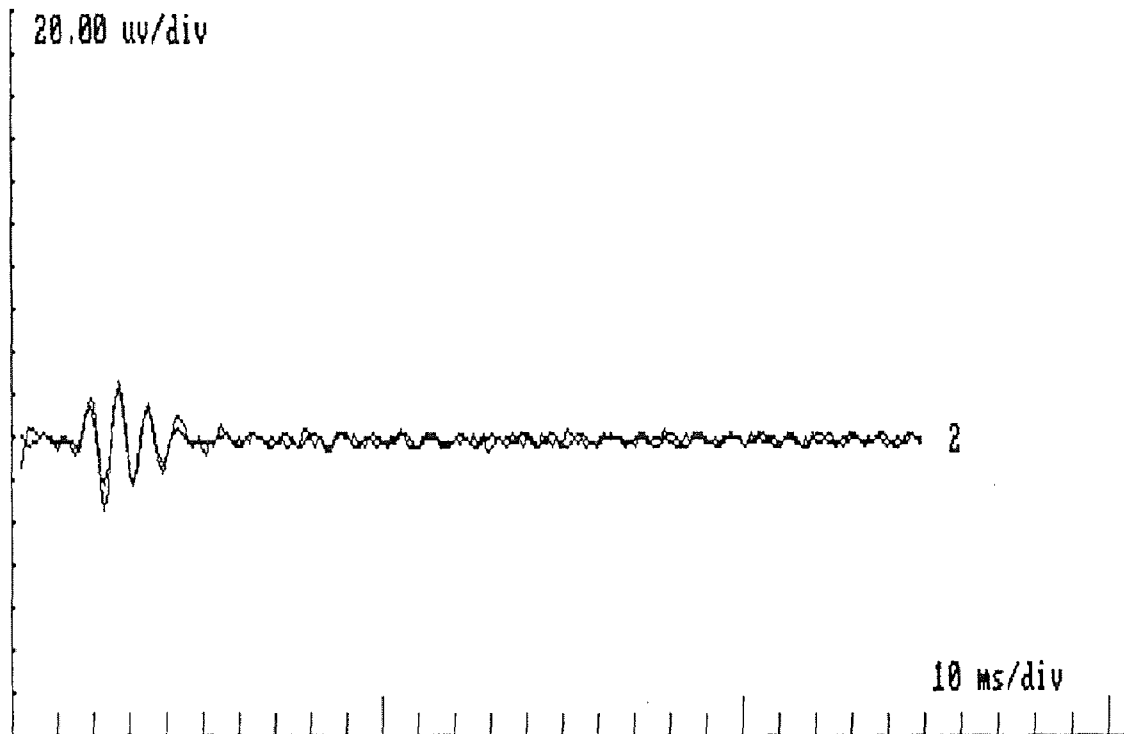
2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.04310 μv

(2) ------------ A_o =   0.21015   1/msec

(3) ------------ f_o =   120.76   Hertz

PATIENT : ODB-4   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

15.00 uv/div

10 ms/div

2

1 : TEST DATE :　　　　　　TEST TYPE : ERG　　　　LABEL :

STIMULUS : 0 dB Scotopic Single White Flash　　　FREQUENCY :　　　EYE : L

FILTER FREQUENCY :　　High Pass : 70 Hz　　Low Pass : 500 Hz
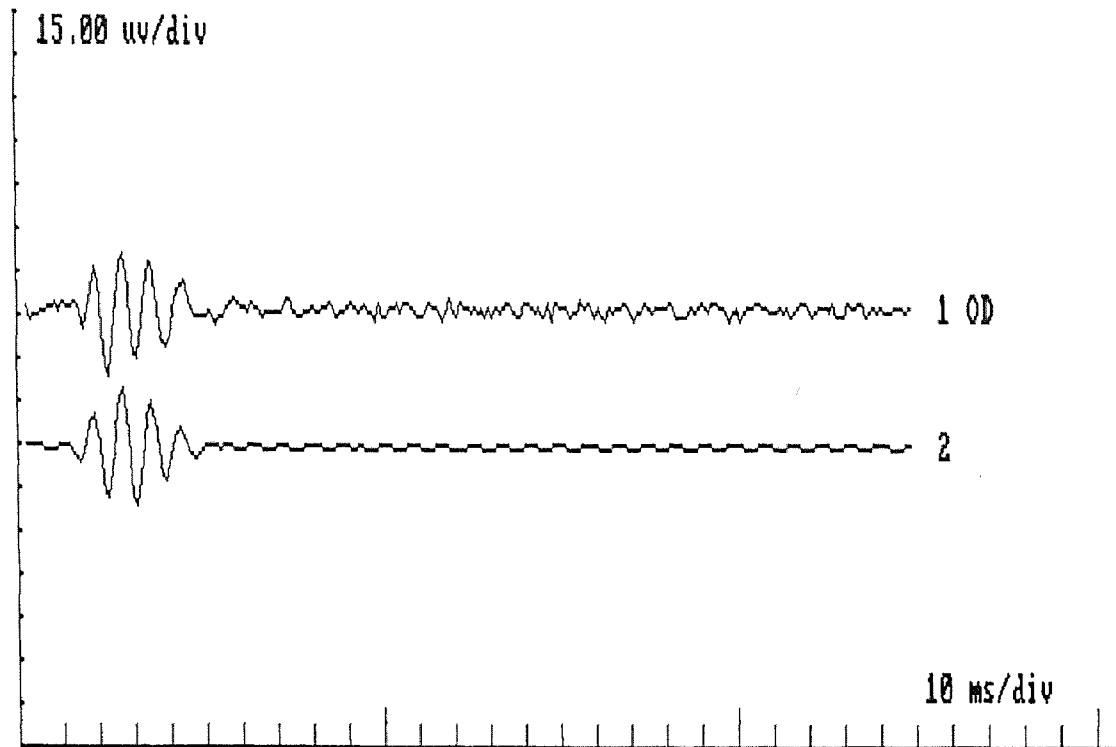
2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =　　0.04113　μv
(2) ------------ A_o =　　0.24240　1/msec
(3) ------------ f_o =　　119.87　Hertz

PATIENT : OSB-4　　　　　DATE OF BIRTH :　　　　SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

15.00 uv/div

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass :   70 Hz   Low Pass :   500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
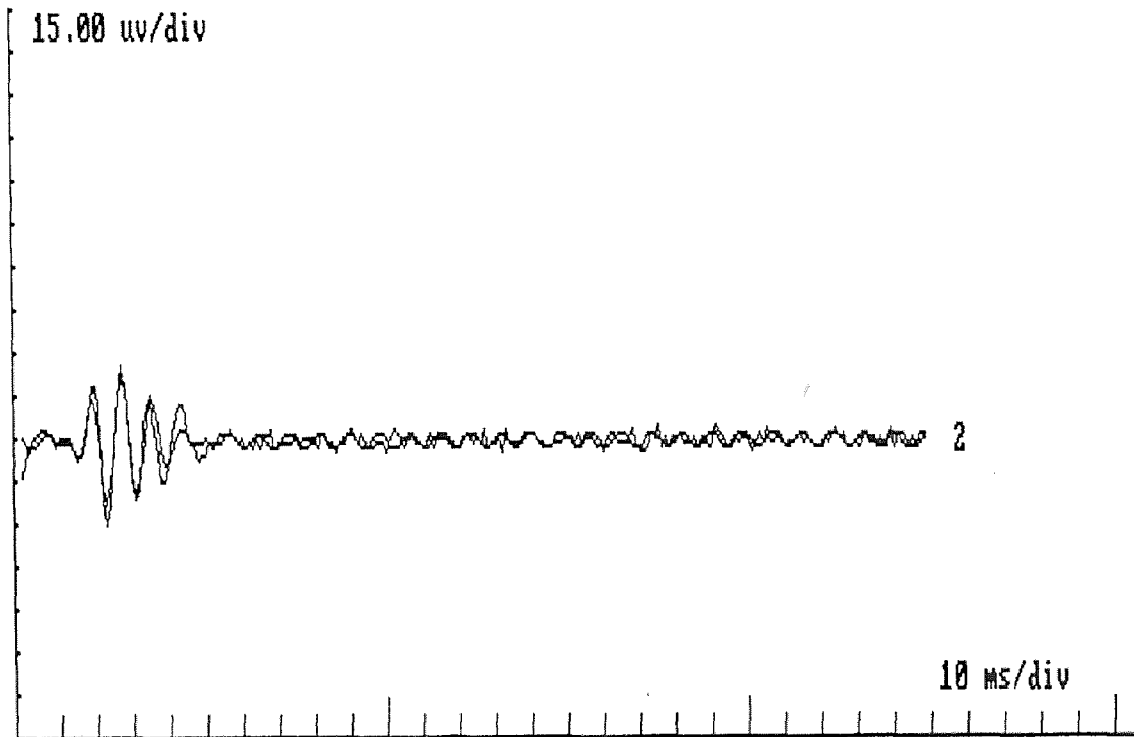
(1) ------------ k_o =   0.05220 μv
(2) ------------ A_o =   0.18994   1/msec
(3) ------------ f_o =   119.05   Hertz

PATIENT : ODB-5   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

20.00 uv/div

10 ms/div

2

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz
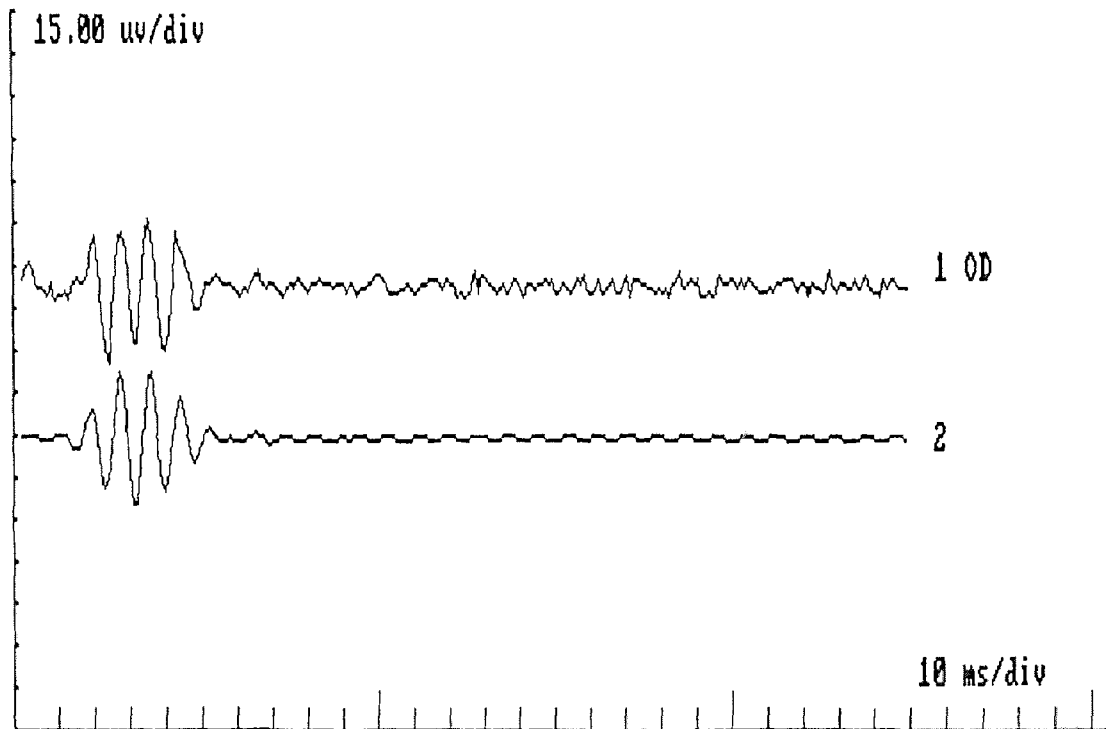
2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.05102 μv
(2) ------------ A_o =   0.21473   1/msec
(3) ------------ f_o =   123.27   Hertz

PATIENT : OSB-5   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

20.00 uv/div

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
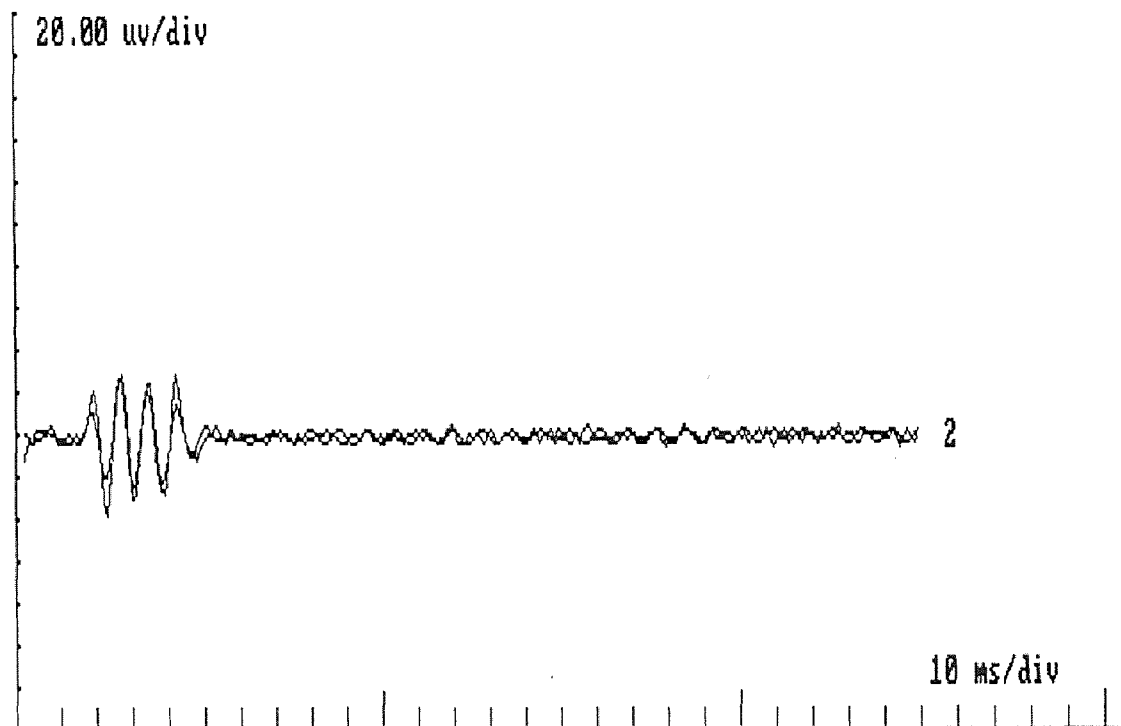
(1) ------------ k_o =   0.05425 μv
(2) ------------ A_o =   0.19532   1/msec
(3) ------------ f_o =   119.39   Hertz

PATIENT : ODB-6   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

20.00 uv/div

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz
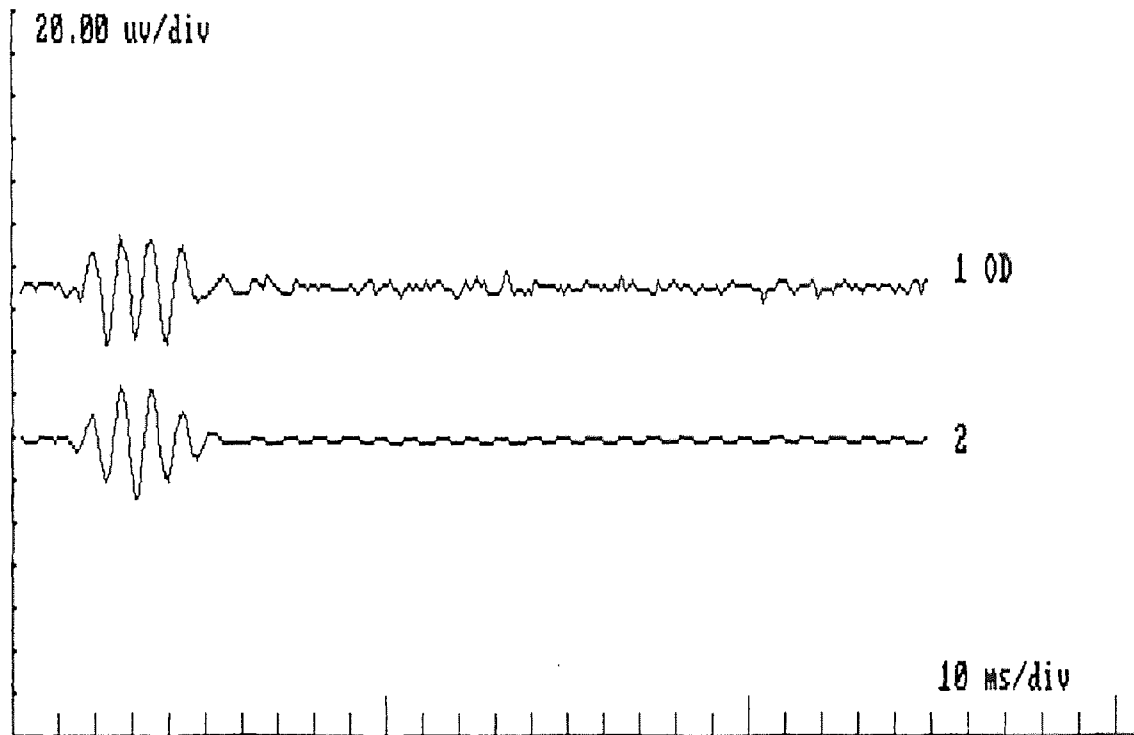
2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.05888 μv

(2) ------------ A_o =   0.22689   msec

(3) ------------ f_o =   119.48   Hertz

PATIENT : OSB-6   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT :

```
20.00 uv/div
```

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
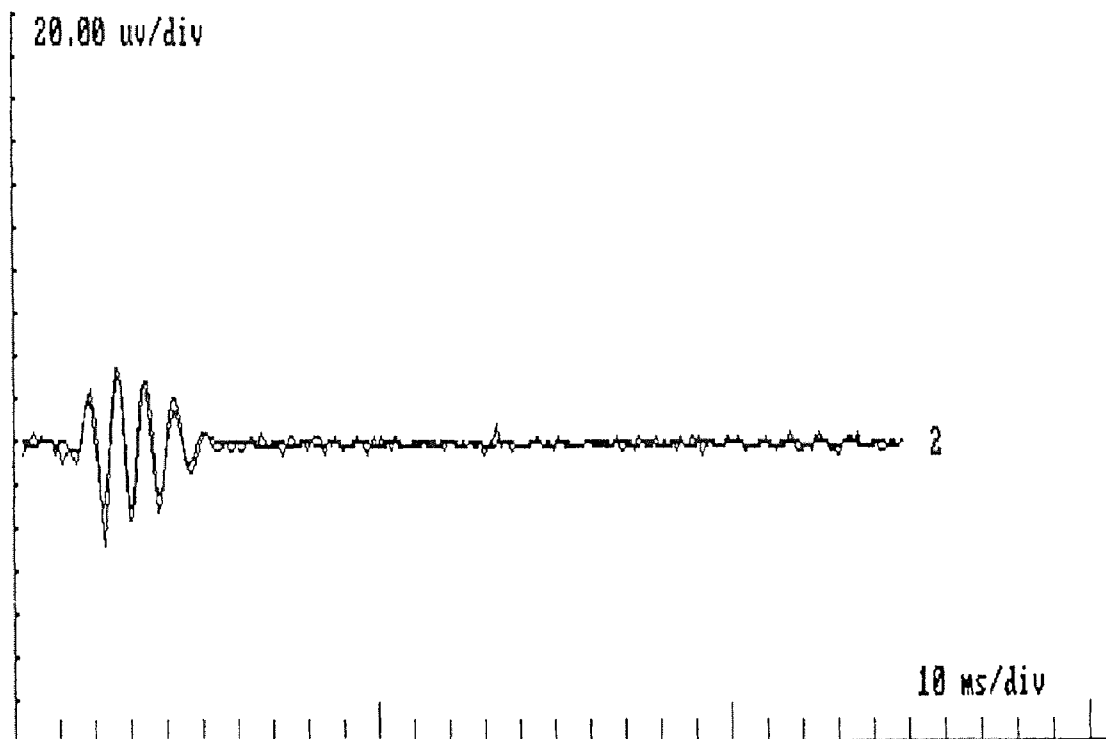
(1) ------------ k_o =   0.04110 μv
(2) ------------ A_o =   0.20227   msec
(3) ------------ f_o =   119.82   Hertz

PATIENT : ODB-7   DATE OF BIRTH :   SEX :
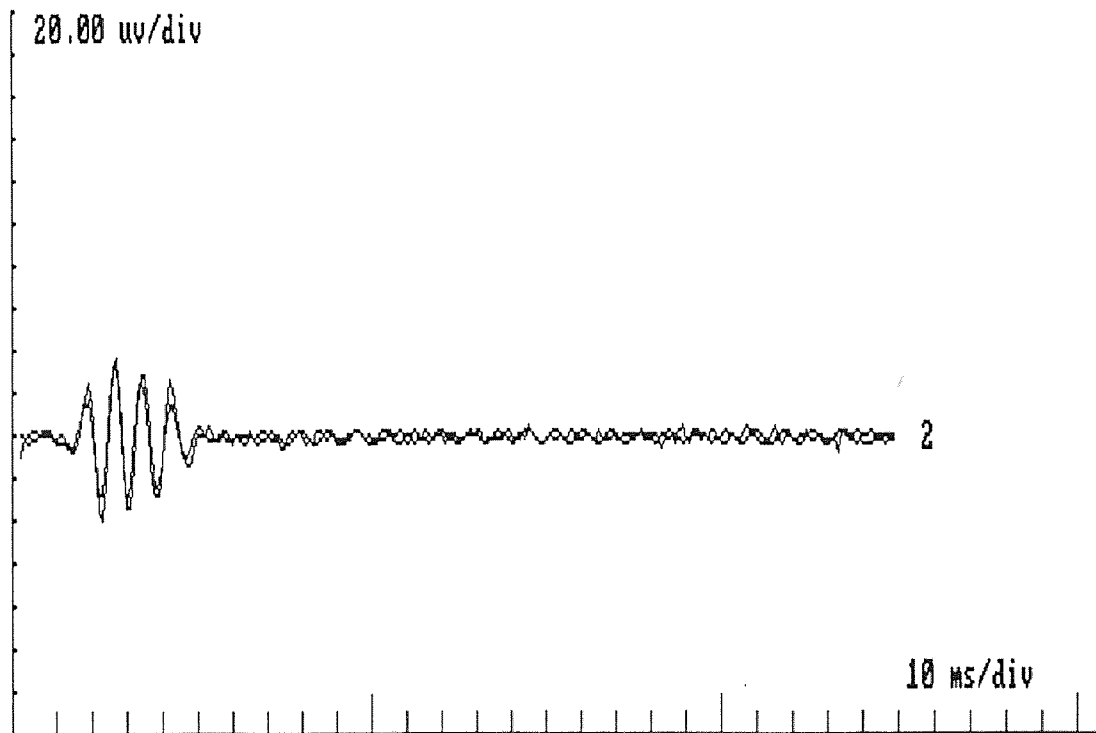
DIAGNOSIS : NORMAL SUBJECT

COMMENT :

20.00 uv/div

10 ms/div

2

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass :   70 Hz   Low Pass :   500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
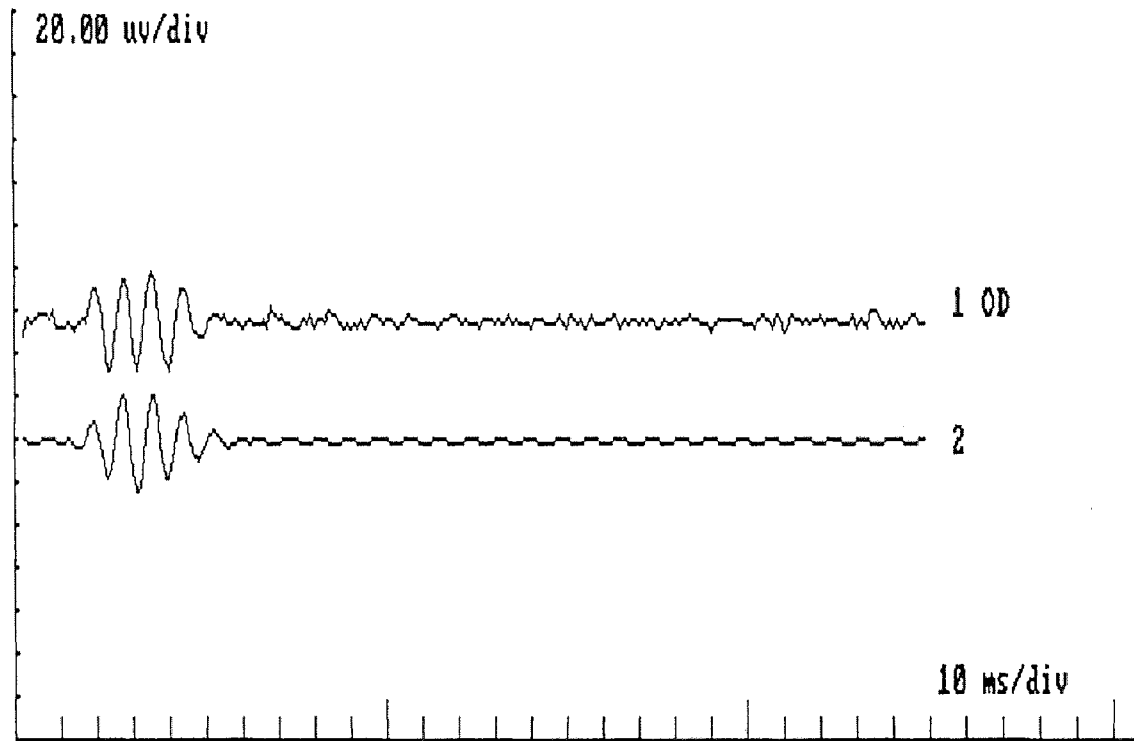
(1) ------------ k_o =   0.05956 μv
(2) ------------ A_o =   0.22305   1/msec
(3) ------------ f_o =   122.99   Hertz

PATIENT : OSB-7   DATE OF BIRTH :   SEX :

DIAGNOSIS : NORMAL SUBJECT

COMMENT

APPENDIX B

OSCILLATORY POTENTIAL RESPONSES AND THEIR
MODEL REPRESENTATION FROM DIABETIC SUBJECTS

This appendix includes oscillatory potential responses
and their parameter identifications from diabetic subjects.
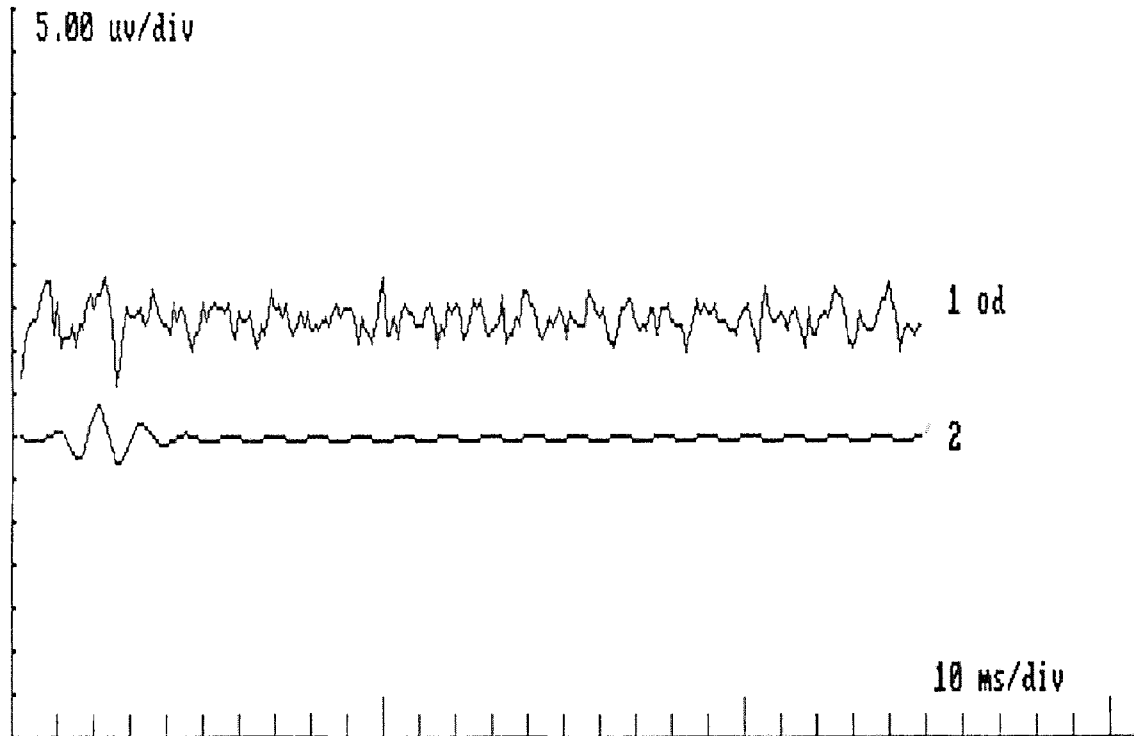
5.00 uv/div

1 od

2

10 ms/div

1 : TEST DATE :　　　　　　TEST TYPE : ERG　　　LABEL :

STIMULUS : 0 dB Scotopic Single White Flash　　FREQUENCY :　　EYE : R

FILTER FREQUENCY :　High Pass : 70 Hz　　Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =　　0.00024　μv

(2) ------------ A_o =　　0.32794　1/msec

(3) ------------ f_o =　　83.02　　Hertz

PATIENT : ODB-1　　　　　DATE OF BIRTH :　　　　SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

```
5.00 uv/div




                                                                    1 OS


                                                                    2


                                                        10 ms/div
```

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   -0.00949 μv

(2) ------------ A_o =   0.26879   1/msec

(3) ------------ f_o =   80.67   Hertz

PATIENT : OSB-1   DATE OF BIRTH :   SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

5.00 uv/div

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
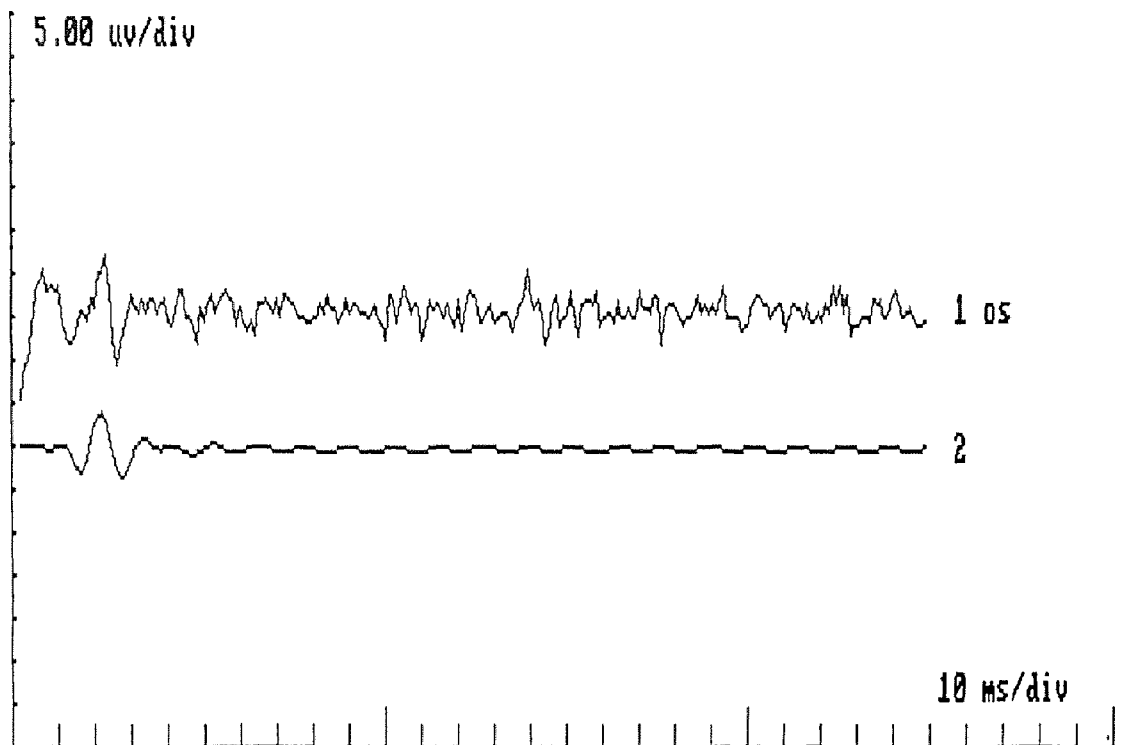
(1) ------------ k_o =   0.00491 μv
(2) ------------ A_o =   0.21046   1/msec
(3) ------------ f_o =   127.51   Hertz

PATIENT : ODB-2   DATE OF BIRTH :   SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

5.00 uv/div

1 OS

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass :   500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.01174 μv
(2) ------------ A_o =   0.21736   1/msec
(3) ------------ f_o =   127.18   Hertz

PATIENT : OSB-2   DATE OF BIRTH :   SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

```
25.00 uv/div
```

1 R

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

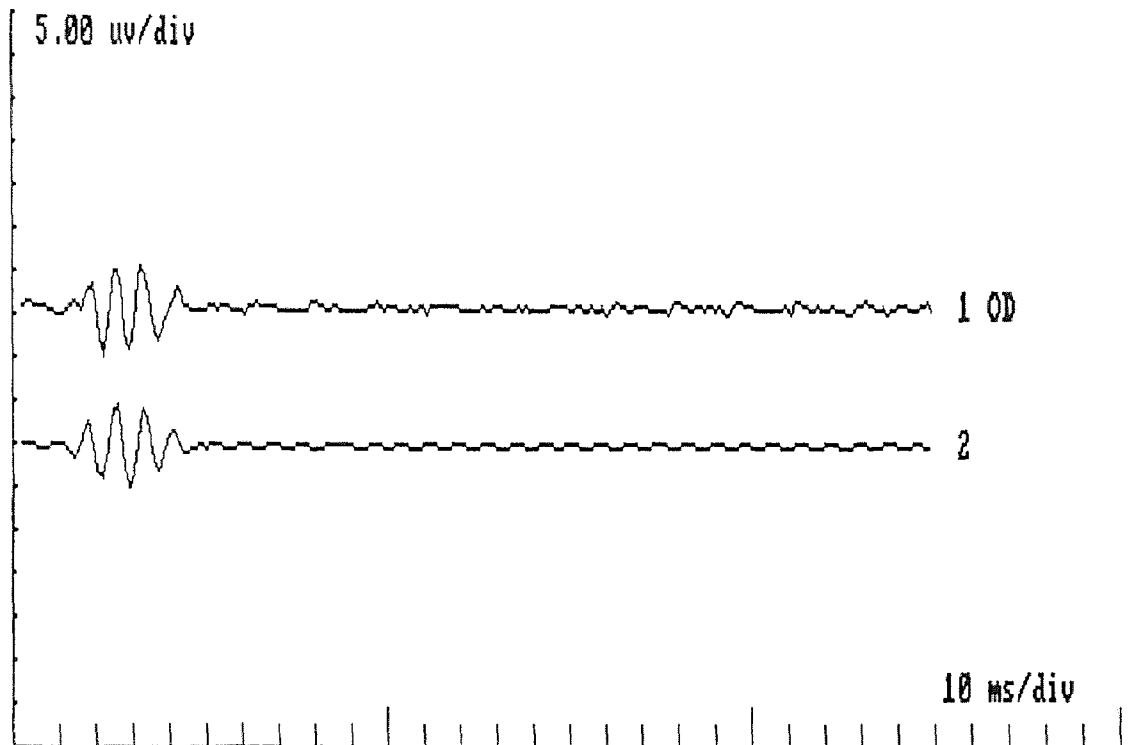$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.01500 μv

(2) ------------ A_o =   0.40468   1/msec

(3) ------------ f_c =   112.44   Hertz

PATIENT : ODB-3   DATE OF BIRTH :   SEX :
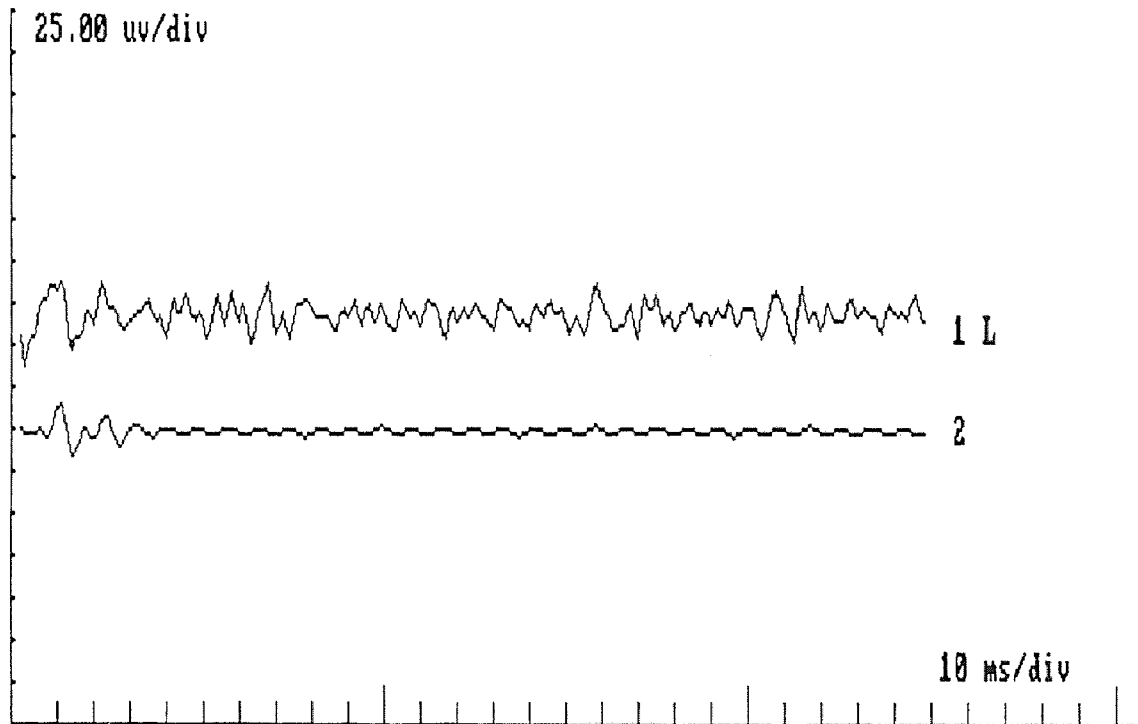
DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

25.00 uv/div

1 L

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

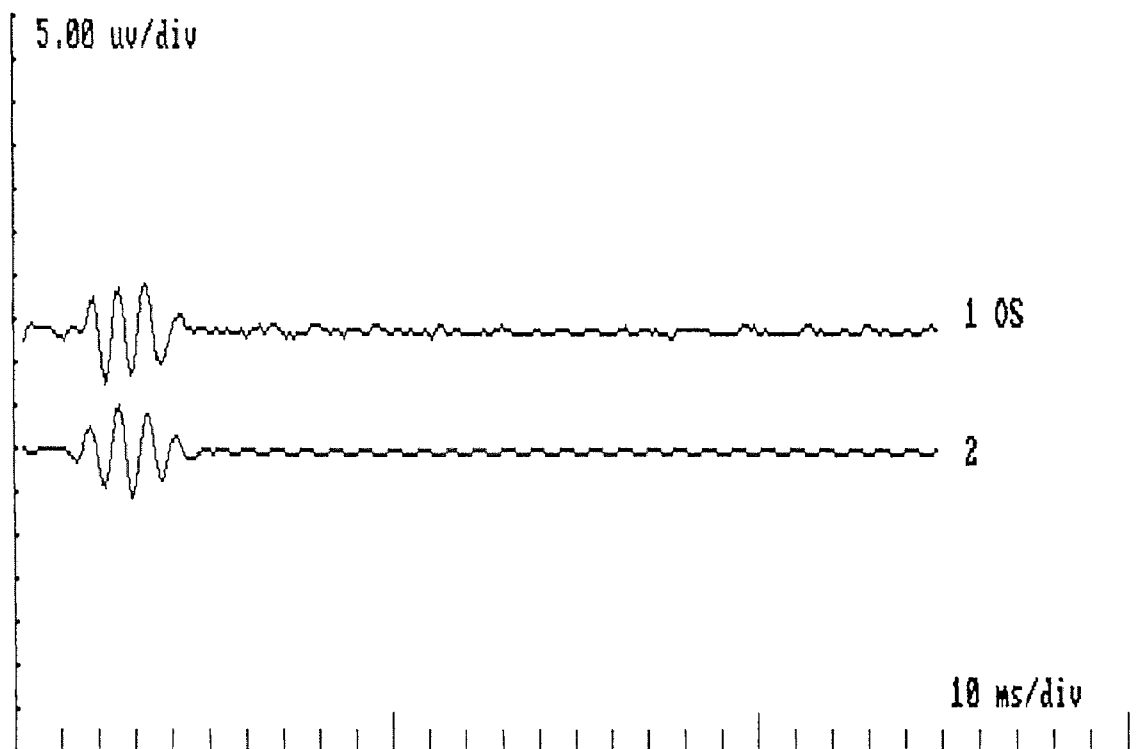FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o =   0.03957 μv

(2) ------------ A_o =   0.41580   1/msec

(3) ------------ f_o =   118.73   Hertz

PATIENT : OSB-3   DATE OF BIRTH :   SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

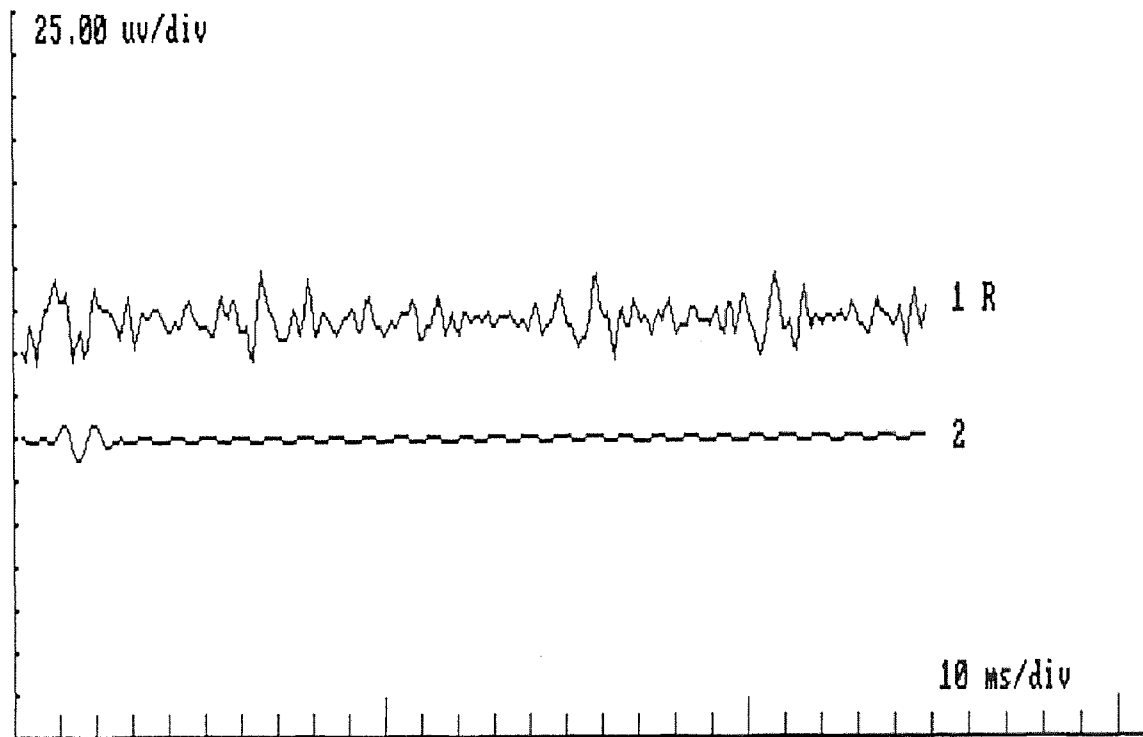FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ $k_o =$ 0.00179 μv

(2) ------------ $A_o =$ 0.21719   1/msec

(3) ------------ $f_o =$ 97.78   Hertz

PATIENT : ODB-4   DATE OF BIRTH :   SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass :   500 Hz

2 : Model   Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$

(1) ------------ k_o = 0.00719 μv

(2) ------------ A_o = 0.82184   1/msec

(3) ------------ f_o =   87.90   Hertz

PATIENT : OSB-4   DATE OF BIRTH :   SEX :
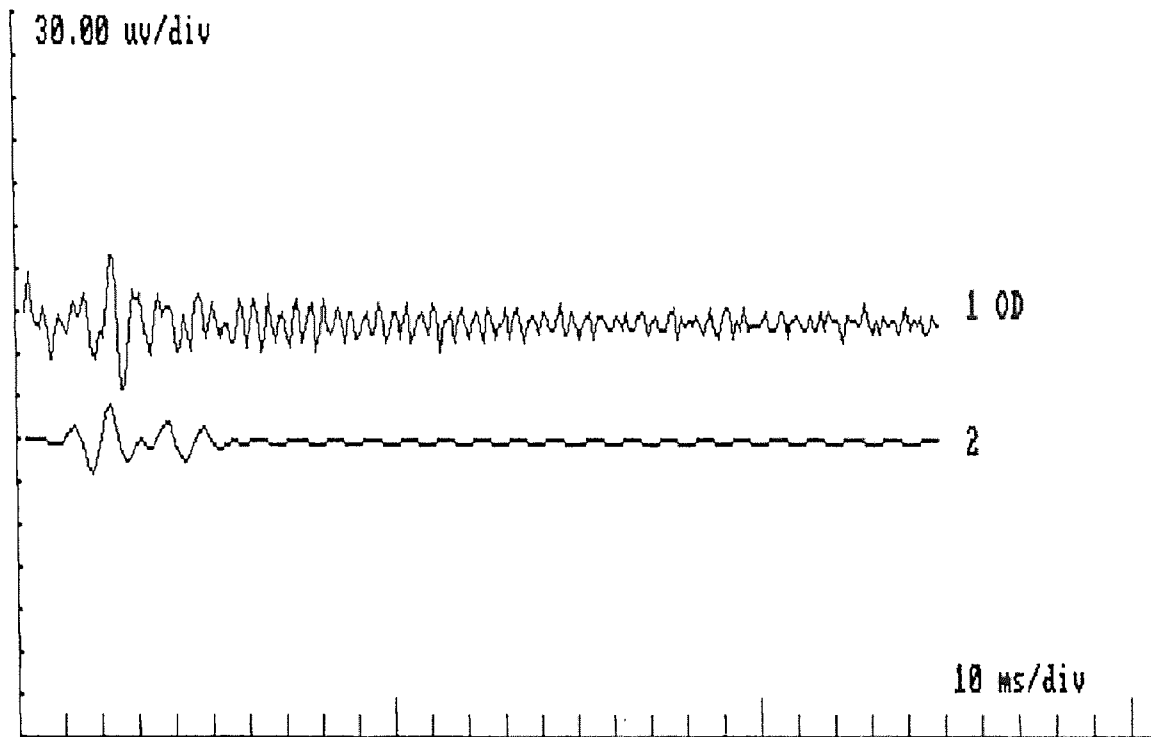
DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

30.00 uv/div

1 OD

2

10 ms/div

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : R

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass : 500 Hz

2 : Model Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
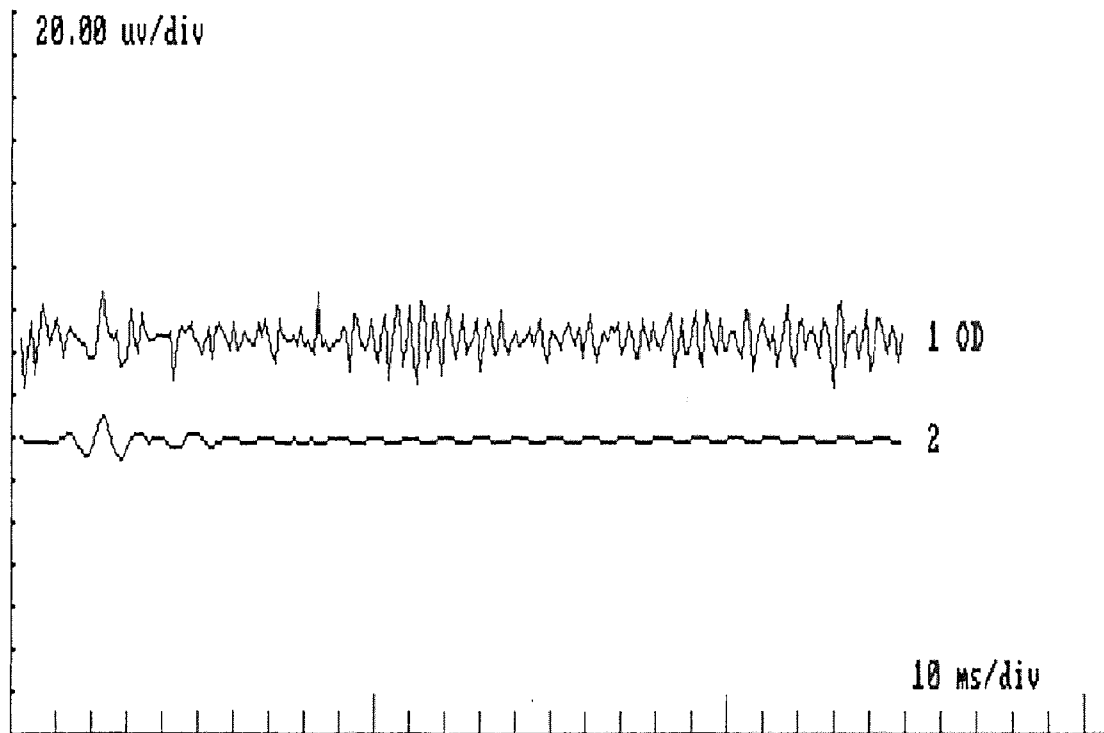
(1) ------------ $k_o =$ 0.01167 μv

(2) ------------ $A_o =$ 0.22041   1/msec

(3) ------------ $f_o =$ 98.67   Hertz

PATIENT : ODB-5   DATE OF BIRTH :   SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

15.00 uv/div

10 ms/div

2

1 : TEST DATE :   TEST TYPE : ERG   LABEL :

STIMULUS : 0 dB Scotopic Single White Flash   FREQUENCY :   EYE : L

FILTER FREQUENCY :   High Pass : 70 Hz   Low Pass :   500 Hz

2 : Model   Waveform

$$OP(t) = k_o \cdot (A_o \cdot t)^7 \cdot e^{-(A_o \cdot t)} \cdot \sin(2 \cdot \pi \cdot f_o \cdot t)$$
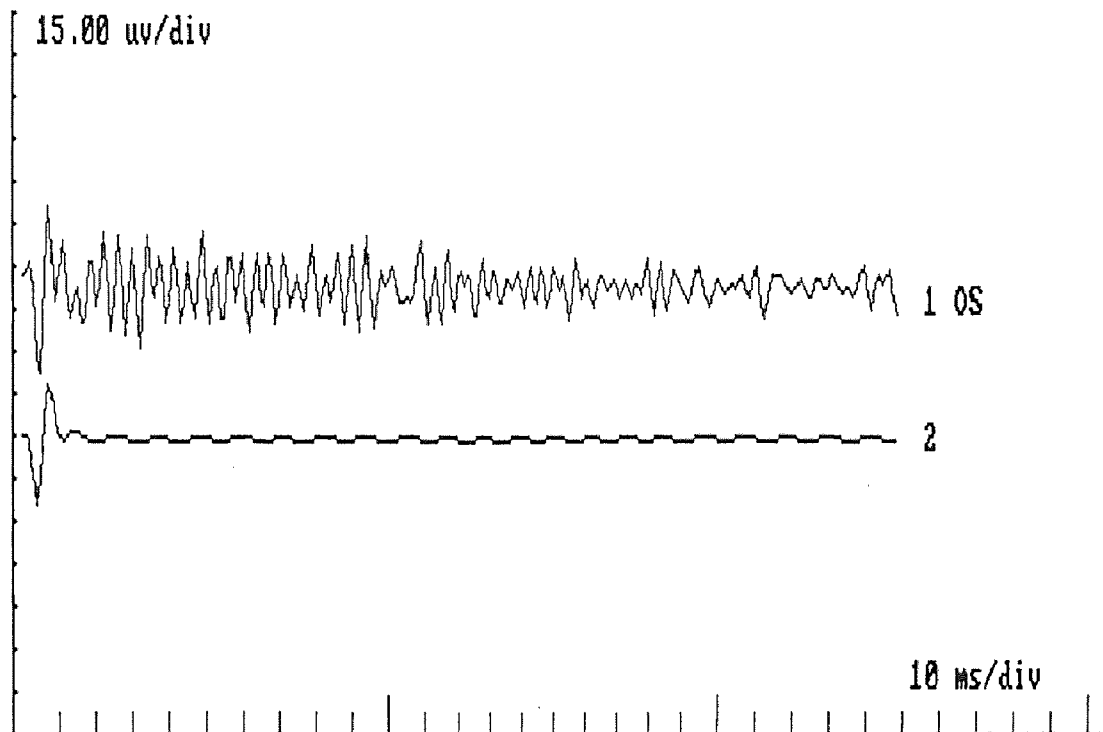
(1) ------------ k_o = 0.00932 μv

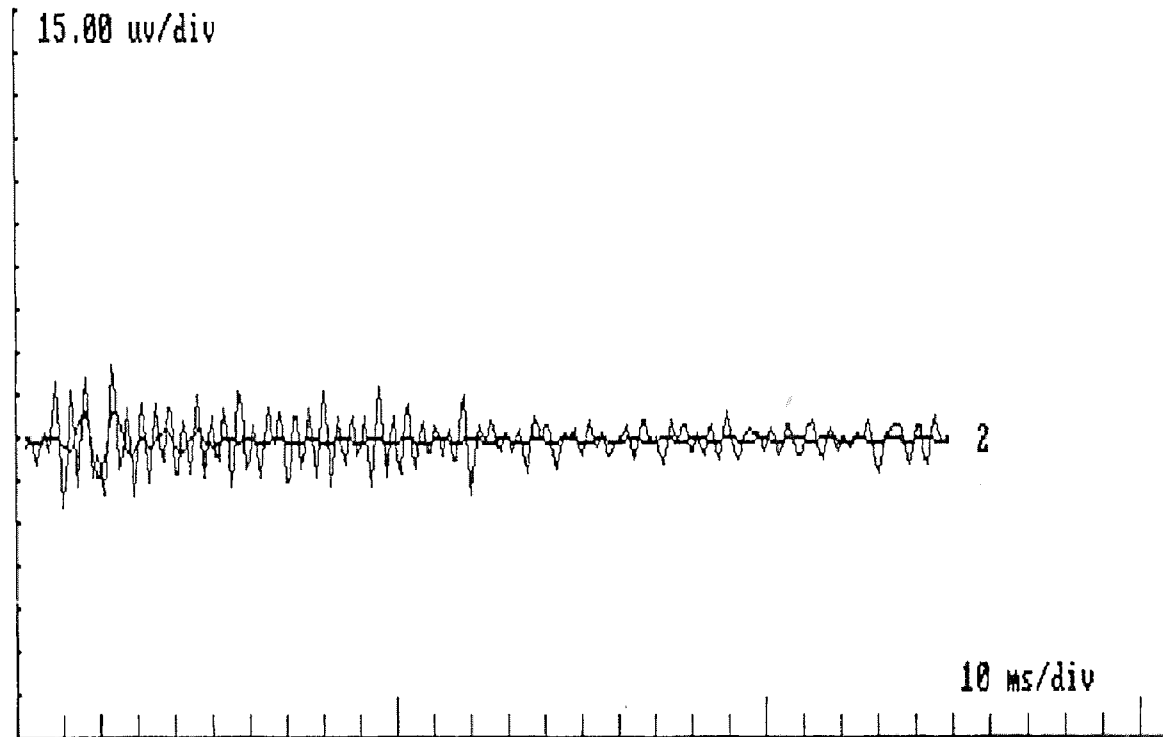(2) ------------ A_o = 0.24986   1/msec

(3) ------------ f_o = 122.08   Hertz

PATIENT : OSB-5   DATE OF BIRTH :   SEX :

DIAGNOSIS : DIABETIC SUBJECT

COMMENT :

APPENDIX C

PROGRAM FOR MEASURING
OSCILLATORY POTENTIAL AMPLITUDES

This appendix includes a program which can measure
oscillatory potential amplitudes and their peak times.

```c
csrm(l)                /* a pair of cursor measure the peak value   */
float l[];
{
    int i,j,k,x,y1,y2,key=49,swch,p=0;
    void g_clean(),position();
    float a,b,c;
    csr_status=1;              /* cursor on        */

    for(i=0;i<chn;++i)         /* the initial position  */
        for(j=0;j<2;++j)
            csrln(i,j,l,1);
    g_clean(95,99);
    position(5,24);
    swch=key-49;          /* channel 1 first */
    cprintf("Cursor of waveform %d;  a:Trough cursor  b:Peak cursor  c:Cursor
off",swch+1);
    while((key=keyin())!=27){ /* not finish  */
        switch(key){
            case 203:          /* move left  */
                csrln(swch,p,l,0);
                --csr[swch][p];
                csrln(swch,p,l,1);
                break;
            case 205:          /* move right*/
                csrln(swch,p,l,0);
                ++csr[swch][p];
                csrln(swch,p,l,1);
                break;
        }          /* end of switch  */
        if(key==97||key==65) /* A cursor       */
            p=0;
        if(key==98||key==66) /* B cursor       */
            p=1;
        if(key==99||key==67)   /* Cursor off       */
        {
            csr_status=0;
            break;
        }
        if(key>48&&key<chn+49){          /* change channel*/
        g_clean(95,99);
            position(5,24);
            swch=key-49;
            cprintf("Cursor of waveform %d;  a:Trough cursor  b:Peak cursor  c:Cursor
```

```
off",swch+1);
                    }    /* end of if   */
              }    /* end of while   */
}


        /* ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ */




opmd(l)             /* op mode */
float l[];
{
     int pkn[4],key=49,swch;
     void g_clean(),position();
     float peak[4][20];
     int i,pkt[4][20],not_done=1;
     extern int chk_csr();
     extern show_op();

     csr_status=1;              /* cursor on        */

     for(i=0;i<4;i++){
     pkn[i]=0;
     csr[i][0]=20;
     }
     csrln(0,0,l,1);

     g_clean(95,99);
     position(5,24);
     swch=key-49;           /* channel 1 first */
cprintf("Cursor of wave %d;  p:set peak position  c:cancel  f:finish  Esc: quit",swch+1);

     while(not_done){ /* not finish  */
      g_clean(95,99);
     position(5,24);
cprintf("Cursor of wave %d;  p:set peak position  c:cancel  f:finish  Esc: quit",swch+1);

          key=keyin();
          switch(key){
               case 27:            /*   exit   */
                    not_done=0;
                    break;
```

```
      case 203:            /* move left  */
          csrln(swch,0,1,0);
          --csr[swch][0];
          csrln(swch,0,1,1);
          break;
      case 205:            /* move right*/
          csrln(swch,0,1,0);
          ++csr[swch][0];
          csrln(swch,0,1,1);
          break;
      }          /* end of switch  */
  if(key==112||key==80)     /* set peak position        */
      {
      pkt[swch][pkn[swch]]=csr[swch][0];
      peak[swch][pkn[swch]]=data[swch][csr[swch][0]];
      ++pkn[swch];
      }
  if(key==99||key==67) /* cancel       */
      for(i=0;i<pkn[swch];++i){
      pkt[swch][i]=0;
      peak[swch][i]=0;
      }
  if(key==102||key==70)   /* finish setting peak    */
      {
      swch=chk_csr(peak,pkn);
      if(swch==chn){
      swch=0;
      show_op(pkt,peak,pkn);
      }
      else{
         for(i=0;i<pkn[swch];++i){
      pkt[swch][i]=0;
      peak[swch][i]=0;
      }          /*  end of for    */
      }          /*  end of else   */
      not_done=0;
      }          /*  end of if     */
  if(key>48&&key<chn+49){          /* change channel*/
      csrln(swch,0,1,0);
      swch=key-49;
      csrln(swch,0,1,1);
      }    /* end of if    */
  }    /* end of while    */
  csr_status=0;
```

```
}


        /* ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ */



csrln(i,j,l,s)   /* draw the little cursor line    */
int i,j;         /* which one */
float l[];       /* vertical shift of the data */
int s;                   /* on or off   */
{
    int x,y1,y2,k,step;

    step=np>300?1:2;
    x=15+step*csr[i][j];
    k=csr[i][j];
    y1=10*data[i][k]/sen+l[i]*20+6;
    y2=y1+10;
    line(x,x,200-y1,200-y2,s);
    if(csr_position)
       if(s)
         for(k=0;k<chn;++k){        /* data   */
             position(40,2+k);
             printf("#%1d: %3d<=>%7.3f",k+1,csr[k][0],data[k][csr[k][0]]);
             }

}


        /* ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ */
int o_mode,mode=6;

plot(n)        /* plot waveforms            */
int n;         /* report mode or test mode     */
{
    int flag=0,i,k,ntst1;
    char key,done=0,loop=1;
    float offset[4];
    void g_clean(),position(),axis();
    extern int prnt1();

    offset[0]=2.5;     /* set the vertical shift */
    offset[1]=4.0;
```

```
offset[2]=5.5;
offset[3]=7.0;
o_mode=getmode();    /* save the old video mode */
cmode(mode);    /* change to graphic mode */
while(done==0){
    g_clean(0,99);
    axis();
    menu1(n);
    for(i=1;i<=chn;++i)
        draw(i,offset[i-1],1);
    if(csr_status)            /*print cursors */
        for(k=0;k<chn;++k)
        {
            csrln(k,0,offset,1);
            csrln(k,1,offset,1);
        }

    loop=1;
    while(loop)
    switch(keyin()){
        case 27:
            done=1;
            loop=0;
            break;
        case 187:    /* digital filter    */
            filter();
            loop=0;
            break;
        case 188:    /* shift waveforms    */
            move(offset);
            loop=0;
            break;
        case 189:    /* change vertical scale    */
            g_clean(95,99);
            position(5,24);
            cprintf("Enter New Scale:");
            scanf("%f",&sen);
            while(getchar()!='\n')
                ;
            loop=0;
            break;
        case 190:
            if(n==2){    /* at report mode this is print function    */
                g_clean(95,99);
```

```
            prnt();
            prnt1();
            menu1(n);
            }
        else{     /* at test mode this is storage function    */
            if(file_flag[0]==0)
                    ++ntk;   /* a new test */
            file_flag[4]=1;     /* data stored      */
            for(i=1;i<=chn;++i)
            savedata(i);
            g_clean(95,99);
            menu1(n);
            }
        break;
case 191:
        flag=1;   /* return mode 1  */
        done=1;
        loop=0;
        break;
case 192:
        flag=2;   /* return mode 2  */
        done=1;
        loop=0;
        break;
case 193:      /* return mode 3  */
        if(n==2)
                flag=3;
        else if(n==1)
                flag=0;
        done=1;
        loop=0;
        break;
case 194:      /* cursor measurement      */
        csr_position=1;
        csrm(offset);
        menu1(n);
        csr_position=0;
        loop=0;
        break;
case 195:      /* op mode   */
        csr_position=1;
        ntst1=ntst;
        opmd(offset);
        if(ntst1!=ntst)
```

```
                    fout();
                    menu1(n);
                    csr_position=0;
                    loop=0;
                    break;
                default:
                    done=0;
                    loop=1;
                    break;
                }
            }

        cmode(o_mode);
        return(flag);
}


    /* ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ */
```

REFERENCES

[1] R. Granit. Sensory Mechanism of the Retina, Oxford University Press, 1947.

[2] J. Dewar. "The Physiological Action of Light." Nature. 15 (1877): 437-445, 453- 454.

[3] R. Kahn, A. Lowenstein. "The Electroretinogram." Graefe's Arch. Ophthal. 114 (1924): 304-331.

[4] H. Hartline. "The Electrical Response to Illumination of the Eye in Intact Animals, Including the Human Subject and in Decerebrate Preparations." Am. J. Physiol. 73 (1925): 600-612.

[5] R. Granit. "The Components of Theoretical Action Potential and Their Relation to the Discharge in the Optic Nerve." J. Physiol. 77 (1933): 207-240.

[6] W. A. Cobb, H. B. Morton. "A New Component of the Human Electroretinogram." J. Physiol. 123 (1953): 36-37.

[7] H. Bornschein, G. Goodman. "Studies of the a-wave in theHumanElectroretinogram." A. M. A. Arch. Ophthal. 58 (1957): 431-437.

[8] D. Yonemula, K. Tsuzuki. "Clinical Importance of the Oscillatory Potential in the Human ERG." Acta. ophthal. Suppl. 70 (1962): 115-122.

[9] L. Wachtmeister. "Basic Research and Clinical Aspects of the Oscillatory Potentials of the Electroretinogram." Doc. Ophthalmol. 66 (1987): 187-194.

[10] W. H. A. Rushton. "Rhodopsin Measurement and Dark Adaptation in a Subject Deficient in Cone Vision." J. Physiol. 176 (1961): 38-45.

[11] Robert A. Moses. Adler's Physiology of the Eye, The C V Mosby Company, 1970.

[12] David Cline, John R Griffin. Dictionary of Visual Science, Third edition, 1980.

[13] H. Pan. Oscillatory Potentials Model and Parameter Identification, Masters Thesis, New Jersey Institute of Technology, Newark, NJ, 07102,1991.

[14] S. Polyak. The Retina, University of Chicago press, 1941.

[15] P. Algvere, L. Wachmeister. "On the Oscillatory Potentials of the Human ERG in Light and Dark Adaptation." Acta. Ophthalmol. 50 (1972): 737-759.

[16] H. Kergoat, J. Lovasik. "The Effect of Altered Retinal Vascular Perfusion Pressure on the White Flash Scotopic ERG and Oscillatory Potentials in Man." Electro. Clinical Neuro. 75 (1990): 306-322.

[17] J. J. Castro: Electroretinogram Modeling: Parameter Identification and Intensity Response- Function Fits, Masters Thesis, New Jersey Institute of Technology, Newark, NJ, 07102, 1991.

[18] A. U. Meyer, E. J. Haupt, J. J. Castro, H. Z. Pan: "Modeling and Parameter Identification in Clinical Electroretinography." IEEE - Regional Control Conference, Brooklyn, NY. (July 1964): 64-67.