Copyright Warning & Restrictions

The copyright law of the United States (Title 17, United States Code) governs the making of photocopies or other reproductions of copyrighted material.

Under certain conditions specified in the law, libraries and archives are authorized to furnish a photocopy or other reproduction. One of these specified conditions is that the photocopy or reproduction is not to be "used for any purpose other than private study, scholarship, or research." If a, user makes a request for, or later uses, a photocopy or reproduction for purposes in excess of "fair use" that user may be liable for copyright infringement,

This institution reserves the right to refuse to accept a copying order if, in its judgment, fulfillment of the order would involve violation of copyright law.

Please Note: The author retains the copyright while the New Jersey Institute of Technology reserves the right to distribute this thesis or dissertation

Printing note: If you do not wish to print this page, then select "Pages from: first page # to: last page #" on the print dialog screen

ABSTRACT

Electroretinography testing provides many useful techniques for clinical diagnosis of the visual system. However, the interpretation of the electroretinogram data involves a great amount of subjectivity. The use of mathematical models and parameter estimation techniques to fit the electroretinogram data supply a non-subjective and more standard way for analysis of the electroretinogram data. Mathematical models provide a way of summarizing the information enclosed in the raw electroretinogram response into a small set of parameters that define the response.

This thesis presents a mathematical model for the electroretinogram response due to light stimuli. It also provides a non-subjective method for obtaining the parameters of an intensity-response function, known as Naka-Rushton function, using the parameters of the mathematical model which define the raw electroretinogram data, instead of quantifying the information from the raw electroretinogram.

The intensity-response function is an example of the use of the information provided by the electroretinogram to evaluate retinal sensitivity to light stimuli. The proposed method for obtaining the intensity-response function consists of fitting the raw electroretinogram responses with the mathematical model of the electroretinogram in order to obtain the parameters which represent each response. These parameters are then used to obtain the intensity-response function instead of having to manually measure the amplitude of each electroretinogram response which is very error prone.

Several subjects were used to obtain electroretinogram responses. Each response was fitted with the mathematical model. The parameters from the electroretinogram model were then used to obtain the intensity-response function, thus providing more consistent and less subjective results.

The intent of this thesis is not to reach any medical conclusions but to provide a method to aid in the clinical diagnosis of the visual system.

Electroretinogram Modeling: Parameter Identification and Intensity-Response Function Fits

By

Juan J. Castro

Thesis submitted to the Faculty of the Graduate School of
the New Jersey Institute of Technology in partial fulfillment of the
requirements for the degree of
Master of Science in Electrical Engineering
1991

APPROVAL SHEET

Title of Thesis: **Electroretinogram Modeling: Parameter Identification and Intensity-Response Function Fits**

Name of Candidate: **Juan J. Castro**

Degree: **Master of Science in Electrical Engineering 1991**

Thesis and Abstract Approval:

Dr. Andrew U. Meyer — Date

Approval of Faculty Committee:

Dr. Stanley S. Reisman — Date

Dr. Edward Haupt — Date

Dr. Nirwan Ansari — Date

VITA

Name: Juan J. Castro

Permanent address: 92 Union St
Newark, NJ
07105

Degree and Date to be Confered: MSEE 1991

Date of Birth:

Place of Birth:

Secondary Education: Liceo La Paz, La Coruña, Spain

Collegiate Institutions Attended:	Date	Degree	Date of Degree
University of Santiago (Spain)	1982-1986	BSIE	June 1986
New Jersey Institute of Technology	1987-1989	BSEE	May 1989
New Jersey Institute of Technology	1989-1991	MSEE	October 1991

ACKNOWLEDGEMENTS

I would like to express my gratitude to the Eye Institute of New Jersey for allowing us the use of their facilities. Special thanks go to Dr. Andrew Meyer and Dr. Edward Haupt for their direction and suggestions, and Mr. Pan Huizhong for his help in the ERG data collection.

CONTENTS

1. INTRODUCTION

The eye is a very complex human organ which provides the sense of sight. The main function of the eye is to transform the light it receives into electrical responses of the nerve cells which the brain can understand and interpret. Light enters the eye through the *cornea*, the outer protective coat of the eye. The first step in focusing the image is provided at the cornea by bending the light and directing it into a small opening in the iris called the *pupil*. The pupil assists in controlling the amount of light that penetrates the eye and in focossing. The pupil adjusts depending on the amount of light that falls upon the eye. When the light is dim the pupil opening increases to permit the necessary amount of light into the eye. But, when the light is very bright the pupil opening tends to decrease to protect the eye from the excess light.

Once the light goes through the pupil it encounters the *lens*. The lens completes focusing light rays to a point image onto the rear part of the eye, the *retina*. This is accomplished by increasing or decreasing the thickness of the lens. The retina is responsible for codifying the light (optical images) into electrical nerve impulses which are transmitted via the optic nerve to the brain. The brain then interprets the signals and configures the visual perception.

A variety of diseases, including diabetes and glaucoma can cause deterioration to the retina and affect the visual process. Researchers have been studying the visual process for many years trying to discover methods for diagnosis and early detection of possible retinal damage. One method for clinical diagnosis of the visual system consists on monitoring the electrical potentials created in the retina as a response to light stimuli. This method is called electroretinography. The ERG[1] detects the variations of electrical

---

1 Electroretinogram

potentials registered in the retina giving an indication of the state of the nerve cells involved in the visual process. A damaged retina will produce a lower electrical response; and therefore, reducing the ERG amplitude considerably.

The Naka-Rushton intensity-response function is used to characterize ERG responses as a function of the maximum amplitude of the receptor cells potentials due to various stimuli intensities. The Naka-Rushton function is obtained by fitting the maximum amplitudes of ERGs recorded at a range of stimuli intensities. The parameters of this intensity-response function can be used as a predictor of some diseases of the visual system. M.A. Johnson,[1] et al used these parameters to discriminate between patients, diagnosed with central retinal vein occlusion, that might require surgery due to neovascularization.[2]

M.A Johnson, et al,[1] used the peak to trough amplitude of the ERG responses to obtain the parameters of the intensity-response function. However, the determination of this amplitude from the ERG response is very subjective. Usually ERGs contain a great amount of noise and the measurement of the peak to trough amplitude from the ERG response is not trivial; it is subject to the individual's interpretation. This can lead to different results when the fitting of the intensity-response function is performed by different individuals.

The use of mathematical models representing the ERG response as a function of a small set of parameters can help eliminate the subjectivity involved in analyzing the ERG responses and produce more consistent results. The parameters of the model are obtained by fitting the ERG raw data to the ERG model using parameter identification techniques. The information contained in the raw ERG can then be compressed into the small set of parameters which define the ERG. Since these parameters identify the ERG response they can be used to obtain the intensity-response function; thus, eliminating the individual's

---

2 Proliferation of weak blood vessels that are very fragile and can produce hemorrhage.

subjectivity and providing more consistent results.

This thesis proposes a model for the ERG response due to light stimuli by breaking down the ERG response into its two major components (A-wave and B-wave) and identifying each component. Some work has been done previously on the parameter identification of ERGs by Zhongquan Li,[2] [3] Ken-Gen Lu,[4] and Yu-Huai Hsiao.[5] My intent is to continue their initial ideas by proposing a model that produces a good fit of the ERG response and has some physiological meaning. The model parameters can be used to obtain other functions, like the intensity-response function, and be used as a tool for clinical diagnosis. In addition, since the model parameters identify the components of the ERG response, they can also be used to observe if a particular component of the ERG has an unusual response, which might not be clearly identifiable from the ERG response.

2. RETINAL CELLS

A brief description of the cells involved in the codification of the visual stimulus into electrical responses is necessary in order to understand the Electroretinogram response and its mathematical model.

The retina is located at the rear part of the eye. It is composed of a great number of light-sensitive cells which convert the optical stimulus they receive into physiological responses that are transmitted to the brain via the optical nerve.

The neural cells involved in transmitting the physiological response to the brain are:

- *photoreceptor cells*
- *bipolar cells*
- *ganglion cells*
- *amacrine cells*
- *horizontal cells*

The photoreceptor, bipolar and ganglion cells form a direct link from the retina to the brain. The amacrine and horizontal cells are laterally situated between the other cells, modifying and controlling the signals on the direct link.[6]

The photoreceptor cells face inward, away from the light, and connect to other neurotransmitter cells forming mesh of nervous tissue directly in the path of the light stimulus. The network of nervous tissue is directed to the brain through an opening in the rear surface of the eye forming the optic nerve. Figure 2.1 shows the interconnections of the neural cells involved in the visual process.

The photoreceptor cells transmit their information, through a *synapse*[3] connection, to

a bipolar cell which in turn transmits it to a ganglion cell whose axon directly connects to the brain. The horizontal cells form connections between photoreceptor cells modifying the activity at the junction between the photoreceptor cells and the bipolar cells. Amacrine cells modify the activity between bipolar cells and ganglion cells.

2.1 PHOTORECEPTOR CELLS

The photoreceptor cells are transducers whose function is to convert light stimuli into neural signals that are transmitted to the brain for processing in order to develop the visual perception. These light-sensitive elements transmit their information to the bipolar and horizontal cells by releasing synaptic neurotransmitters when light fall upon them.

There are two types of photoreceptor cells: *rods* and *cones*. Humans contain approximately 6 million cones and 120 million rods in each eye.[7] Cones and rods have different response characteristics. Cones provide color and high resolution information, however, their sensitivity is limited. Rods, on the other hand, are 500 times more sensitive to light but provide low resolution and no color information. Together cones and rods complement each other providing an ideal system for transforming light stimulus into responses that can be transmitted to the brain.

Photoreceptor cells have three distinct regions: the outer segment, the inner segment and the synaptic ending.[8]

The transduction of light stimuli into neural signals starts at the outer segment of the photoreceptor cells. The outer segment is located in the far end of the cell. This region contains photosensitive pigment molecules which absorb light energy creating conductance changes in the surface of the outer segment. The changes in conductance

---

3. A synapse is a connection between neuron cells where one neuron transmits information to the adjacent neuron by releasing chemical messengers, called neurotransmitters.

produce movements of ions throughout the outer segment area altering the electrical potentials on the surface of the photoreceptor cell. These electrical potential changes reach the synaptic-ending area and modulate the secretion of neurotransmitters. This way they transfer neural information to the bipolar and horizontal cells.

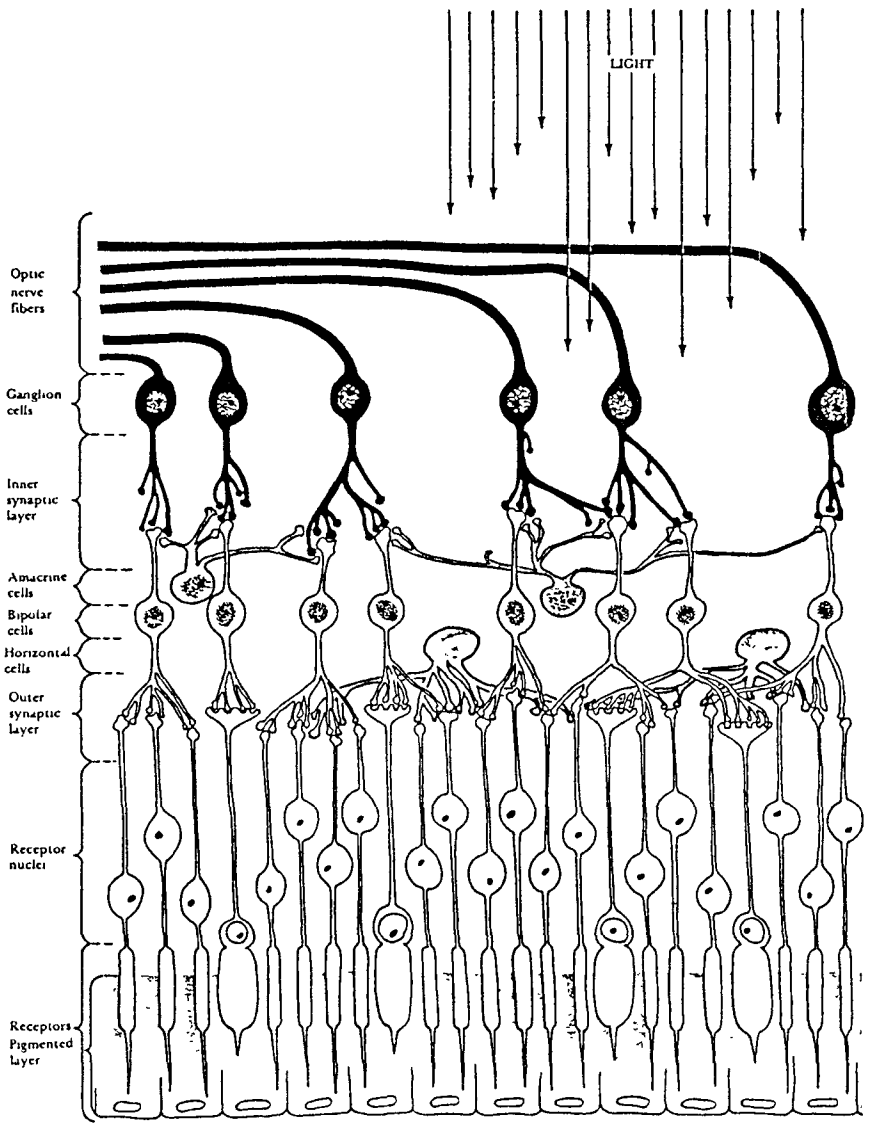


Figure 2.1. Interconnections of neural cells involved in the visual process (from [6])

3. ELECTRORETINOGRAM AND MODEL

The electroretinogram is a useful clinical technique for diagnosis of the visual system. The ERG detects the alteration of electrical potential in the retina when it is stimulated by light, giving an indication about the state of the neuroreceptor and neurotransmitter cells involved in the visual process, thereby, providing a powerful tool for the diagnosis of the type and evolution of retinal diseases.

The first ERG recorded on humans dates from 1877 when Dewar was able to measure the light evoked response of the retinal cells. Since then, many researchers have been involved in the study of the ERG and its clinical application.

The ERG is not the result of a single response but a gross potential resulting from the algebraic summation of several individual responses. Observations of ERGs show two possible components which appear as two prominent peaks in the ERG response. Brown in 1968 separated the response of the ERG into two main components:[9]

- A cornea-negative potential (A-wave) generated by the receptor cells.
- A cornea-positive potential (B-wave) generated by the inner nuclear layer.

Figure 3.1 shows the representation of the ERG as the summation of its individual components.

Having the ERG response divided into its individual components a model can be specified for each component. Therefore, the ERG response can be represented as the algebraic summation of the two components:

$$ERG(t) = E_A(t) + E_B(t) \tag{3.1}$$

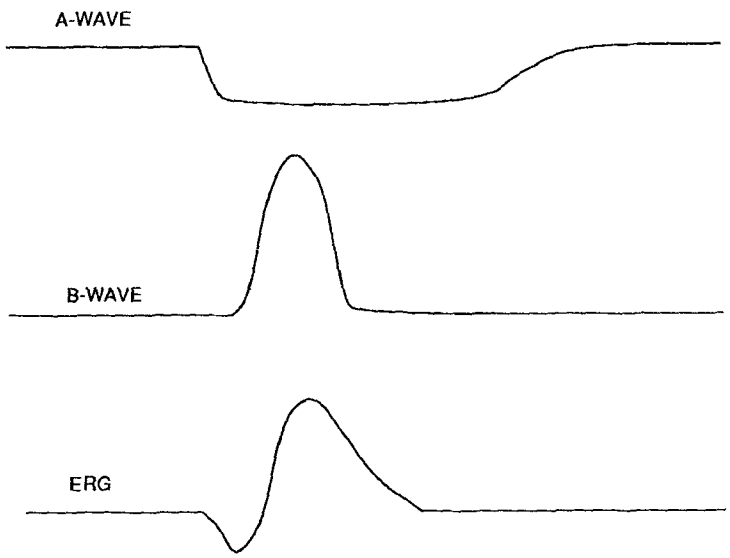


Figure 3.1. Representation of the ERG response as the summation of its individual components

where $E_A(t)$ and $E_B(t)$ represent the A-wave and B-wave potentials respectively.

The A-wave is the result of the activity of the receptor cells. Its magnitude varies with the intensity of the flash stimulus and the time after the onset of the flash. The A-wave increases in magnitude for higher stimulus intensities and during the first 50 msec after the onset of the stimulus. [10] In general, there is agreement on the components that form part of the model for the A-wave. Penn and Hagins,[11] and Baylor, Numm and Schnapf[12] came up with two similar models representing the response of rods to light stimuli. The models are defined by two components: the first component is a linear transduction process which converts the light stimuli into electrical responses. The second component is an instantaneous nonlinearity.[13]

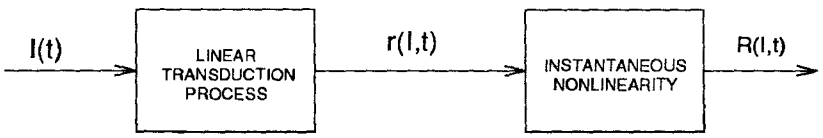


Figure 3.2. Representation of the rod model as the function of two components[13]

The first component of the model for the rod response to light stimuli is a linear transduction process that converts light stimuli into electrical signals. This component can be represented in the model by a low-pass filter with *n* stages. The filter consists of a series of resistor (R) and capacitor (C) stages connected by isolating amplifier units (K) as proposed by M. G. F. Fuortes and A. L. Hodgkin[14] earlier in 1964. Figure 3.3 shows a representation of the low-pass filter used to represent the linear transduction component of the rod response model.

The output of the linear transduction component is the input into the nonlinear component. When the output of the first component is small the second component behaves like a linear process. However, as the output of the first component increases the output of the second component saturates and therefore, becomes nonlinear. This nonlinearity is possibly due to the limited number of response generators available. When the output of the linear transduction is small there are many response generators available. Therefore, increasing the output of the linear transduction will increase the output of the second component by the same amount. However, as the output of the linear transduction increases to a certain level, the number of response generators in use approaches the total number of response generators available. Therefore, the output of the second component will increase by smaller quantities.[13]

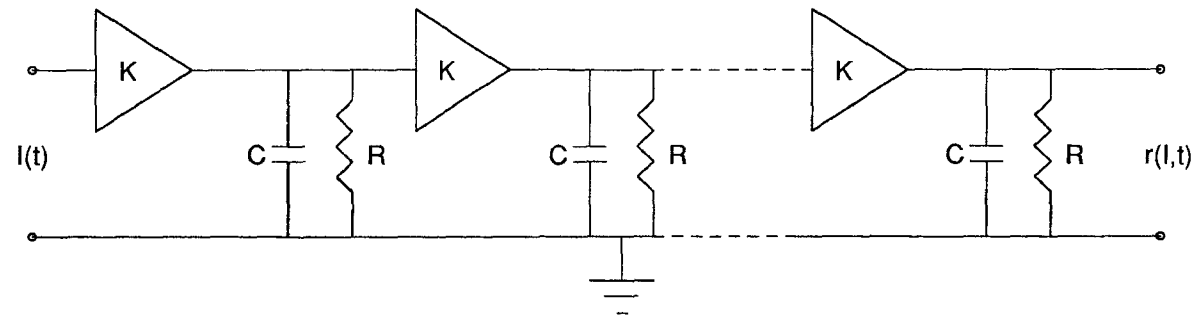


Figure 3.3. Low-pass filter representing the linear transduction component of the rod response model

The ERGs we are concerned with in this work are those obtained from very brief flash stimuli (10 μsec). Therefore, we can consider the input to the linear transduction component an impulse. If this is the case, the output of the linear transduction component due to a unit impulse will be the impulse response of the filter function, h(t):

$$h(t) = \left[(t/t_p) \cdot e^{[1 - (t/t_p)]}\right]^{(n - 1)} . \tag{3.2}$$

Therefore, the output of the linear transduction process due to different stimuli (I) will be:

$$r(I,t) = I \cdot c \cdot h(t), \tag{3.3}$$

where:

- t: time in seconds
- t_p: time of the peak response in seconds
- n: number of stages of the low-pass filter
- I: intensity of the stimuli expressed in $scot\ td \cdot sec$
- c: conversion constant expressed in $\frac{response\ units}{scot\ td \cdot sec}$
- h(t): low-pass filter unit impulse response

The rod response R(I,t) is a nonlinear function of the output of the low-pass filter r(I,t). This nonlinearity was defined by Baylor et al[12] as:

$$R(I,t) = R_m \cdot \left[1 - e^{-r(I,t)/r_0}\right], \tag{3.4}$$

where R_m is the maximum receptor response and r_0 is a constant. We can define a semisaturation intensity K_a as the stimulus intensity required to produce a response equal to one-half of the maximum response at the time of the peak response (t_p); that is:

$$R(K_a,t_p) = 1/2\ R_m. \tag{3.5}$$

Then from the rod response R(I,t) in Equation 3.4 we obtain:

$$R(K_a,t_p) = 1/2\ R_m = R_m \cdot \left[1 - e^{-r(K_a,t_p)/r_0}\right],$$

which gives r_0:

$$r_0 = \frac{r(K_a,t_p)}{ln(2)},$$

where $r(K_a,t_p)$ can be obtained from Equation 3.3:

$$r(K_a,t_p) = K_a \cdot c \cdot h(t_p).$$

And from Equation 3.2 we can obtain the response of the filter for $t = t_p$: $h(t_p) = 1$. Therefore, r_0 becomes:

$$r_0 = \frac{c \cdot K_a}{ln(2)}. \tag{3.6}$$

Fixing the number of low-pass filter stages to $n=6$ and substituting Equations 3.6 and 3.3 into Equation 3.4, the rod response due to light stimuli becomes:

$$R(I,t) = R_m \cdot \left[1 - e^{-r(I,t) \cdot \frac{ln(2)}{c \cdot K_a}}\right]$$

$$= R_m \cdot \left[1 - e^{-\alpha_1 \cdot \left[(t/t_p) \cdot e^{[1-(t/t_p)]}\right]^5}\right] \tag{3.7}$$

where $\alpha_1 = I \cdot (\frac{ln(2)}{k_a})$.

Since the A-wave magnitude is linearly related to the receptor response we can assume that the A-wave is defined by[13]:

$$E_{A(t)} = d \cdot R(I,t), \tag{3.8}$$

where d is a constant that depends on the number of receptors recorded and other factors influenced by the recording situations.

Therefore, the A-wave response can be approximated by the following function:

$$E_{A(t)} = K_1 \cdot \left[1 - e^{-\alpha_1 \cdot \left[(t/t_p) \cdot e^{[1 - (t/t_p)]}\right]^5}\right], \tag{3.9}$$

where $K_1 = R_m \cdot d$ represents the amplitude of the A-wave.

The B-wave response is due to the response activity of the cells in the iner-nuclear layer. This response can be approximated by a delayed damped sinusoid as expressed by the following equation:

$$E_{B(t)} = K_2 \cdot t^n \cdot e^{-\alpha_2 \cdot n \cdot t} \cdot \sin(\omega \cdot t), \tag{3.10}$$

where K_2 is related to the amplitude of the B-wave response, and n is the order of the function. Setting $n=3$, the B-wave becomes:

$$E_{B(t)} = K_2 \cdot t^3 \cdot e^{-3 \cdot \alpha_2 \cdot t} \cdot \sin(\omega \cdot t). \tag{3.11}$$

The ERG response is defined as the algebraic summation of the A-wave and B-wave. Therefore, the electroretinogram response due to brief stimuli becomes:

$$ERG(t) = E_A(t) + E_B(t), \tag{3.12}$$

or

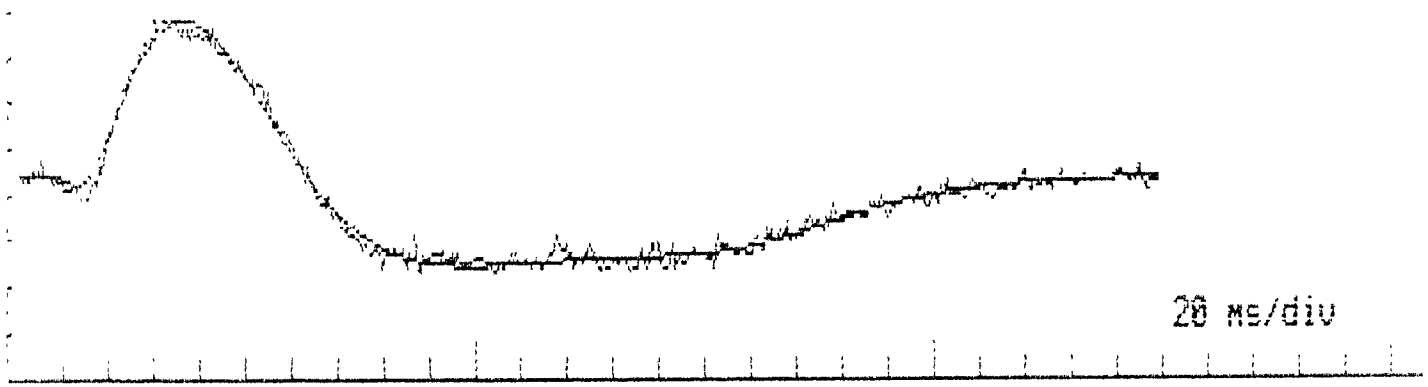
$$ERG(t) = K_1 \cdot \left[1 - e^{-\alpha_1 \cdot \left[(t/t_p) \cdot e^{[1 - (t/t_p)]}\right]^5}\right] + K_2 \cdot t^3 \cdot e^{-3 \cdot \alpha_2 \cdot t} \cdot \sin(\omega \cdot t).$$

Figure 3.4 displays an example of an ERG recording due to a white flash together with the model response. As can be seen from this figure the ERG model gives an

accurate representation of the ERG response. However, the information provided by the ERG has been compressed into a small set of six parameters: K_1, t_p, α_1, K_2, α_2, and ω.

Figure 3.5 shows the breakdown of the model of a fitted ERG into its individual components: A-wave and B-wave.

Once the parameters that represent the ERG response are obtained the analysis of the ERG becomes more standard and consistent eliminating the subjectivity of the analyzer.



1: TEST DATE: 3/27/91 TEST TYPE: ERG LABEL: R
STIMULUS : 10 db Scotopic Single Flash, White FREQUENCY: EYE: S
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

Figure 3.4. Example of an ERG recording due to a white flash together with the model response

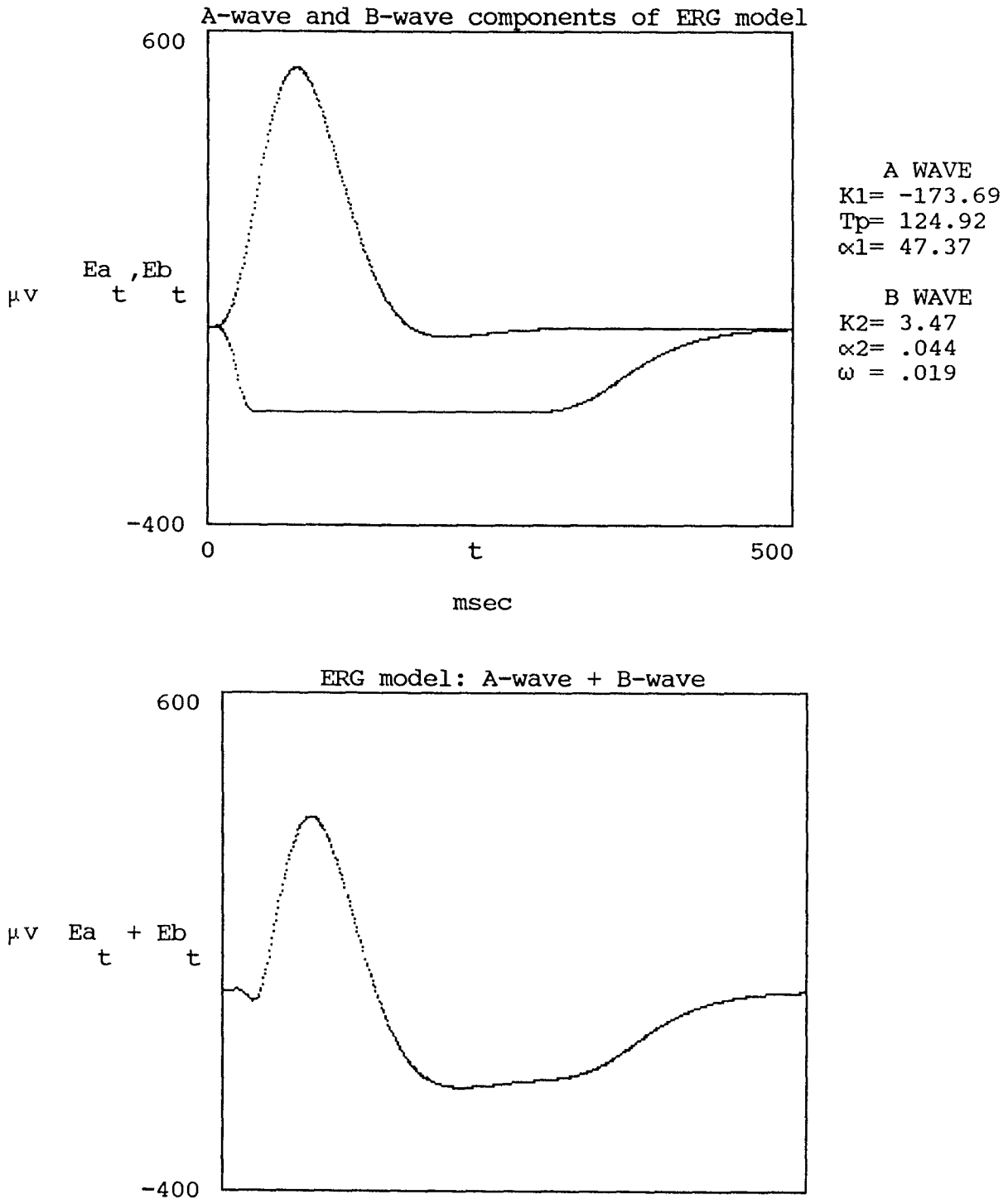


Figure 3.5. Breakdown of the model response from Figure 3.2 into its individual components

4. NAKA-RUSHTON INTENSITY RESPONSE FUNCTION

K. I. Naka and W. A. Rushton, in 1966, discovered that the amplitude response of the photoreceptor cells can be defined as a function of the stimulus intensity that produced the response.[15] Using this idea, Massof and Wu[16] described the human ERG as a function of maximum amplitude responses due to varying stimulus intensities:

$$R = R_{\max} \frac{I^n}{I^n + K^n}, \tag{4.1}$$

where:

R = ERG amplitude (b-wave amplitude)

$R_{\max}$ = Maximum ERG amplitude (μv)

I = Stimulus intensity (log $cd \cdot \frac{s}{m^2}$)

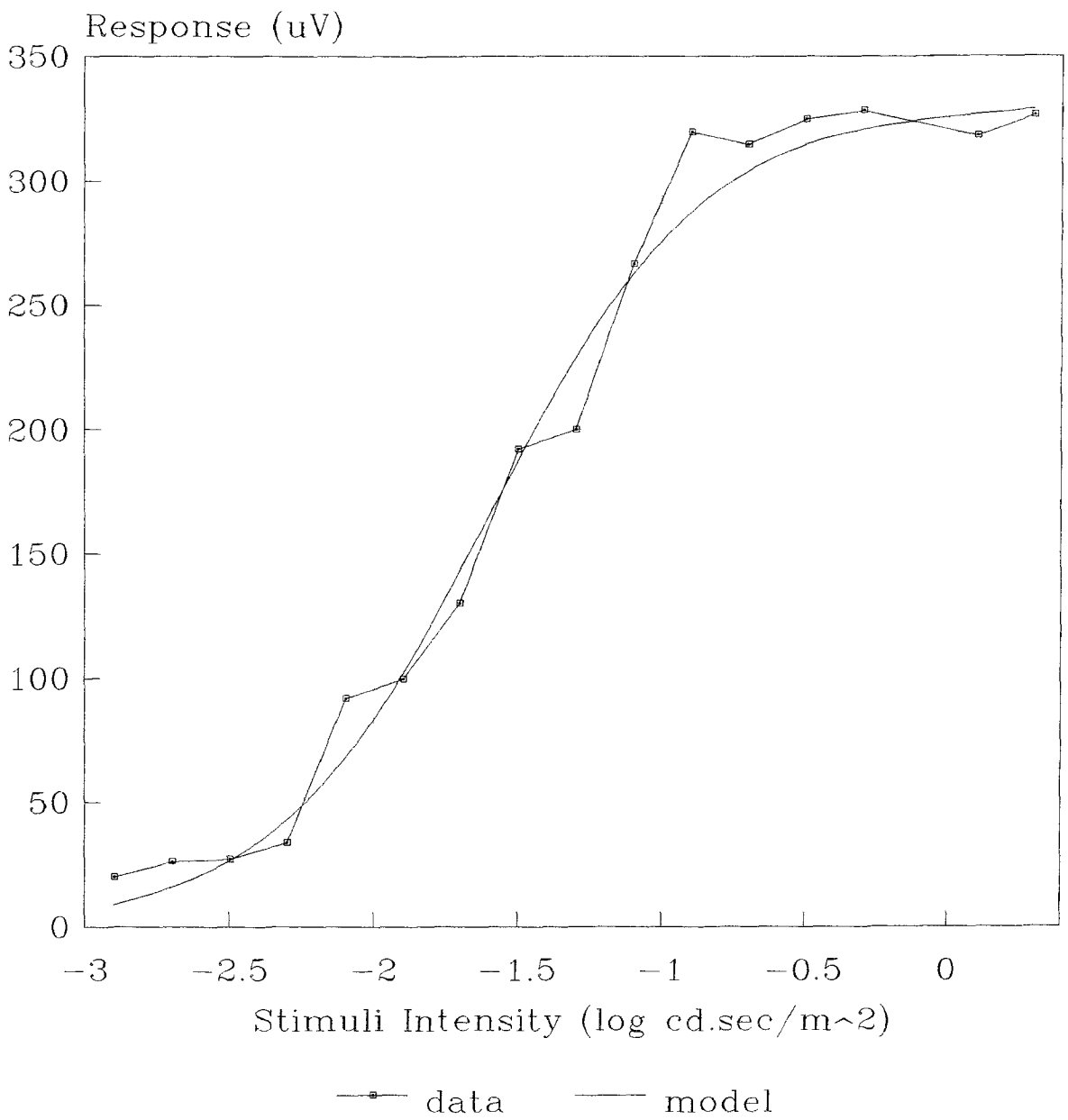
K = Semisaturation constant. Intensity required to produce an ERG amplitude equal to $\frac{1}{2} R_{\max}$

n = Factor related to the steepness of the curve

The parameters from this function, $R_{\max}$, n and K, seem to be a good predictor of diseases of the visual system[1]. $R_{\max}$ corresponds to the maximum amplitude response due to the strongest stimulation. Damaged photoreceptor cells will reduce this maximum value considerably. K is a sensitivity parameter indicating the amount of light that is needed to elicit a response of normal amplitude. An increase in the *log K* will shift the curve to the right indicating that more light is required to produce a normal response. The parameter n relates to the steepness of the curve.

Previously, the parameters of the Naka-Rushton function were obtained by taking the peak to trough amplitude of ERG responses measured at various intensities and fitting this data to the Naka-Rushton function in equation 4.1. However, a problem occurs when identifying the peak to trough amplitude of the ERG responses. This measurement is not trivial because the ERG recording is usually affected by noise and it can lead to different interpretations. However, since the ERG model, described in Section 3, gives an adequate representation of the ERG response, and parameter K_2 of the model represents the amplitude of the B-wave, the Naka-Rushton function can be fitted using this parameter. Once the ERG model parameters are obtained for the different set of stimuli intensities, the Naka-Rushton parameters can be obtained using the simplex method for parameter identification described in appendix C. This technique should provide less interpretation errors and more consistent results.

A Naka-Rushton fit of ERG responses from a subject is shown in Figure 4.1. The horizontal axis of the plot corresponds to the light intensities (in a logarithmic scale) and the vertical axis to the ERG amplitude responses. The data for this plot was obtained by manually measuring the peak to trough amplitudes of the raw ERG responses from a diabetic subject.



Diabetic subject (CJ).Data obtained
using manual measurement of peak–trough.
Figure 4 1

5. TEST PROTOCOL

To obtain the intensity response function as a function of the ERG model parameters, the electroretinograms should first be recorded using a protocol introduced by Massof.[17] This protocol consists of gathering ERG responses due to white flash stimuli starting with a very low stimulus intensity The intensity is then increased in small steps up to the maximum stimulus intensity. After the ERGs are recorded, the model parameters are identified using the simplex method. Finally the ERG model parameters, in particular K_2, are used to fit the Naka-Rushton function, again using the simplex method.

The following list provides a summary of the steps required to obtain the Naka-Rushton intensity response function using the ERG model parameters:

- Dilate the subject's pupils
- Dark adapt the subject for 45 minutes
- Place anesthesia drops on the corneas
- Connect electrodes to the subject
- Record the ERG responses, starting with the lowest stimulus intensity that produces some response, increasing the intensity in small steps up to the maximum intensity.
- Fit the raw ERG data to the ERG model to obtain the parameters that identify the ERG
- Use the ERG model parameters to fit the Naka-Rushton function

5.1 Methods and Materials Used to Obtain the ERGs for This Work

The ERG data gathered for this work were recorded using the MFTS2 system described in section 6. The analog filter settings of the GRASS amplifiers were set to the highest bandwidth (.1 Hz to 10 kHz) in order to avoid distorting the signal as little as

possible. This increased the noise (high frequency and 60 Hz noise) on the signals recorded but avoided any distortions that might be introduced by the time constants of the filters. The parameter identification procedure is not affected by the amount of noise introduced using these filter settings; therefore, this method produces more reliable results. If desired, the raw ERG data can be filtered, after recording, using a bandpass acasual digital filter incorporated into the MFTS2 system.

ERGs were simultaneously recorded on both eyes. The active electrodes were placed on the surface of the subjects corneas using *ERG-jet*[4] corneal contact lens electrodes. The reference electrode for both eyes was placed on the forehead using a skin electrode with Aquasonic 100[5] transmission gel. The subjects were grounded using a skin electrode attached to the earlobe.

The pupils were dilated with a mydriatic (Mydriacyl 1% and Neo-Synephrine hydrochloride 2 1/2%) before the dark adaptation process. Proparacaine hidrochloride 0.5% was used to anesthetize the corneas in order to minimize the discomfort produced by the contact lens electrodes.

4. ERG-jet is made by Universo SA, La Chaux de Fonds, Switzerland
5. Parker Laboratories

6. TESTING SYSTEM

In order to facilitate the recording of ERGs and to provide adequate data for the purpose of this work and other works a system was developed in the Electrophysiology Laboratory of the Eye Institute of New Jersey. The MFTS2 (MultiFunction Testing System Version 2) system was constructed using standard equipment available in the laboratory. The main components of the testing system are:

- IBM/XT Compatible Computer.
- GRASS Model 8 Amplifiers and Analog Filters.
- Metrabyte DASH-16 Data Acquisition Board.

The IBM/XT compatible computer runs the software that interacts with the user and processes the data. The software was mostly written in C language except for a small portion that reads the data acquisition board, which was implemented in assembly language. The program guides the user through the testing procedure providing instructions and help. The system is very flexible allowing the use of any variety of protocols for testing. However, the Massof protocol, used for this work, and the standard clinical test protocols are facilitated by the system stepping the user through the different stimuli. Data recorded on the system can be digitally filtered (low pass, band pass and high pass digital filters are implemented). This is not only useful for eliminating high frequency or 60 Hz noise but also to view certain bands of frequencies which provide some clinical information such as high frequency components referred to as *oscillatory potentials*.[18] The recorded data is displayed on the screen in real time and can be stored on disk for later evaluation, further processing or generation of written reports.

A data base, essential for research, was implemented in order to keep records of the subjects. The data base contains demographic information, clinical subject history as well as the recorded data. An interface was written in C in order to allow the transfer of information recorded with the testing system to the data base in a single step. This provides a very good platform to perform research since queries can be performed to

discriminate between subjects with a particular disease.

The system utilizes the amplifiers and analog filters of a GRASS Model 8 machine previously used for recordings on paper of electro encephalograms. The output of the GRASS amplifiers is converted into digital form by the DASH 16 data acquisition board which in turn feeds the data into the IBM/XT compatible computer. A Ganzfeld unit from an LKC[6] machine was used to produce the light stimulus for this work. The Ganzfeld unit produces 10 μsec flashes with a maximum intensity of 2 $cd \cdot \frac{s}{m^2}$ that can be attenuated in 2 db steps. Also available in the laboratory are two pattern stimulators which produce a checkerboard pattern used for other physiological tests such as pattern electroretinogram (PERG) or visual evoked response (VER). ERGs, PERGs and VERs, as well as, electrooculograms (EOGs) can be recorded with this system. Figure 6.1 displays the configuration of the testing system. For a more detail description of the system refer to the MFTS2 system manual[19] and Appendix D.

6 LKC Systems Inc, Gaithersburg, MD

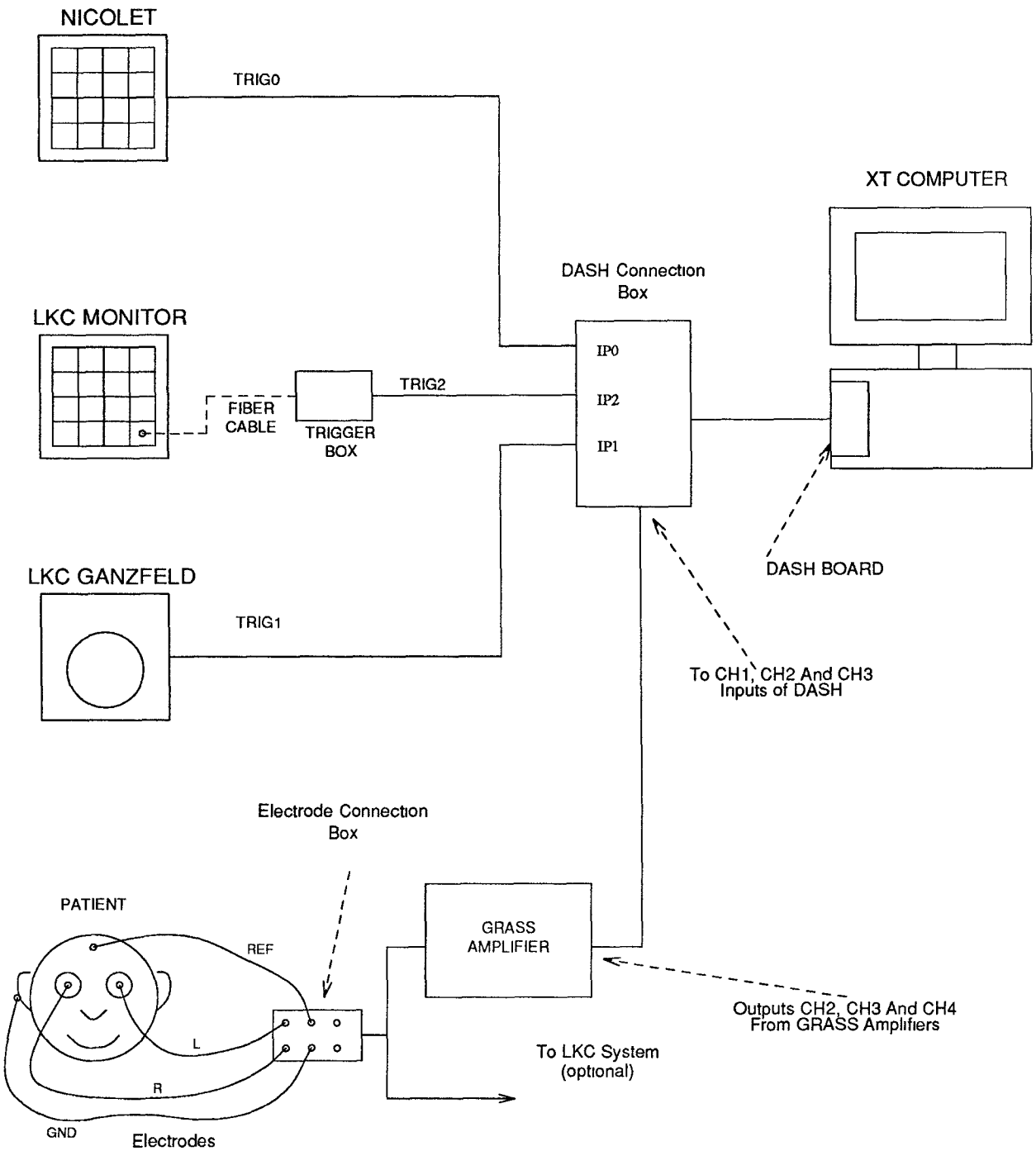


Figure 6.1. Configuration of the MFTS2 testing system

7. RESULTS

Appendix A displays a set of ERGs recorded on a normal subject (only the right eye is shown). The recordings were obtained during 500 msec to allow the wave to reach its steady-state value. The numbers at the right of the waveforms identify the ERG by relating it to the legend located underneath the waveforms. The letter besides the number identifier indicates to which eye the recording belongs, R for the right eye and L for the left eye.

The legends give miscellaneous information about the recordings, such as, stimulus intensity, digital filter frequency, date of the test, etc. Note that the stimulus intensity is given in terms of loss in dB referenced to highest intensity (0 dB) which corresponds to 2 $cd \cdot \frac{s}{m^2}$.

The legends also indicate the peak to trough amplitude of each waveform. This measurement is obtained by having the user of the system manually place cursors at the peak and trough locations on each waveform. The implicit time, also displayed on the legends, is the time at which the peak of the waveform occurs.

It is clearly seen from these waveforms that the determination of the peak to trough amplitude is affected by the recording noise. If the peak to trough cursors are moved even by 1 msec the peak to trough amplitude can vary considerably.

The peak to trough amplitude gathered from these recordings was use to obtain the parameters of the Naka-Rushton intensity-response function. The following parameters were obtained:

$$R_{\max} = 485.84\ \mu v \qquad n = 1.158 \qquad \log k = -1.71\ \log cd \cdot \frac{s}{m^2}.$$

Figure 7.1 displays the intensity-response function obtained from the parameter identification of the manual peak to trough amplitude of these ERGs together with the peak to trough amplitudes.

Appendix B displays the same set of ERGs with the model representation of each ERG. The top two waveforms represent the breakdown of the ERG into its two model components (A-wave and B-wave). The bottom curves show the raw ERGs superimposed by the model representation. The parameters for each waveform are identified in the text of each waveform and are summarized on table 7.1.

Parameter K_2 of the ERG model, for the different intensities, was used to obtain the parameters of the intensity-response function. The following parameters were obtained:

$$R_{\max} = 601.8\ \mu v \qquad n = 1.56 \qquad \log k = -.0734 \log cd \cdot \frac{s}{m^2}.$$

Figure 7.2 displays the intensity-response function obtained from the parameter identification of parameters K_2 from the ERG model together with the value of this parameter for each intensity.

This curve does not produce the saturation at higher amplitudes as it is seen by using the peak to trough amplitude values. This indicates that parameter K_2 of the B-wave is much more sensitive at high stimuli intensities then the peak to trough value of the ERG. However at low stimuli intensities parameter K_2 of the B wave has very little sensitivity. It is required to obtain some more recordings at higher stimuli intensities in order to obtain the expected saturation. However, at the moment it is not possible to increase the stimuli intensity with the equipment available in the lab.

Figures 7.3 and 7.4 display the intensity-response functions corresponding to another normal subject; and, table 7.2 shows the parameters of the ERG model for this same subject. The following intensity-response function parameters were obtained.

Using the peak to trough manual measurement:

$$R_{\max} = 400.26\ \mu v \qquad n = 1.28 \qquad \log k = -1.777\ \log cd \cdot \frac{s}{m^2}.$$

Using parameter K_2 of the ERG model:

$$R_{\max} = 650.6\ \mu v \qquad n = 1.31 \qquad \log k = 0.12\ \log cd \cdot \frac{s}{m^2}.$$

The intensity-response function of a diabetic subject is displayed on Figures 7.5 and 7.6. The following intensity-response parameters were obtained:

Using the peak to trough manual measurement:

$$R_{\max} = 330.19\ \mu v \qquad n = 1.20 \qquad \log k = -1.60\ \log cd \cdot \frac{s}{m^2}.$$

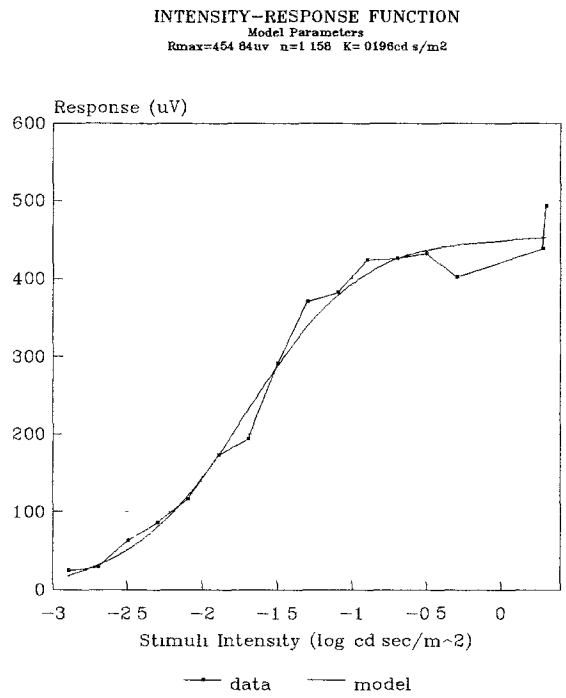
Using parameter K_2 of the ERG model:

$$R_{\max} = 265.5\ \mu v \qquad n = 0.82 \qquad \log k = -0.49\ \log cd \cdot \frac{s}{m^2}.$$

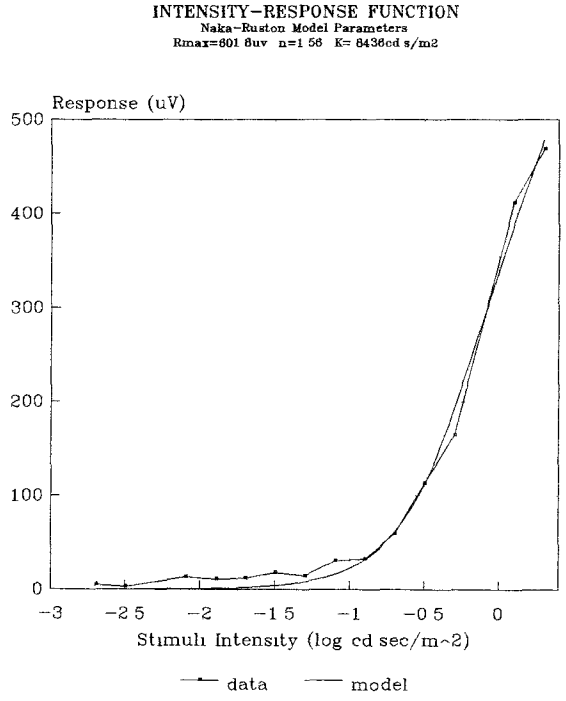
Comparing the intensity response parameters for the normals and diabetic subject we clearly see how the response $R_{\max}$ for the normals is much greater then for the diabetic subject. This is also shown of Figure 7.7 which shows a plot of parameter K_2 for the mentioned subjects. This figure shows the lower K_2 value at high stimuli intensities for the diabetic subject.

Also included in Figures 7.8 through 7.12 are the plots of the other parameters, besides K_2, that represent the ERG model for two normal subjects and a diabetic. Figure 7.8 shows the A-wave response versus stimulus intensity, represented by parameter K_1. This plot shows how the A-wave response increases in magnitude as the stimulus intensity increases. We can also identify from this plot the lower A-wave response of the diabetic subject compared with the normals, specially at higher stimuli intensities.

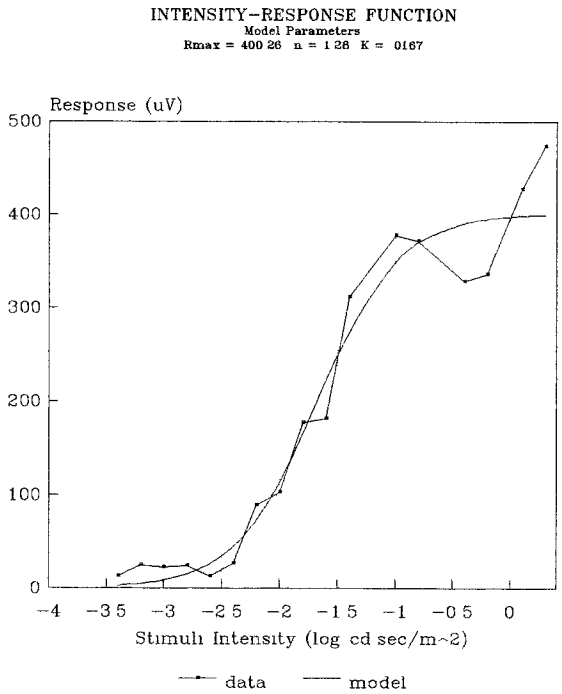
An interesting parameter is α_2 (B-wave parameter) which produces a sigmoid type curve characteristic of the Naka-Rushton function.



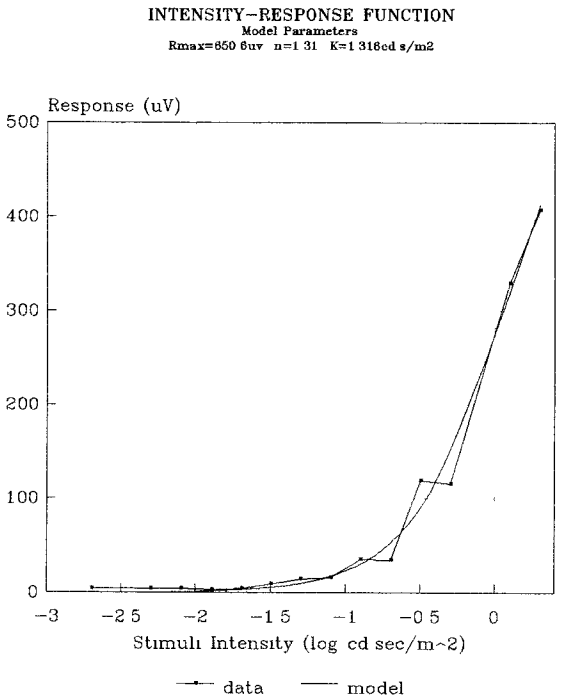
Normal subject (GC) Data obtained using manual measurement of peak to trough
Figure 7 1



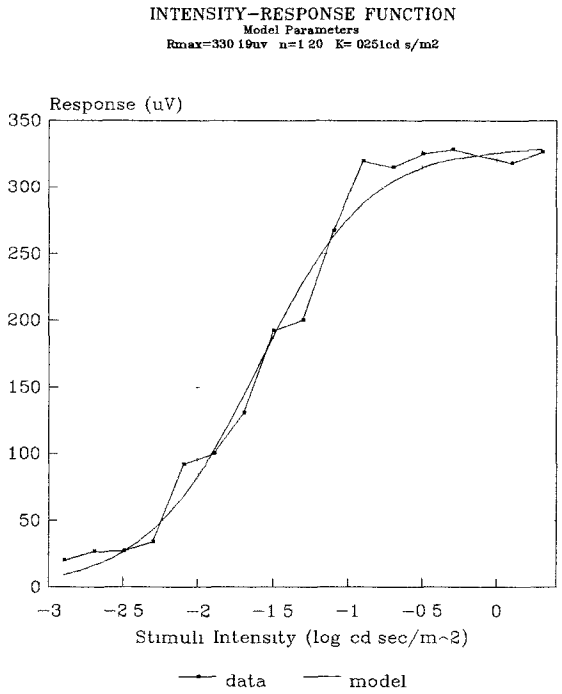
Normal subject (GC) Data obtained using parameter k2 from the ERG model
Figure 7 2



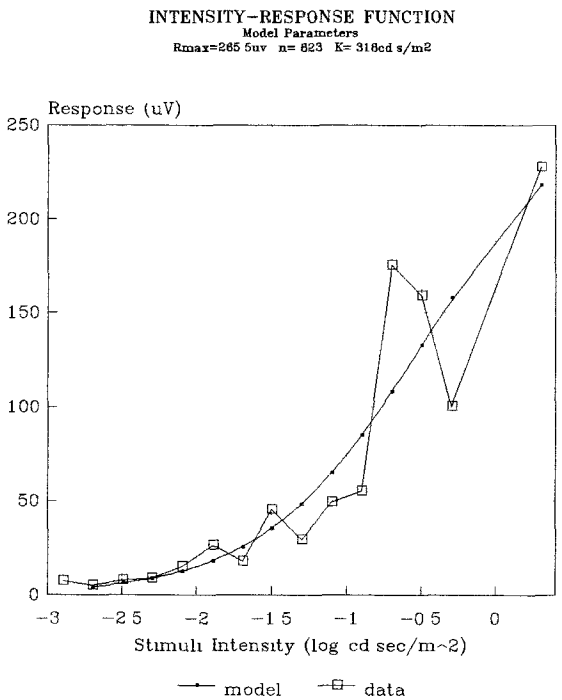
Normal (JC) Data obtained using
manual measurement of peak to trough
Figure 7 3



Normal subject (JC) Data obtained
using parameter K2 from the ERG model
Figure 7 4

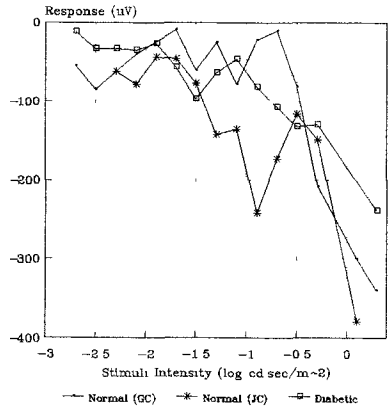


Diabetic subject (CJ) Data obtained
using manual measurement of peak-trough
Figure 7 5



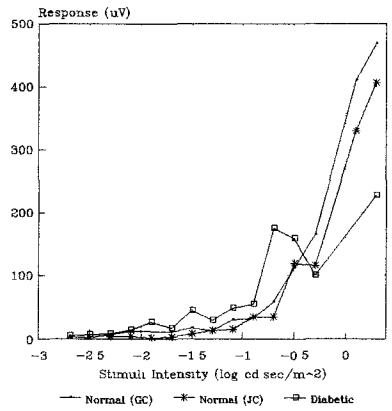
Diabetic subject Data obtained
using parameter K2 from the ERG model
Figure 7 6

PARAMETER K1 (A-WAVE) vs STIMULUS



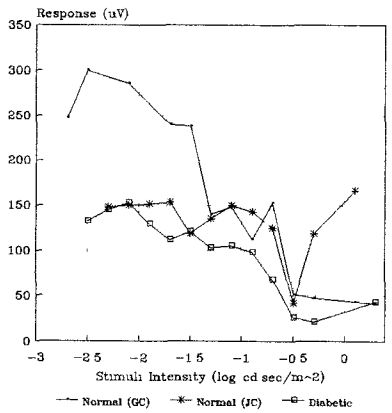
Normals(JC,GC),Diabetic Data obtained using parameter K1 from the ERG model
Figure 7.8

PARAMETER K2 (B-WAVE) vs STIMULUS



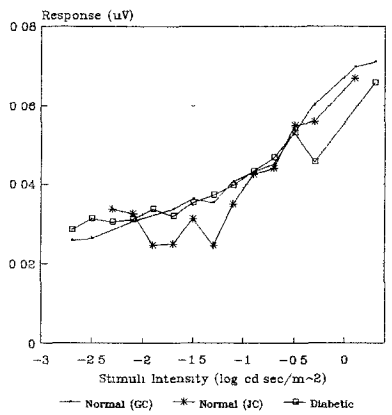
Normals(JC,GC),Diabetic Data obtained using parameter K2 from the ERG model
Figure 7.7

PARAMETER Tp (A-WAVE) vs STIMULUS



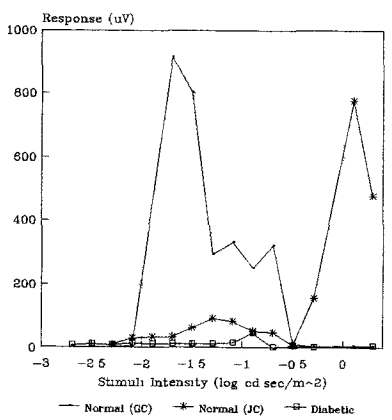
Normals(JC,GC),Diabetic Data obtained using parameter Tp from the ERG model
Figure 7.9

PARAMETER a2 (B-WAVE) vs STIMULUS



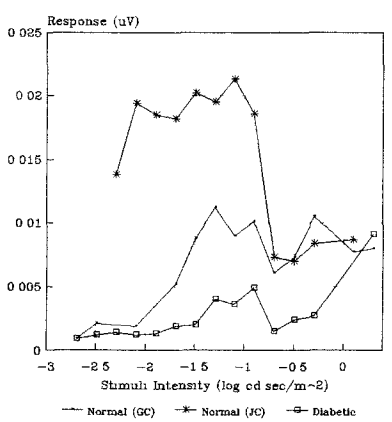
Normals(JC,GC),Diabetic Data obtained using parameter a2 from the ERG model
Figure 7 10

PARAMETER a1 (A-WAVE) vs STIMULUS



Normals(JC,GC),Diabetic Data obtained using parameter a1 from the ERG model
Figure 7.12

PARAMETER w (B-WAVE) vs STIMULUS



Normals(JC,GC),Diabetic Data obtained using parameter w from the ERG model
Figure 7 11

ERG MODEL PARAMETERS						
Stimulus (dB)	K_1	t_p	α_1	K_2	α_2	ω
0	-340.42	41.93	4.16	468.6	.071	.008
2	-300.62	43.18	4.01	410.1	.0696	.0077
6	-208.23	47.84	3.79	164.7	.0603	.0105
8	-81.77	51.48	10.26	112.6	.0534	.0073
10	-10.37	152.55	321.50	58.8	.0452	.0061
12	-22.18	112.38	250.55	32.5	.0431	.0101
14	-78.50	148.62	331.05	30.4	.0406	.0090
16	-24.78	140.05	292.64	14.0	.0354	.0112
18	-60.75	238.49	803.38	17.2	.0363	.0088
20	-9.18	239.76	914.38	11.2	.0338	.0052
24	-39.23	285.95	2.32	12.7	.0307	.0019
28	-84.97	299.91	.72	2.7	.0264	.0021
30	-54.61	247.07	1.54	4.6	.0258	.0009

TABLE 7.1. Parameters of the ERG model for a normal subject (GC)

ERG MODEL PARAMETERS						
Stimulus (dB)	K_1	t_p	α_1	K_2	α_2	ω
0	-755.65	198.91	477.48	406.7	.062	.0059
2	-379.56	166.21	776.37	329.2	.067	.0087
6	-149.12	118.62	155.86	115.4	.056	.0084
8	-116.25	42.14	7.20	118.8	.055	.007
10	-173.69	124.92	47.37	34.77	.044	.0073
12	-241.42	142.46	50.36	35.1	.0424	.0186
14	-135.04	149.54	82.73	15.6	.035	.0213
16	-142.60	134.91	91.56	14.0	.0245	.0195
18	-76.29	118.52	62.04	8.378	.0313	.0202
20	-45.34	153.61	34.00	3.75	.025	.0182
22	-43.25	151.27	33.43	2.853	.0247	.0185
24	-78.31	149.91	28.16	4.026	.0326	.0194
26	-62.48	147.85	9.6071	4.068	.0337	.0138

TABLE 7.2. Parameters of the ERG model for a normal subject (JC)

ERG MODEL PARAMETERS						
Stimulus (dB)	K_1	t_p	α_1	K_2	α_2	ω
0	-238.71	43.36	4.23	227.5	.0658	.0091
6	-129.86	19.87	.7352	100.4	.0456	.0027
8	-132.59	21.73	4.42	158.9	.0531	.0024
10	-107.45	26.55	1.82	174.9	.0468	.0015
12	-81.59	68.17	44.66	55.1	.0432	.0049
14	-46.07	98.09	14.33	49.1	.0397	.0036
16	-63.73	105.38	10.53	29.2	.0373	.0040
18	-96.64	103.14	10.68	45.2	.0353	.0020
20	-56.07	120.57	10.71	17.6	.0320	.0019
22	-26.29	111.44	10.80	26.2	.0338	.0013
24	-34.83	129.51	12.41	14.9	.0312	.0012
26	-33.27	152.67	7.5	8.6	.0305	.0014
28	-33.47	144.46	10.21	7.9	.0313	.0012
30	-11.47	132.32	6.96	5.0	.0286	.0009

TABLE 7.3. Parameters of the ERG model for a diabetic subject

8. CONCLUSION

The representation of the ERG response to light stimuli by the proposed mathematical model provides a way of compressing the information enclosed in the ERG response into a small set of six parameters. The parameters, together with the model, include most of the information supplied by the ERG raw data.

The use of mathematical models can be a helpful tool in the clinical diagnosis process since the interpretation of the model parameters, instead of the raw ERG data, can lead to more objective results. The determination of maximum amplitude responses or the time of peak responses from the raw ERG data can be very subjective due to the influence of recording noise. However, the determination of the model parameters is a more objective procedure; and the parameters can easily provide the required information.

The proposed model for the ERG response decomposes the response into its two principal components, the A-wave and the B-wave, giving information about each of the two components of the ERG. This information is not clearly detectable from the raw ERG data since the A-wave and B-wave intrude, and only the gross response is visible. Therefore, the model parameters can provide information about the neurotransmitter and neuroreceptor cells that is not immediately detectable from the raw ERG response. For example, an abnormally low K_1 parameter value (A-wave amplitude) might indicate a problem with the receptor cells. Or, a low K_2 parameter value might suggest a problem with the cells in the inner nuclear layer.[7]

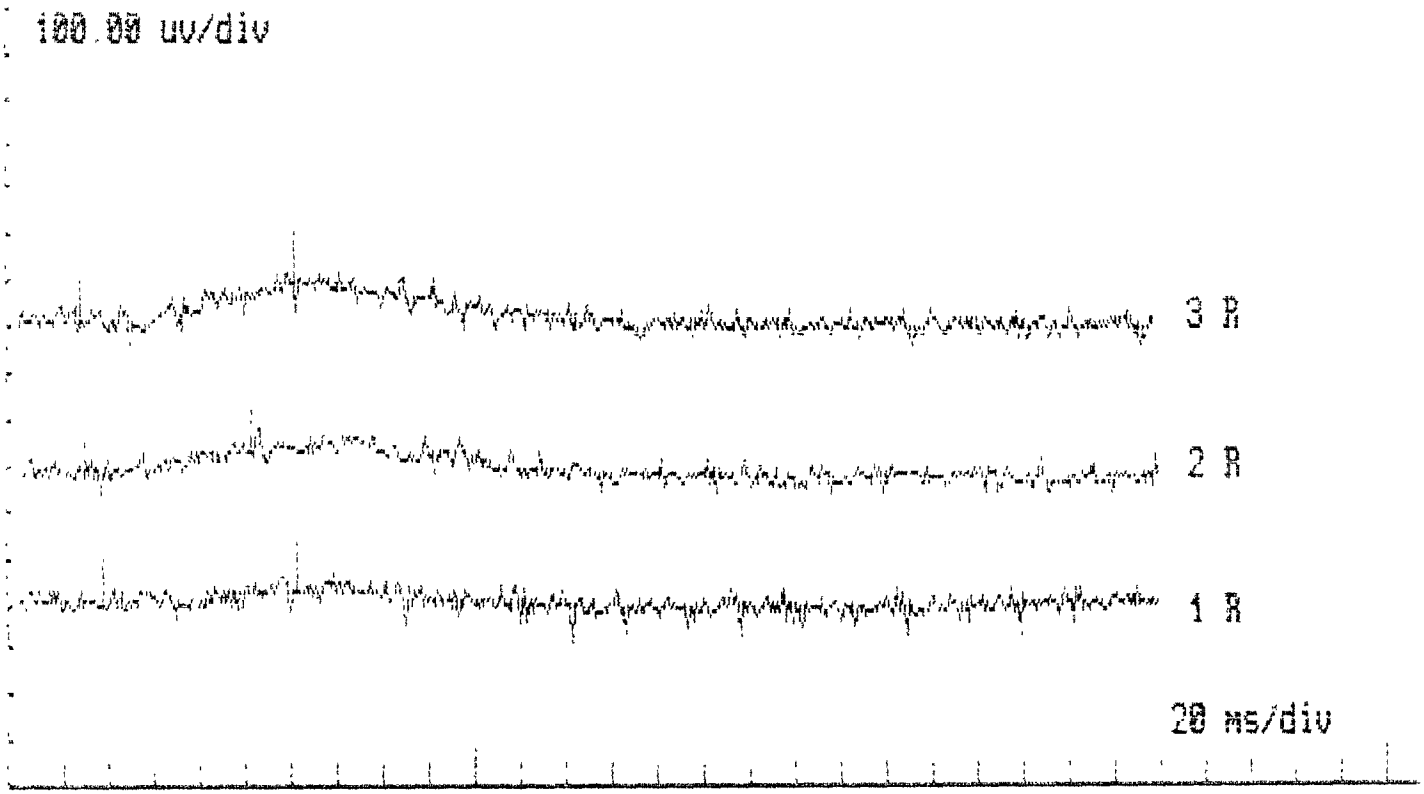
Parameter K_2 of the ERG model was used to obtain the parameters of the intensity-response or Naka-Rushton function. This produces more objective and consistent results than using the peak to trough amplitude of the raw ERG. However, this parameter did not show the saturation of the response at high stimuli intensities, as it is seen when using the

7. The photoreceptor cells generate the A-wave response and the cells in the inner nuclear layer are responsible for the B-wave response.

peak to trough values. The plot of parameter K_2 versus logarithmic stimulus intensity indicates that this parameter is much more sensitive to high stimuli intensities than to the lower intensities. This provides the grounds for future study in order to determine how this parameter behaves under higher stimuli intensities. Also future work should include more testing of normal and abnormal subjects to determine if there are any rages of parameter values that might be indicative of some abnormalities.

APPENDIX A

RAW ERGs OBTAINED FROM A NORMAL SUBJECT



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :30 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 29.54 uV IMPLICIT TIME : 123 ms

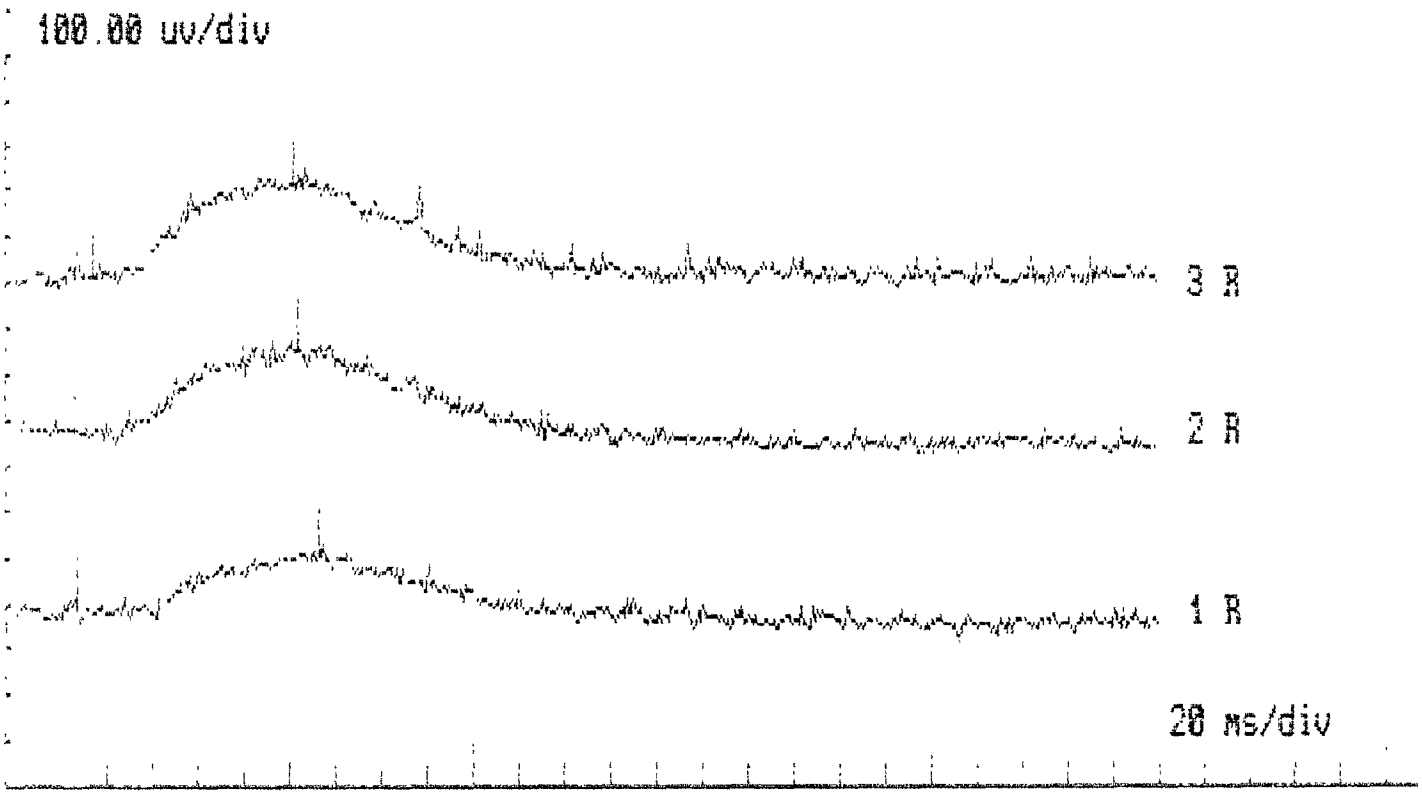
2: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :28 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 62.55 uV IMPLICIT TIME : 103 ms

3: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :26 db Scotopic Single Flash White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 85.14 uV IMPLICIT TIME : 122 ms

PATIENT: c .o BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :24 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 116.42 uV IMPLICIT TIME : 133 ms

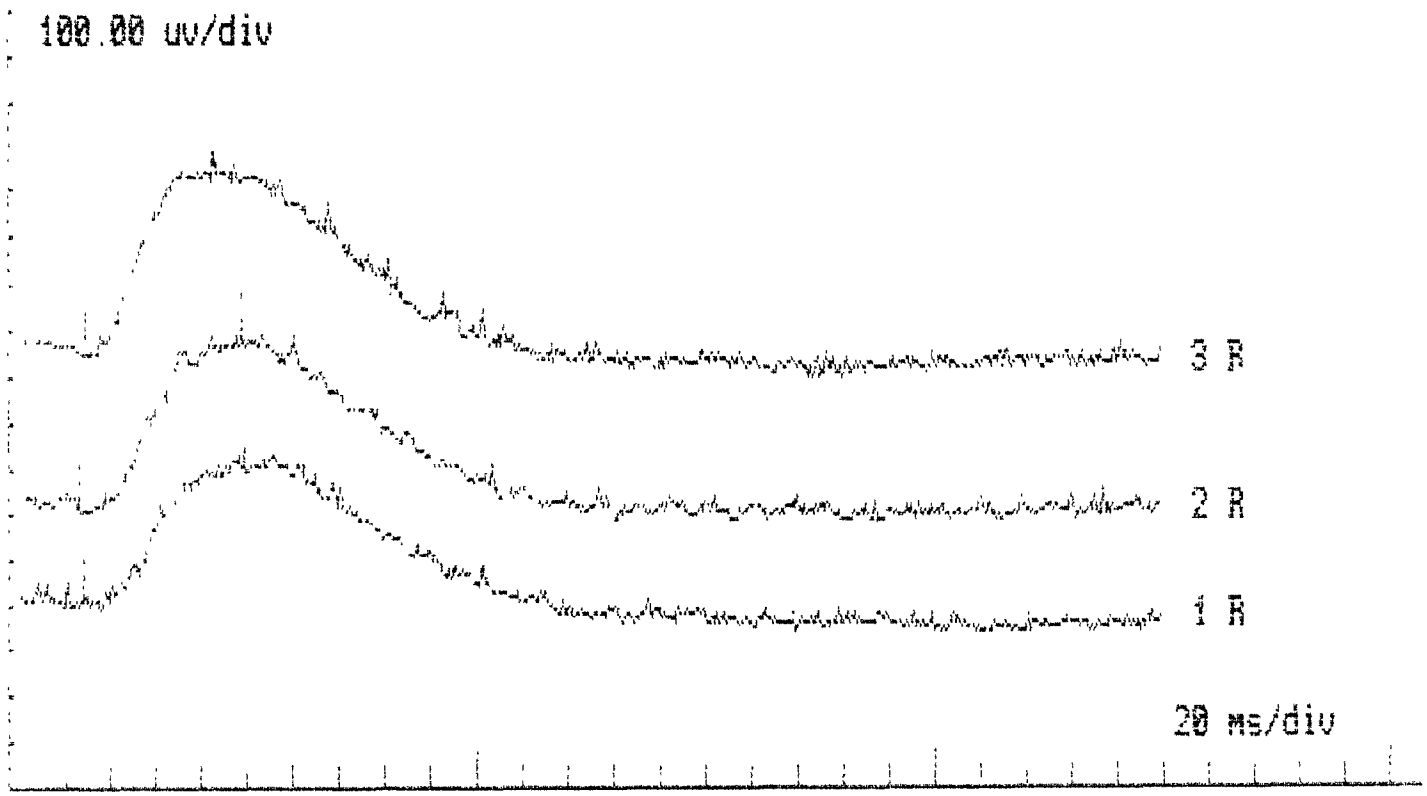
2: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :22 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 172.89 uV IMPLICIT TIME : 124 ms

3: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :20 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 192.88 uV IMPLICIT TIME : 122 ms

PATIENT: c .o BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :18 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 290.18 uV IMPLICIT TIME : 99 ms

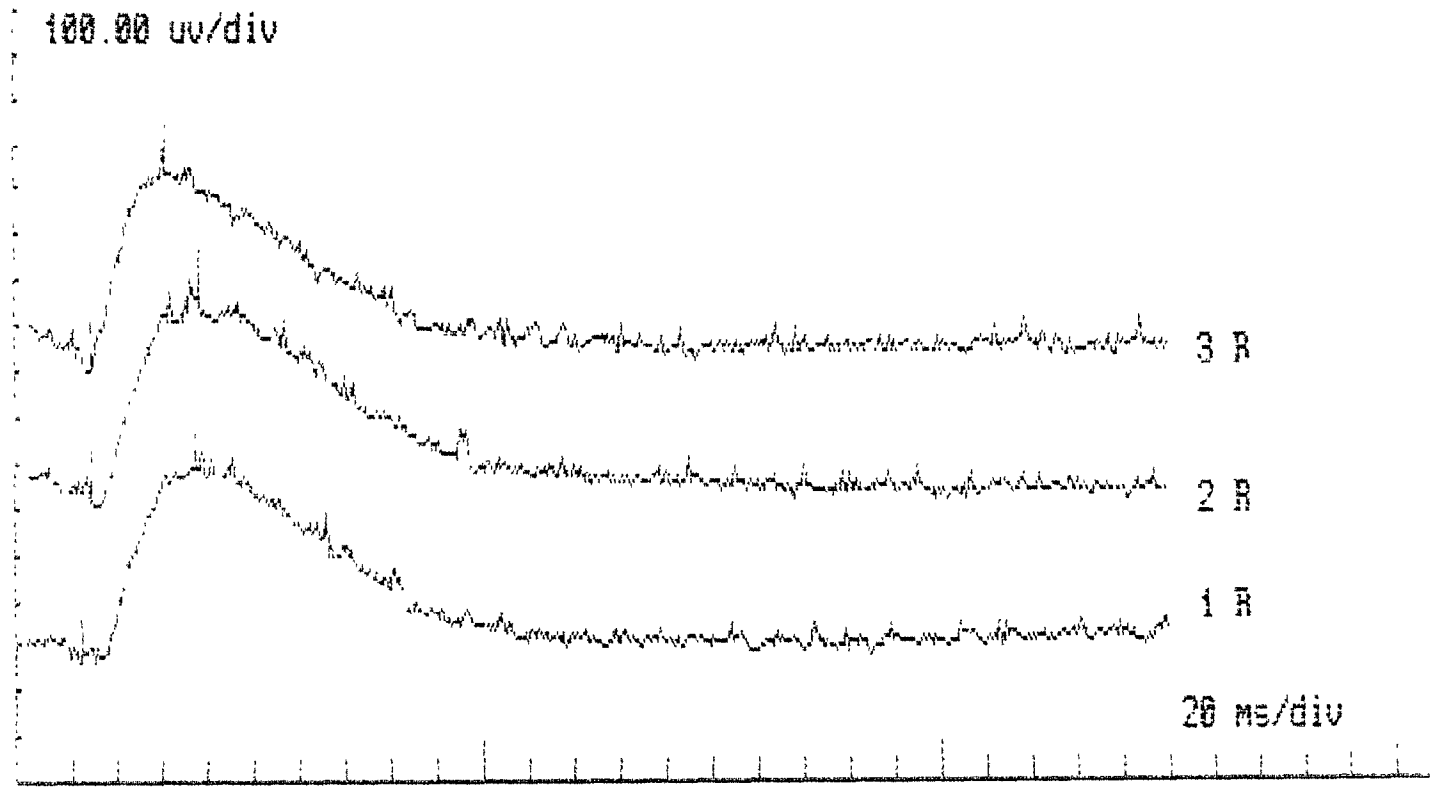
2: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :16 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 369.24 uV IMPLICIT TIME : 98 ms

3: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :14 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 381.41 uV IMPLICIT TIME : 85 ms

PATIENT: c .a BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :12 db Scotopic Single Flash. White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 423.11 uV IMPLICIT TIME : 75 ms

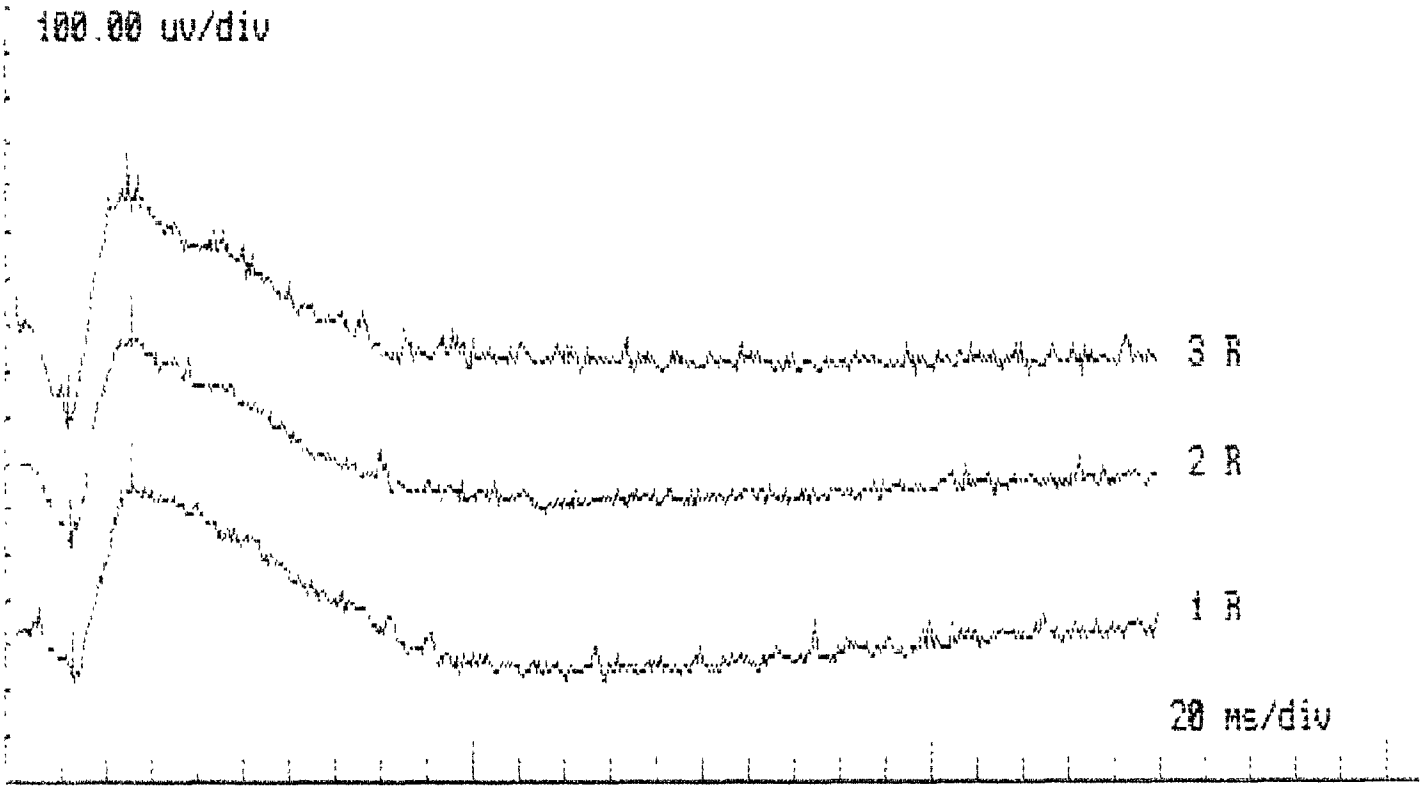
2: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :10 db Scotopic Single Flash. White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 424.85 uV IMPLICIT TIME : 77 ms

3: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :8 db Scotopic Single Flash White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 432.67 uV IMPLICIT TIME : 62 ms

PATIENT: c .o BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :6 db Scotopic Single Flash White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 401.39 uV IMPLICIT TIME : 51 ms

2: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :2 db Scotopic Single Flash. White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 437.88 uV IMPLICIT TIME : 51 ms

3: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :0 db Scotopic Single Flash. White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz
PEAK-TO-TROUGH AMPLITUDE : 492.62 uV IMPLICIT TIME : 49 ms

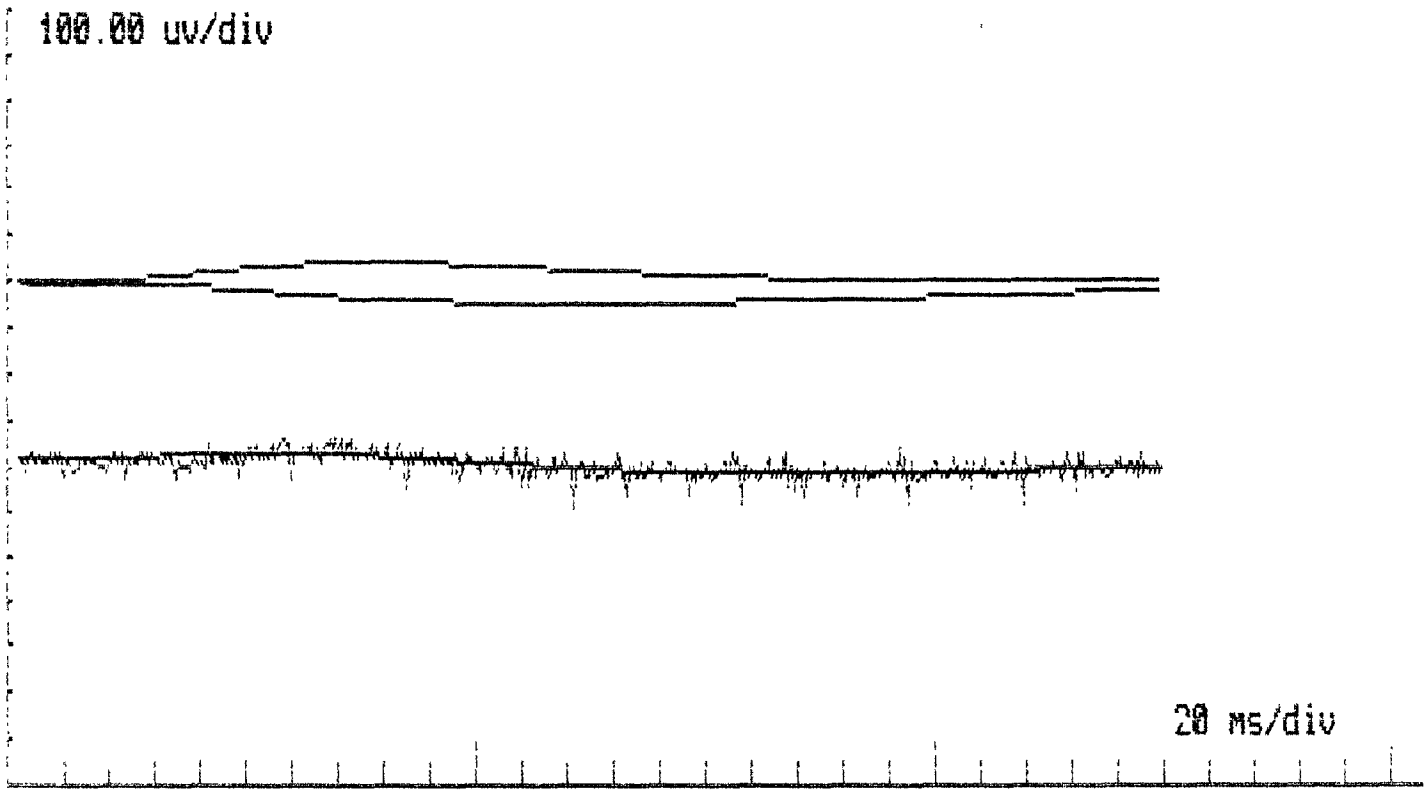
PATIENT: c .a BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT

APPENDIX B

RAW ERGs FROM APPENDIX A AND THEIR MODEL REPRESENTATION



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :30 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform

$$Y(t)=K1*(1 - exp(-\alpha 1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha 2*t)*sin(Wt)$$

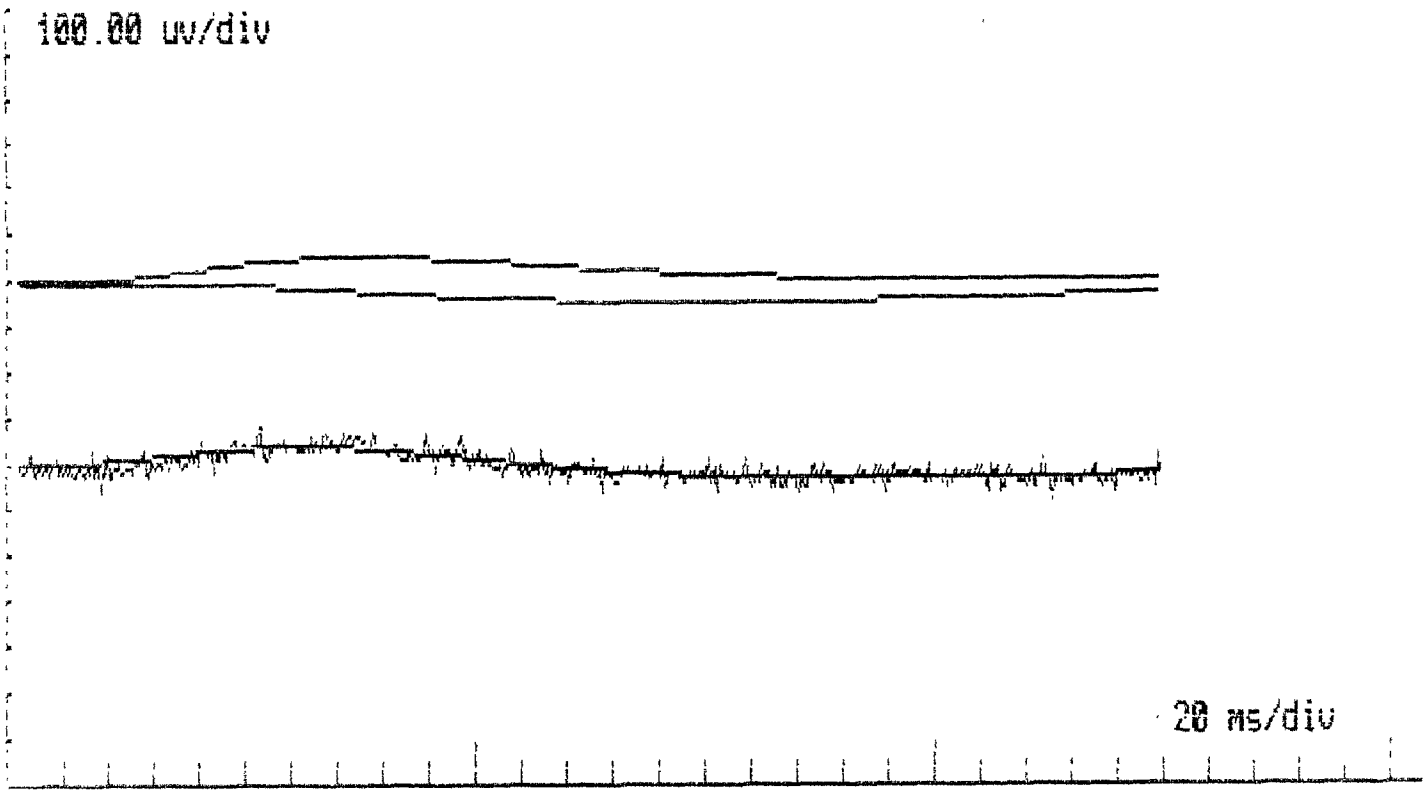
(1)----	K1=	-54.6163 uv
(2)----	To=	247.0693 ms
(3)----	α1=	1.5399
(4)----	K2=	4.587 uv
(5)----	α2=	0.0258 ms
(6)----	W=	0.0009

PATIENT: c . o BIRTHDATE: 05/05/40 SEX: f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO: .1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :28 db Scotopic Single Flash White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform

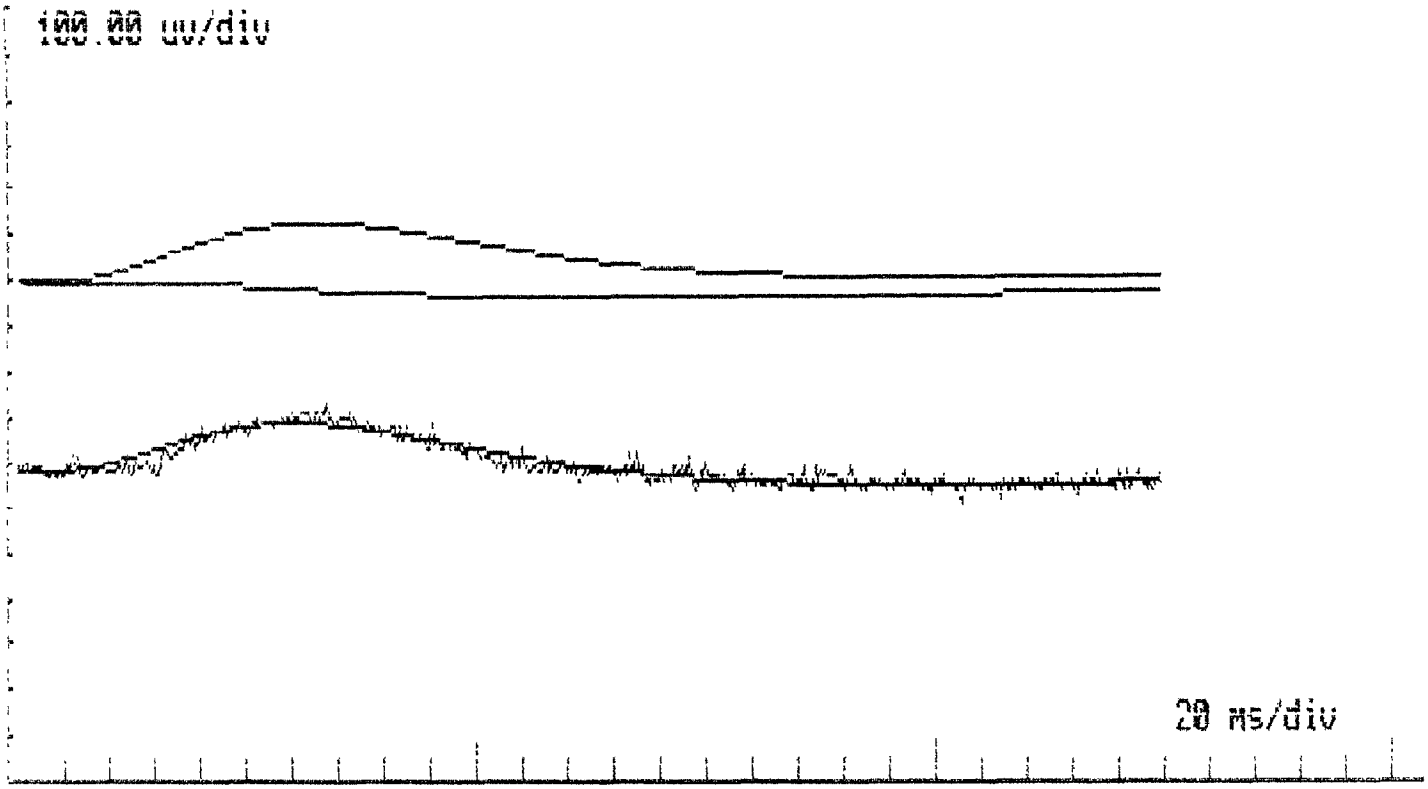
$$Y(t)=K1*(1 - exp(-\alpha 1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha 2*t)*sin(Wt)$$

(1)---- K1=	-84.9784	uv
(2)---- To=	299.9169	ms
(3)---- α_1=	0.7282	
(4)---- K2=	2698	uv
(5)---- α_2=	0.0264	ms
(6)---- W=	0.0021	

PATIENT: c . o BIRTHDATE: 05/05/40 SEX: f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :24 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

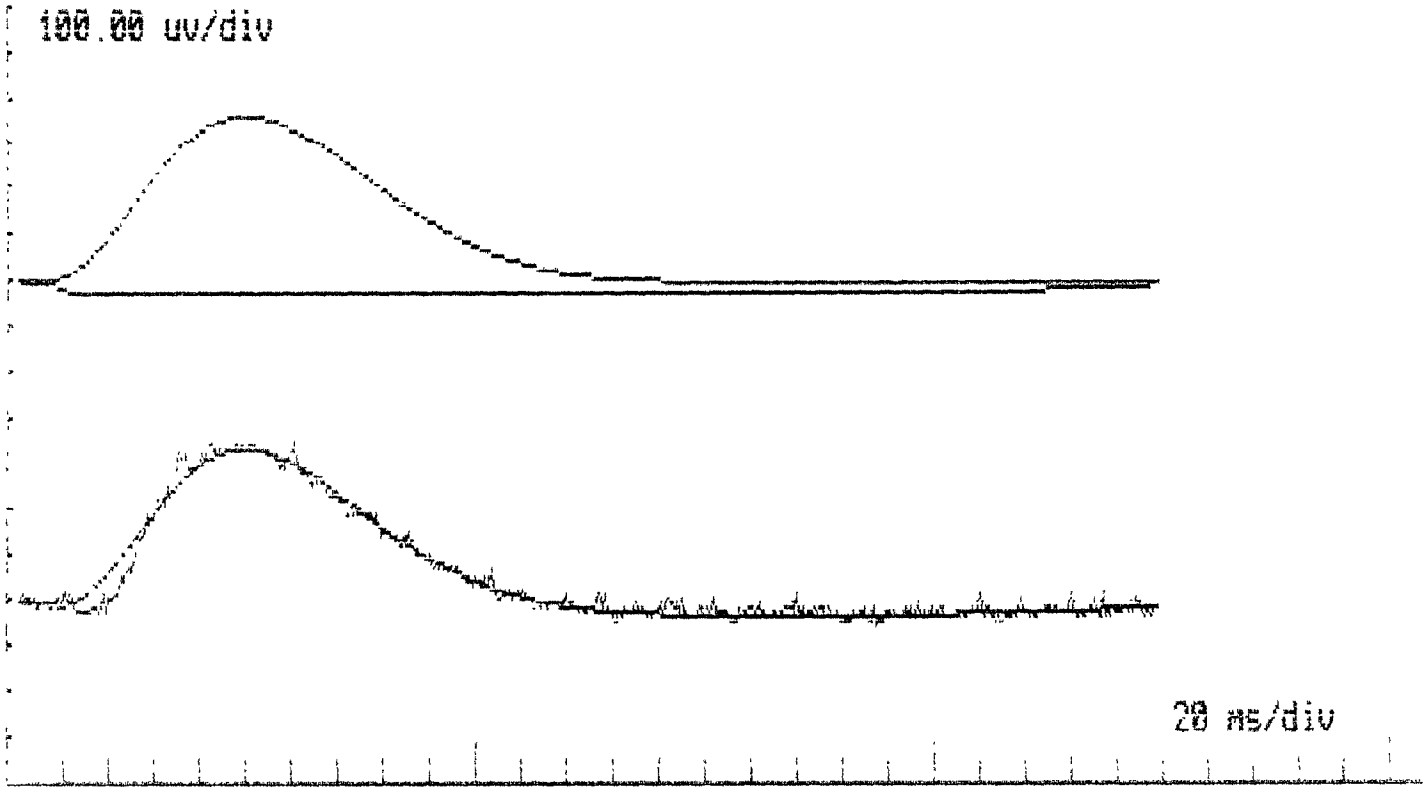
2: Model Waveform
$Y(t)=K1*(1 - exp(-'1((t/Tp1)exp(1-t/Tp1))^3)) + K2*t^3*exp(-3*'2*t)*sin(Wt)$

(1)----	K1=	-39.2349 uv
(2)----	Tp=	285.9536 ms
(3)----	α_1=	2.3249
(4)----	K2=	12.712 uv
(5)----	α_2=	0.0307 ms
(6)----	W=	0.0019

PATIENT: c o BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :16 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass 1 Hz Low Pass 500 Hz

2: Model Waveform
$Y(t)=K1*(1 - exp(-\alpha 1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha 2*t)*sin(Wt)$

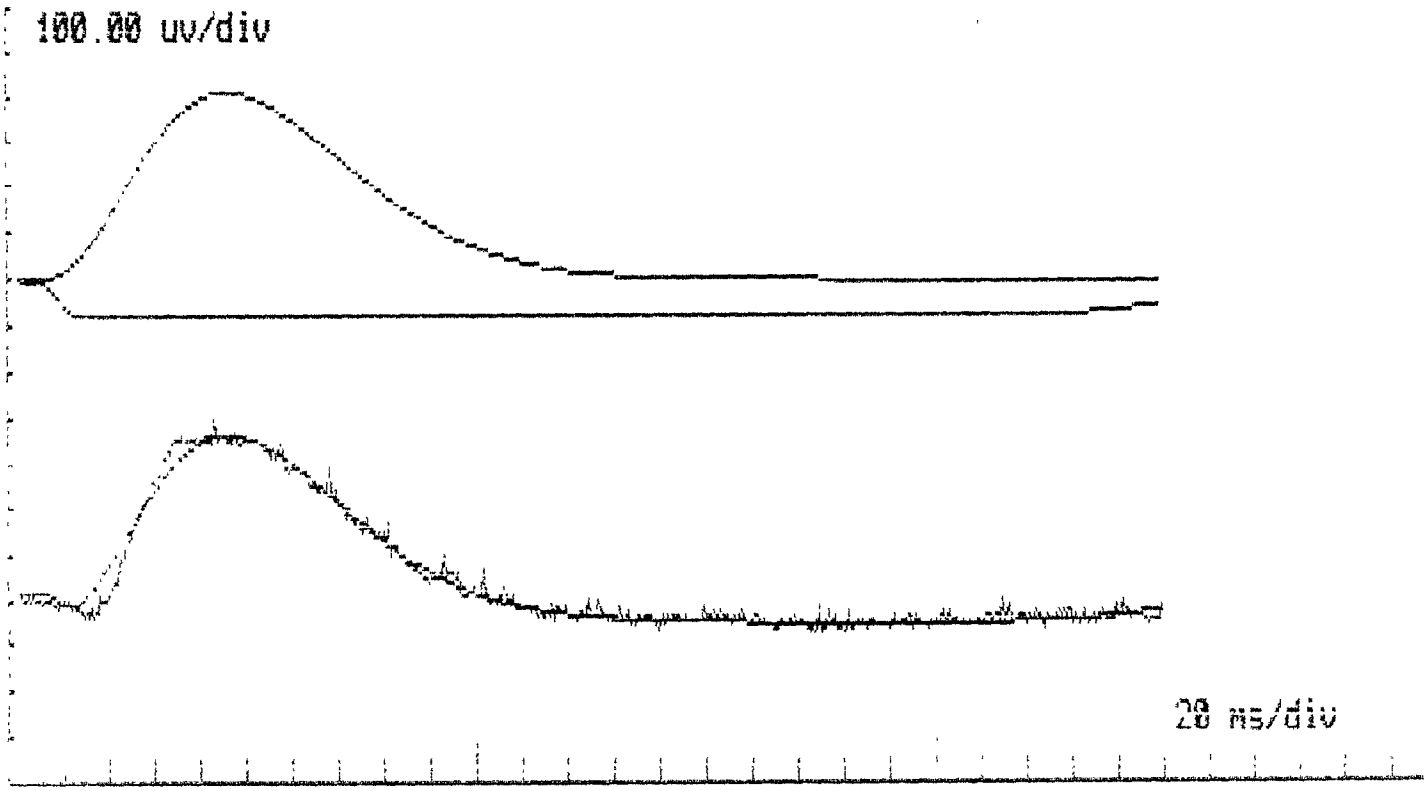
(1)----	K1=	-24.7854 uv
(2)----	To=	140.0558 ms
(3)----	$\alpha 1$=	292.6468
(4)----	K2=	14,018 uv
(5)----	$\alpha 2$=	0.0354 ms
(6)----	W=	0.0112

PATIENT: c o BIRTHDATE: 05/05/40 SEX: f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :14 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass 1 Hz Low Pass 500 Hz

2: Model Waveform
$Y(t)=K1*(1 - exp(-\alpha 1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha 2*t)*sin(Wt)$

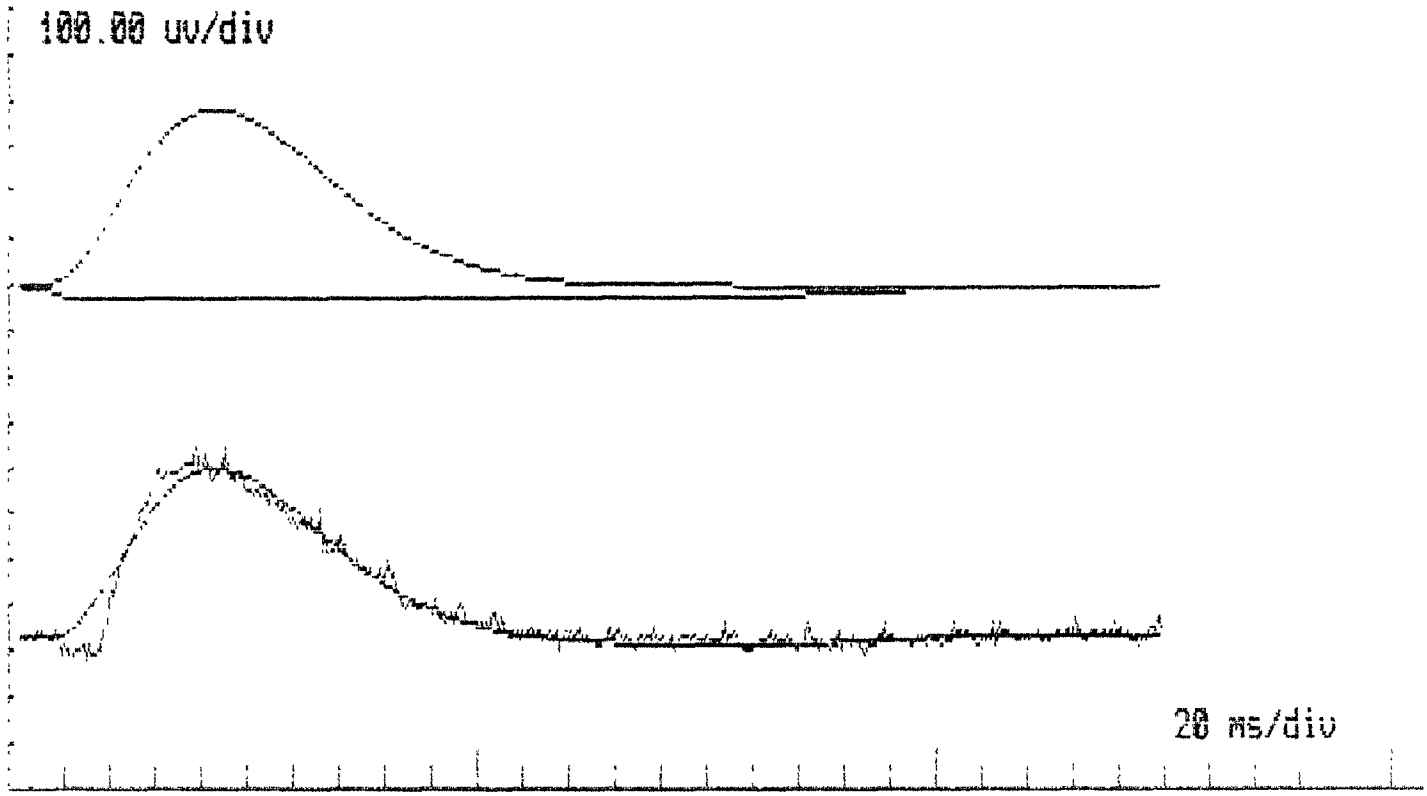
(1)---- K1=	-78.5049	uv
(2)---- To=	148.6291	ms
(3)---- $\alpha 1$=	331.0566	
(4)---- K2=	30,438	uv
(5)---- $\alpha 2$=	0.0406	ms
(6)---- W=	0.0090	

PATIENT: c o BIRTHDATE: 05/05/40 SEX: f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO: .1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :12 db Scotopic Single Flash White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform

$$Y(t)=K1*(1 - \exp(-\alpha1((t/To1)\exp(1-t/To1))^3)) + K2*t^3*\exp(-3*\alpha2*t)*\sin(Wt)$$

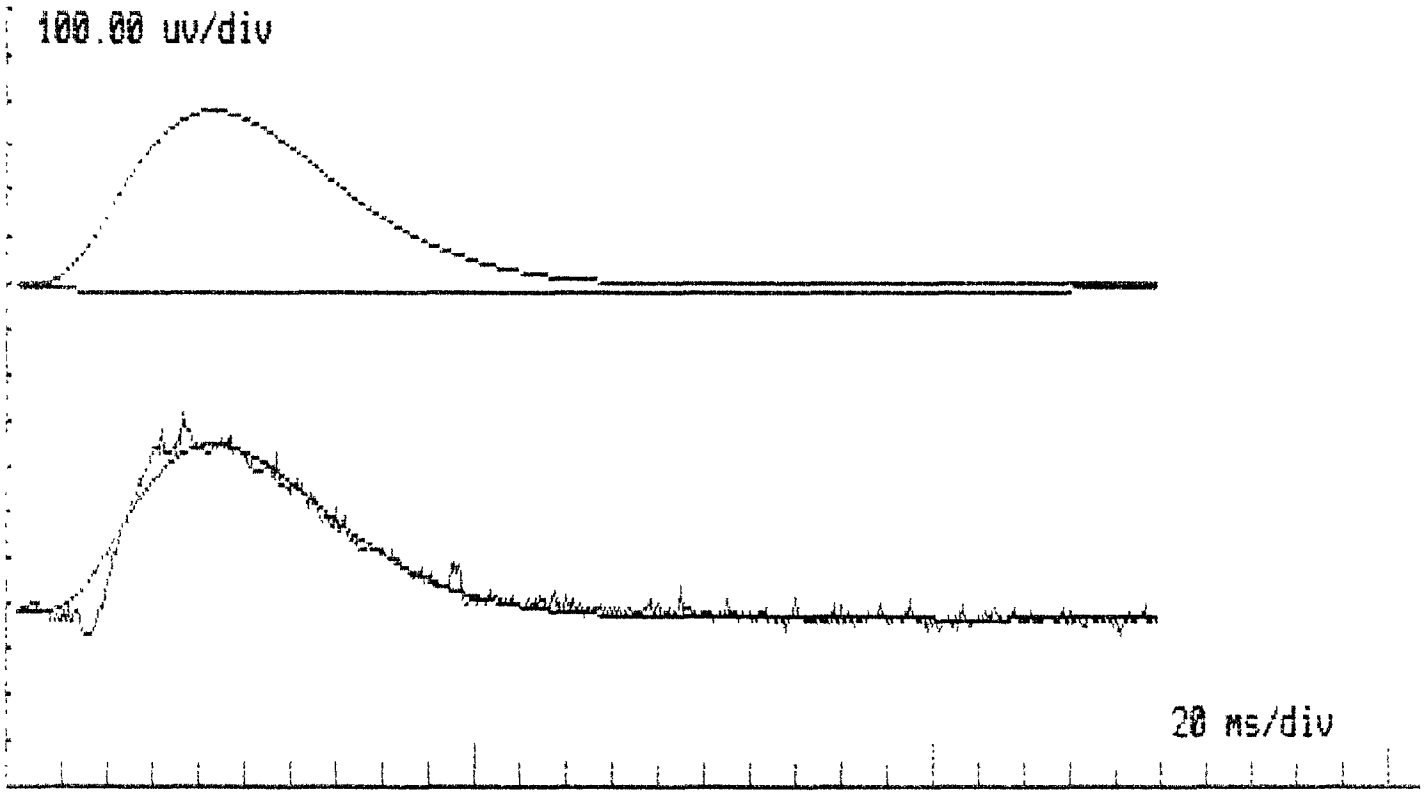
(1)---- K1=	-22.1875	uv
(2)---- To=	112.3877	ms
(3)---- $\alpha1$=	250.5561	
(4)---- K2=	32.507	uv
(5)---- $\alpha2$=	0.0431	ms
(6)---- W=	0.0101	

PATIENT: c o BIRTHDATE: 05/05/40 SEX: f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :10 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform
$Y(t)=K1*(1 - exp(-\alpha 1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha 2*t)*sin(Wt)$

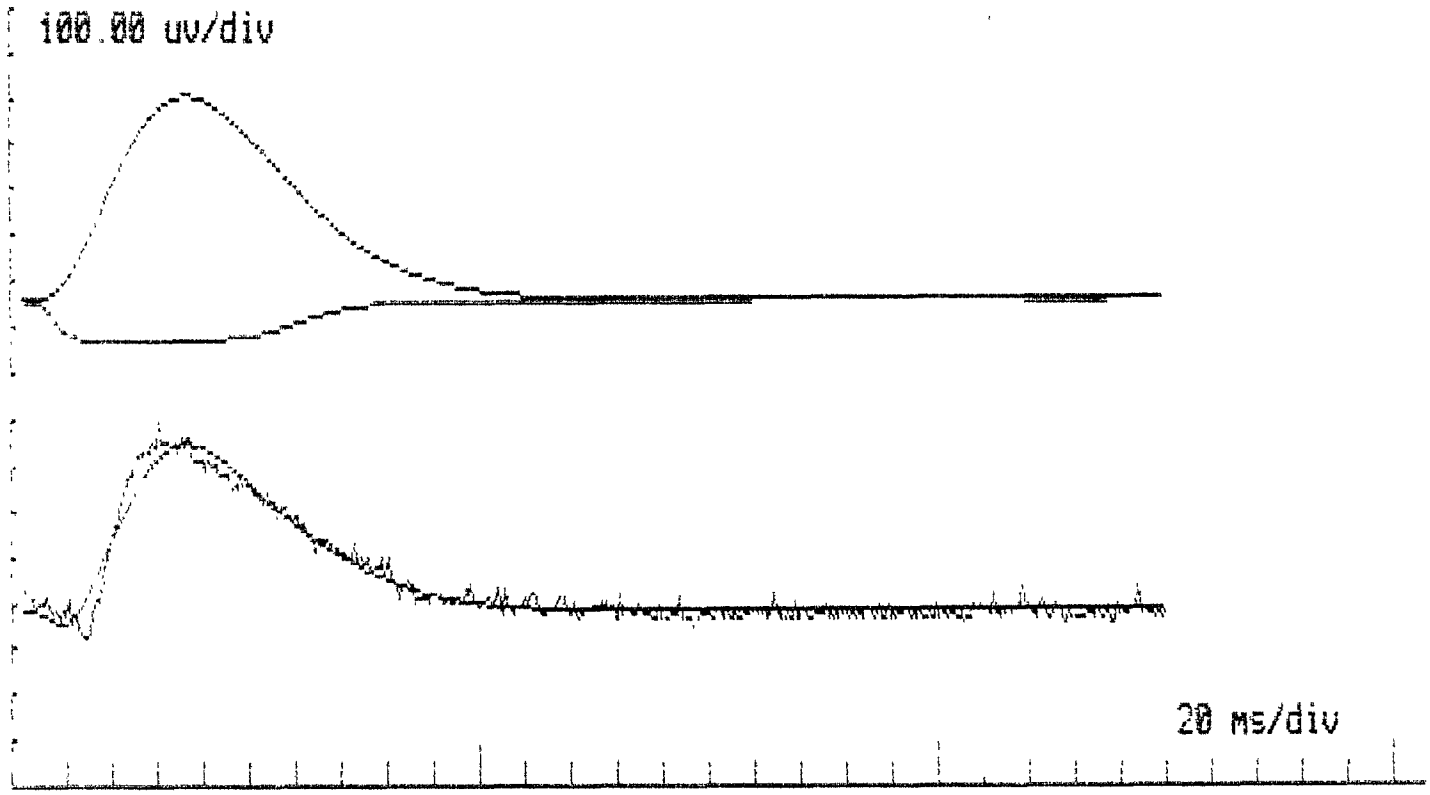
(1)----	K1=	-10.3790 uv
(2)----	To=	152.5556 ms
(3)----	$\alpha 1$=	321.5053
(4)----	K2=	58.824 uv
(5)----	$\alpha 2$=	0.0452 ms
(6)----	W=	0.0061

PATIENT: c o BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :8 db Scotopic Single Flash, White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform

$$Y(t)=K1*(1 - exp(-\alpha1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha2*t)*sin(Wt)$$

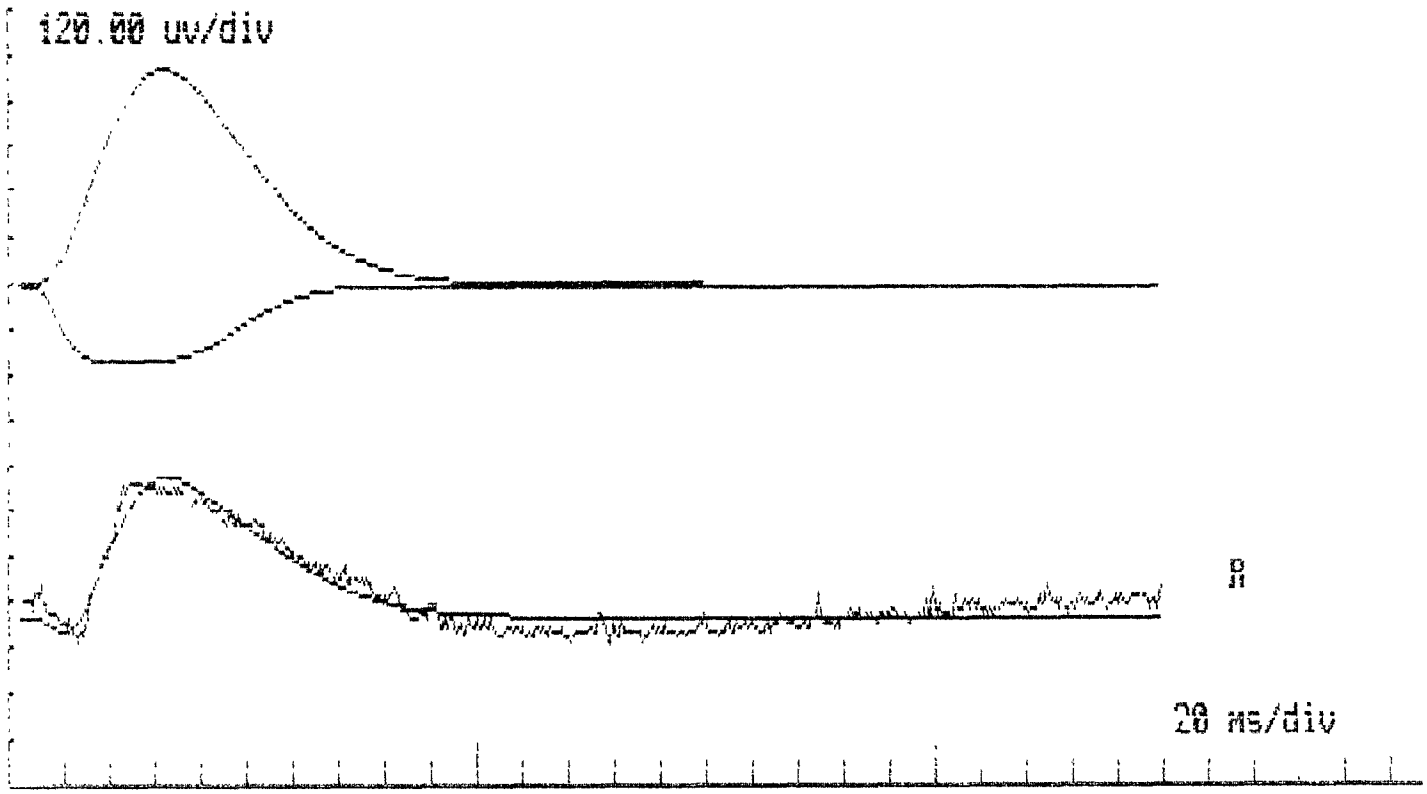
(1)----	K1=	-81.7754 uv
(2)----	To=	51.4882 ms
(3)----	α1=	10.2621
(4)----	K2=	112610 uv
(5)----	α2=	0.0534 ms
(6)----	W=	0.0073

PATIENT: c . o BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :6 db Scotopic Single Flash White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform
$Y(t)=K1*(1 - exp(-\alpha1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha2*t)*sin(Wt)$

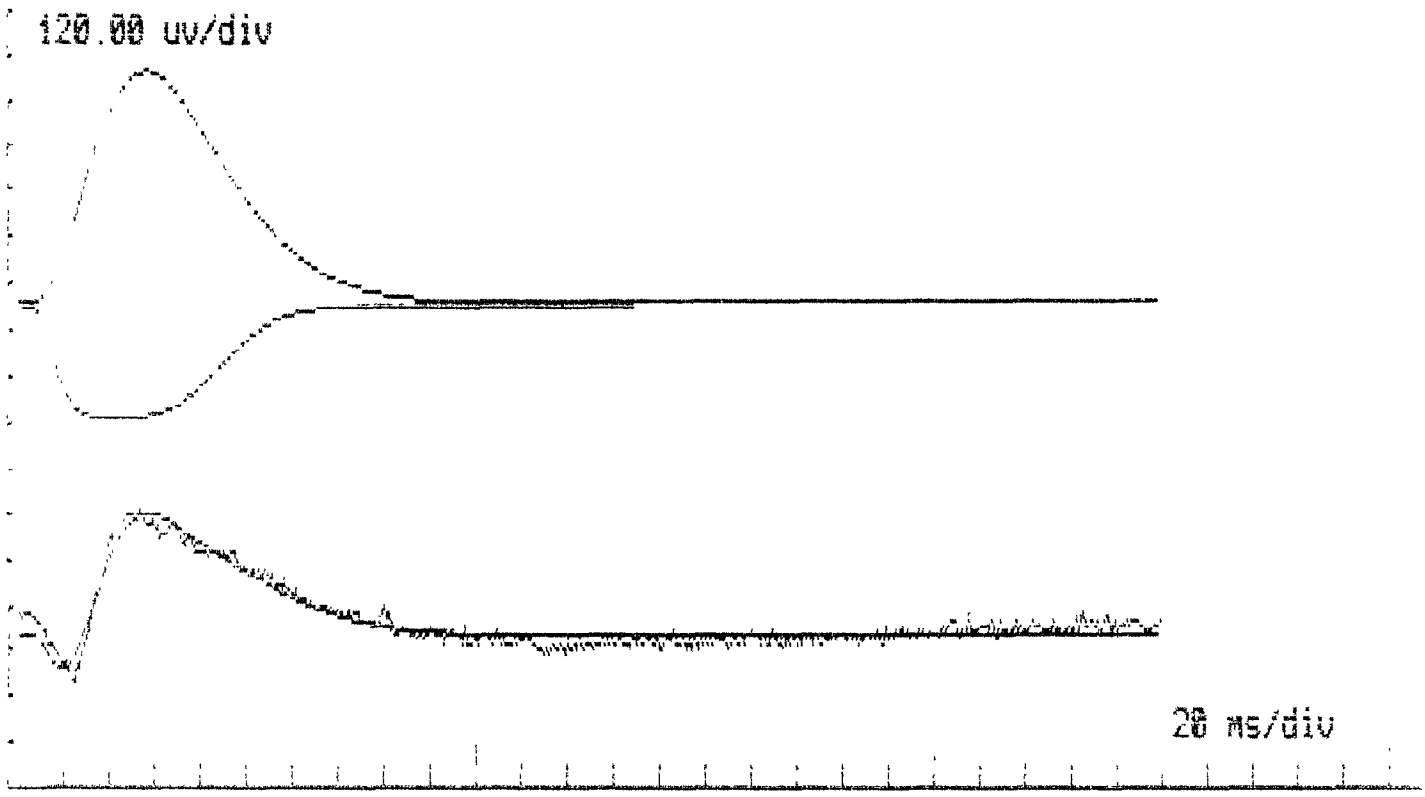
(1)----	K1=	-208.2374 uv
(2)----	To=	47.8408 ms
(3)----	α1=	3.7969
(4)----	K2=	164.758 uv
(5)----	α2=	0.0603 ms
(6)----	W=	0.0105

PATIENT: c . o BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :2 db Scotopic Single Flash White FREQUENCY: EYE: R
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform
$Y(t)=K1*(1 - exp(-\alpha1((t/Tp1)exp(1-t/Tp1))^3)) + K2*t^3*exp(-3*\alpha2*t)*sin(Wt)$

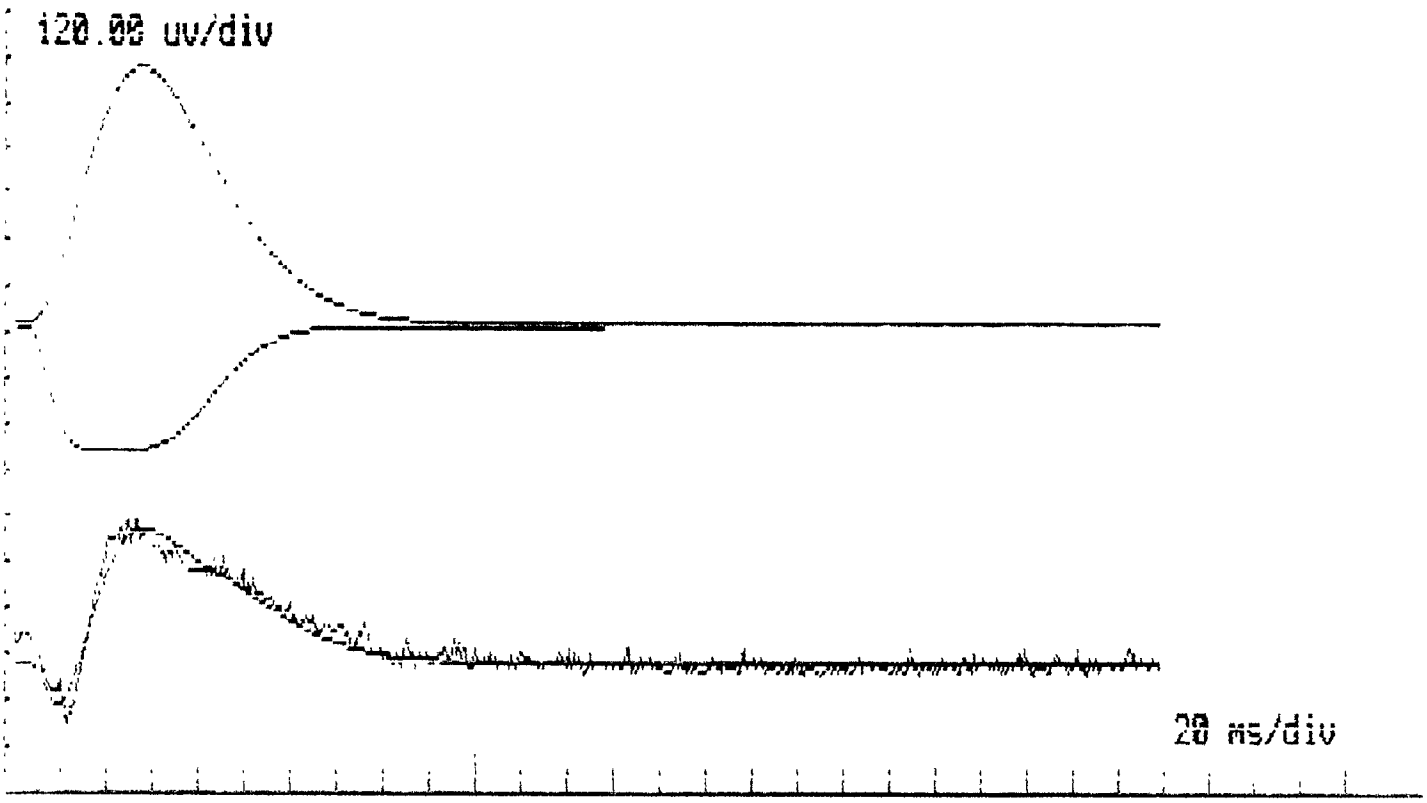
(1)---- K1= -300.6210 uv
(2)---- Tp= 43.1892 ms
(3)---- α1= 4.0129
(4)---- K2= 411.404 uv
(5)---- α2= 0.0696 ms
(6)---- W= 0.0077

PATIENT: C . O BIRTHDATE: 05/05/40 SEX: F

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO: 1Hz HI: 10KHz 60Hz: OUT

ERG



1: TEST DATE: 04/20/91 TEST TYPE: ERG LABEL: R
STIMULUS :0 db Scotopic Single Flash White FREQUENCY: EYE: b
FILTER FREQUENCY : High Pass .1 Hz Low Pass 500 Hz

2: Model Waveform
$Y(t)=K1*(1 - exp(-\alpha 1((t/To1)exp(1-t/To1))^3)) + K2*t^3*exp(-3*\alpha 2*t)*sin(Wt$

(1)----	K1=	-340.4220 uv
(2)----	To=	41.9355 ms
(3)----	$\alpha 1$=	4.1631
(4)----	K2=	46.8659 uv
(5)----	$\alpha 2$=	0.0710 ms
(6)----	W=	0.0081

PATIENT: castro gina BIRTHDATE: 05/05/40 SEX:f

DIAGNOSIS:

COMMENT:
ERGs recorded using Massof's protocol
Analog Filters (GRASS): LO:.1Hz HI: 10KHz 60Hz: OUT

APPENDIX C

PARAMETER IDENTIFICATION OF THE ERG MODEL

SIMPLEX ALGORITHM

In this work, the model parameters were estimated using a Simplex algorithm based on a non-linear least-squares criterion. The algorithm fits the ERG model to the raw ERG data computing the parameter values that best fit the raw data.[19] [20]

Assume that the raw data consists of n points; Where each value of the independent variable is represented by: $t_1, t_2, \ldots, t_n$; the dependent variable by $E_1, E_2, \ldots, E_n$; and the parameters by $a_1, a_2, \ldots, a_m$. Then for a set of predicted parameter values we will obtain the following dependent variables: $E'_1, E'_2, \ldots, E'_n$. The sum of squared residuals (SS_R) is defined as:

$$SS_R = (E_1 - E'_1)^2 + (E_2 - E'_2)^2 + \cdots + (E_n - E'_n)^2$$

$$= \sum_{i=1}^{i=n} (E_i - E'_i)^2 \qquad \text{(C.1)}$$

The lower the SS_R is the best the model will fit the data. Therefore, the problem of estimating the parameters of the model consists in determining the minimum of the new function: SS_R; where the parameters a_i become the independent variables and SS_R become the dependent variable.

To determine the minimum of SS_R the simplex method was used. The main idea of the simplex method is to construct a simplex[8] in the space described by the m parameters to fit (m+1 vertices). Each vertex of the simplex is defined by m parameters plus the

8. A simplex is a geometric figure that has one more vertex than the space where it is defined has dimensions. A simplex on a plane (2 dimensions) would be a triangle (3 vertices); A simplex on a three dimensional space would be a tetrahedron, etc.

SS_R.

The first vertex of the simplex is defined by the initial parameters $a_1{}^{(0)}, a_2{}^{(0)}, \ldots, a_m{}^{(0)}$ and the SS_R defined by these parameters.

The remaining m vertices are defined by another set of parameters: $a_1{}^{(i)}, a_2{}^{(i)}, \ldots, a_m{}^{(i)}$. Where $i = 1,2,..m$; and the SS_R defined by these parameters. The parameters for these vertices are calculated by the following equations:

$$a_j{}^{(i)} = \begin{cases} a_j{}^{(0)} + \delta_1 & \text{if } j = i \\ a_j{}^{(0)} + \delta_2 & \text{if } j \neq i \end{cases} \tag{C.2}$$

Where $i,j = 1,2,...,m$, and δ_1, δ_2 are the parameter increments which depend on the number of parameters m and a user selected scale step α:

$$\delta_1 = \left[\frac{\sqrt{(m+1)} + m - 1}{\sqrt{2} \cdot m} \right] \cdot \alpha \tag{C.3}$$

$$\delta_2 = \left[\frac{\sqrt{(m+1)} - 1}{\sqrt{2} \cdot m} \right] \cdot \alpha \tag{C.4}$$

Therefore, the vertices ($V^{(i)}$ i=0,1,...,m) for the initial simplex are defined as:

$$V^{(0)} = (a_1{}^{(0)}, a_2{}^{(0)}, \ldots, a_m{}^{(0)}, SS_R{}^{(0)})$$
$$V^{(1)} = (a_1{}^{(1)}, a_2{}^{(1)}, \ldots, a_m{}^{(1)}, SS_R{}^{(0)})$$

$$V^{(m)} = (a_1{}^{(m)}, a_2{}^{(m)}, \ldots, a_m{}^{(m)}, SS_R{}^{(0)})$$

The minimum is obtained by rejecting the worst vertex, the one that gives the highest

response (SS_R); And substituting it by a new value that is obtained by one of the following mechanism:

- *Reflection*: A new vertex is created on the line that joins the worst vertex with the midpoint of all the other vertices (centroid) at the same distance that the worst vertex is from this point but in the opposite direction.
- *Expansion*: A new vertex is created on the line that joins the worst vertex with the midpoint of all the other vertices (centroid) at twice same distance that the worst vertex is from this point but in the opposite direction.
- *Contraction*: A new vertex is created on the line joining the worst vertex with the midpoint of all the other vertices (centroid) at halve the distance that the worst vertex is from this point in the direction of the midpoint.
- *Shrinkage*: All vertices except the best one move toward the best one by half of the original distance from it.

The rules for estimating the parameters of the ERG model using the Simplex method are described in figure C.1.

First, the worst vertex of the simplex is identified. If we assume $V^{(j)}$ to be the worst vertex, then the centroid (C_i) for each parameter ($a_i{}^{(J)}$) is calculated as:

$$C_i = \frac{1}{m} \sum_{\substack{k=0 \\ k \neq j}} a_i{}^{(k)} \qquad \text{(C.5)}$$

$i = 1,2,..,m$

The parameters for the new vertex $V^{(new)}$ are determined based on the type of mechanism used as described on figure C.1.

For a reflextion the new parameters will be:

$$a_i^{(new)} = 2 \cdot C_i - a_i^{(j)} \tag{C.6}$$

For a expansion the new parameters will be:

$$a_i^{(new)} = 2 \cdot a_i^{(j)} - C_i \tag{C.7}$$

For a contraction the new parameters will be:

$$a_i^{(new)} = \frac{1}{2} \cdot a_i^{(j)} - C_i \tag{C.8}$$

$i = 1,2,..,m$

The simplex method provides an adequate tool for identifying the parameters of the ERG model that best fit the raw data. The parameter identification program was implimented in C language. It contains a user interface wich allows the user to select the raw ERG data for a particular subject from the database and obtain the parameters which identify the ERG. The program running under an IBM compatible 386 computer with a math coprocessor produces the nine parameters of the ERG model in a reasonable amount of time.

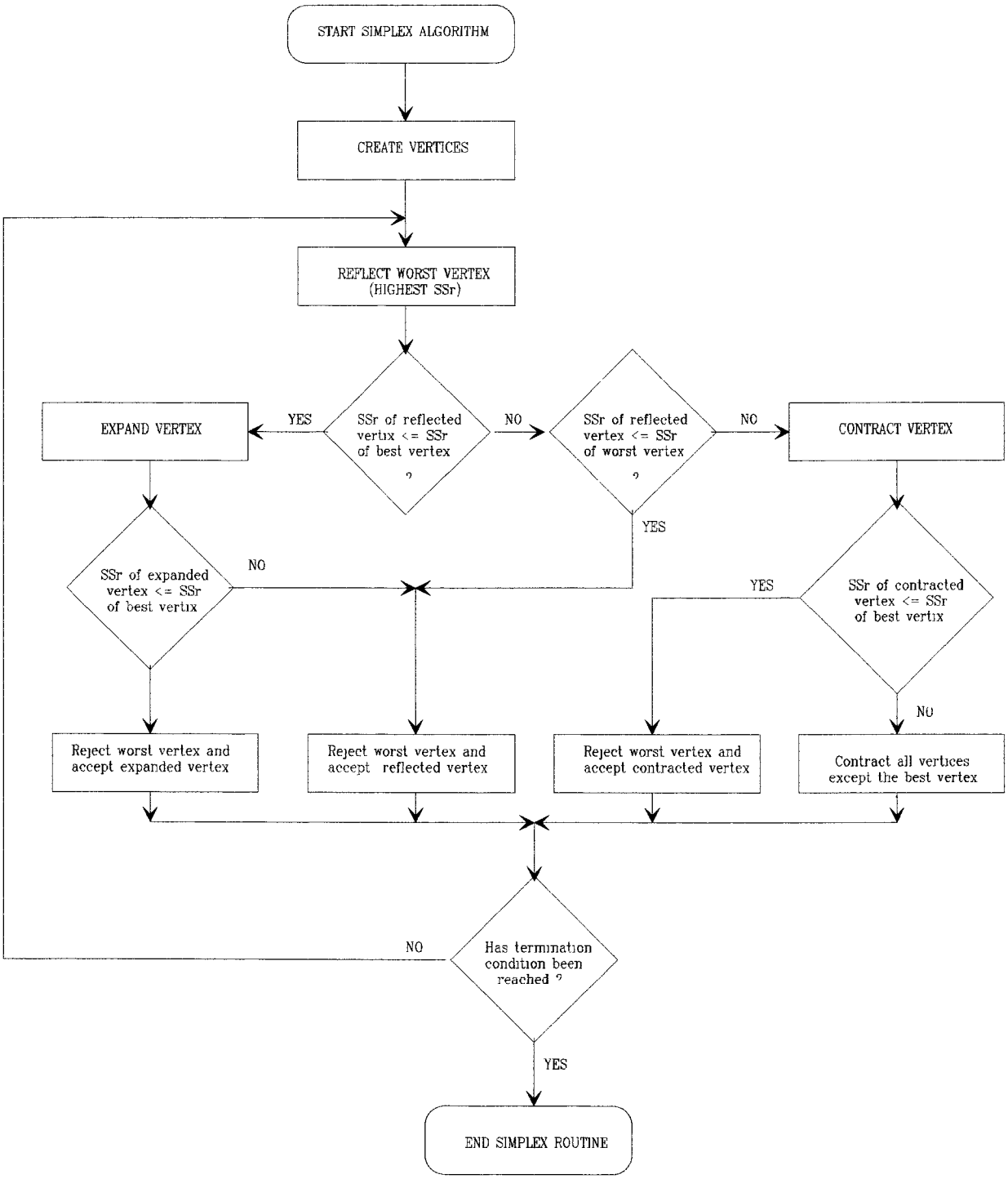


Figure C.1: Simplex Algorithm

APPENDIX D

MULTI-FUNCTION TEST SYSTEM VERSION 2

MANUAL

MULTI-FUNCTION TEST SYSTEM VERSION 2.0

1. INTRODUCTION

Electrophysiologic testing provides a way for diagnosis of the visual system. The Multi-Function Test System Version 2.0 (MFTS2) described in this manual, can be used for three different electrophysiologic tests: Electroretinography (ERG), Visual Evoked Response (VER) and Electrooculograpy (EOG).

Single flash electroretinogram measures the alteration of electrical potential in the retina when it is stimulated by a flash of light. For this type of recording a Ganzfeld unit is used to provide the visual stimulus to elicit the ERG response. Since we do not have a direct control over the Ganzfeld unit available in the Electrophysiology Laboratory at the Eye Institute of New Jersey, the LKC UTAS-1000 system which controls the Ganzfeld unit, must be operated at the same time as the system described here.

For pattern ERG or VER recordings a pattern monitor is used to provide the stimulus. This type of recording creates a very low amplitude response, therefore, averaging of the response is required in order to eliminate external noise. Two pattern monitors are available: a Nicolet monitor and a monitor supplied by the LKC UTAS-1000 system. If the LKC monitor is used, the LKC system must be operated in order to control the monitor. The Nicolet monitor can be directly controlled on the monitor itself and the LKC system is not required if the Nicolet monitor is used.

This manual describes the operation of the MFTS2 system developed using an IBM/XT compatible computer. For a description and operation of the LKC UTAS-1000 system refer to the LKC operations manual.

2. THE SYSTEM

The Multi-Function Test System was developed using an IBM/XT compatible computer, a Metrabyte DASH-16 data acquisition board and a GRASS 8-10 multichannel recording amplifier. The system also utilizes the LKC Ganzfeld unit, LKC pattern monitor and Nicolet pattern monitor as stimulating devices.

2.1 EQUIPMENT CONNECTIONS

The patient's electrodes connect to an Electrode Connection Box which routes the signals to the LKC system and the MFTS2 system. The jacks in the electrode connection box contain the same labels as the pushbuttons in the Pushbutton Electrode Selector Panel on the GRASS machine. Once the system is calibrated the pushbuttons for the channels used in the test, must be set to the position that the electrodes are connected in the Electrode Connection Box.

In the MFTS2 system the signal is amplified by the analog filters of the GRASS amplifier, then it is converted into digital form by the DASH-16 board and fed into the XT computer.

2.1.1 Electrodes To GRASS Amplifier:

The electrodes which capture the response from the patient should be connected to the Electrode Connection Box. This box allows the signal to be routed to either, or both, the LKC or MFTS2 systems. The Electrode Connection Box connects to the GRASS amplifier by a flexible cable with a 25 pin

connector.

Once the system is calibrated the pushbuttons in the pushbutton electrode selector panel of the GRASS machine must be set to the position in which the electrodes are connected to in the electrode connection box. Make sure that the positive (+) and negative (-) poles are selected properly in the GRASS machine.

2.1.2 GRASS Amplifier To DASH Data Acquisition Board:

Channels labeled Ch2, Ch3 and Ch4 in the GRASS amplifier are used for the MFTS2 system testing. The output from the GRASS amplifier, for these channels, should be connected to the A/D conversion inputs (CH1, CH2 and CH3 respectively) of the DASH connection box. The wire connecting each output from the GRASS amplifier to the A/D inputs is a one conductor shielded wire. The shield (ground) for each channel must be connected to the A/D converter inputs labeled "CHx LO" (where x = 1,2,3) and the center conductor must be connected to the A/D input labeled "CHx HI".

The DASH connection box connects to the DASH-16 data acquisition board via an 18 inch ribbon cable with 37 pin connectors at each end. The DASH-16 board is located in one of the expansion slots inside the IBM/XT compatible computer.

2.1.3 Triggers:

Triggers are used to indicate to the data acquisition board when a stimulus occurs. The MFTS2 system starts to acquire data as soon as the trigger is received. Since there are three stimulating devices (LKC Ganzfeld, LKC pattern monitor and Nicolet pattern monitor) three trigger inputs are used to detect to occurrence of each stimulus. The triggers connect from the trigger outputs of the stimulating devices to the DASH connection box. One conductor shielded wires are used. The shields (ground) of the wires connect to the pin labeled GND in the DASH connection box and the conductors connect to the pins labeled IP0, IP1 and IP2.

2.1.3.1 LKC Ganzfeld Trigger:

The trigger for the LKC Ganzfeld dome is bridged from the "STR TRIG" output of the LKC system located at the LKC interface rear panel, and connects to the IP1 input of the DASH connection box.

2.1.3.2 LKC Pattern Monitor Trigger:

The LKC pattern monitor does not have an external trigger signal. Therefore, a photodiode is used to convert the pattern reversal into an electrical trigger. A fiber optic cable is used to transfer the light stimulus from the LKC monitor to a photodiode in the Trigger Box.

One termination of the fiber optic cable box should be taped to the front of LKC pattern monitor. The fiber tip should be placed in contact with the center of the lowest and rightmost square of the checkerboard pattern on the monitor. The other termination of the fiber cable should be connected to the photodiode in the Trigger Box. The output of the Trigger Box should connect to the IP2 of the DASH connection box.

If this trigger is going to be used to switch in the Trigger Box should be turn to the ON position (green light should turn on). The trigger box requires a 9 volt battery. Turn the switch to the OFF position after using the system, to avoid draining the battery.

2.1.3.3 Nicolet Pattern Monitor Trigger:

The trigger from the Nicolet pattern monitor connects to the IP0 input of the DASH connection box.

3. MFTS2 TEST

The MFTS2 program can be used for the recording of electrophysiological tests such as electroretinogram, electrooculogram and visual evoked potentials. Once the data is recorded it can be digitally filtered, displayed on a screen, stored on disk or used for generation of reports. The program is stored on the XT computer in the electrophysiology laboratory of the Eye Institute of New Jersey, in the ERGVER directory. To run the test, type "mfts2" at the DOS (c:>) prompt and hit [ENTER]:

C:> mfts2 [ENTER]

This will execute the mfts2 program and present the main menu of the program:

[T]: TEST
[R]: REPORT
[C]: CALIBRATION
[Q]: QUIT

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

3.1 CALIBRATION

The MFTS2 system must be calibrated before any test is performed. This process will measure the actual gain of the GRASS amplifiers. It is essential for the system to be calibrated before testing, otherwise, the results will not be accurate. To calibrate the MFTS2 system select CALIBRATION at the main menu then follow the directions presented on the screen.

The following instructions involve the GRASS machine. Refer to the GRASS manual for a detailed description of its features.

1.- Make sure that the pushbuttons which select the electrodes in the GRASS Pushbutton Electrode Selector Panel are released. If not, they can be released by pressing the left release lever located at the Pushbutton Electrode Selector Panel.

2.- All switches of the GRASS amplifiers (8A5) for channels 2, 3 and 4 should be set to the ALL CHANNEL CONTROL position.

3.- The filter switches in the ALL CHANNEL CONTROL panel should be set to the red positions: 1Hz, 70Hz and 60Hz OUT.

4.- Select the test to be performed. Enter 1 for ERG or 2 for VER.

5.- If ERG test is selected set the SENSITIVITY switch in the ALL CHANNEL CONTROL panel to one of the following positions 20, 15 or 10. The highest sensitivity value will give the lowest gain. A good choice is to set the sensitivity factor to 20 when contact lens electrodes are used and 10 for skin electrodes. Then set the reference voltage in the GRASS CALIBRATOR to 100 μv.

If VER test is selected set the SENSITIVITY switch in the ALL CHANNEL CONTROL panel to the position labeled 3. Then set the reference voltage in the GRASS CALIBRATOR to 20 μv.

6.- Push and release the CALIBRATOR button firmly in equal intervals of approximately 1/2 second until a sound comes. Usually it takes 10 seconds to calibrate.

After the system is calibrated the gain of the three channels will be displayed. The three gains should be positive and close to equal. If any of the gain factors is negative or very different from the others the calibration process did not work and you must try again. Make sure that the instructions are followed correctly.

After the system is calibrated the analog filter settings in the GRASS machine can be individually adjusted for each channel, to the desire values. However, for VER tests the filters should not be set to the 10 Khz position.

Select the pushbuttons in the GRASS Pushbutton Electrode Selector Panel that correspond to the jacks in which the electrodes are connected in the Electrode Connection Box. The jacks in the Electrode Connection Box contain the same labels as the pushbuttons in the GRASS electrode selector panel. Depress the pushbutton that corresponds to the positive (+) and the negative (-) electrode for each of the channels used.

The system is now ready for testing.

3.2 TEST

To perform a test select the TEST option at the main menu of the MFTS2 program. Remember that the system must be calibrated before a test can be performed. Follow the protocol required for the particular test that you are going to perform on the patient. Make sure that the electrodes are connected properly and the pushbuttons in the Pushbutton Electrode Selector Panel of the GRASS machine depressed to the correct position.

The system will ask if the patient has a record on file, that is , if the patient was tested with the MFTS2 system before. Enter "N" if the patient was tested with the MFTS2 system before or enter "Y" if this is the first visit.

It the test corresponds to the first visit, the user will have to enter some general information about the patient, such as: name, address, birth date, etc. If the patient has a record already in the system, the user will have to insert the disk with the patient's information on the disk drive and press [ENTER]. The system will then display the names of the patients that have information on the disk. Select the patient's name by using the up and down cursor keys. The information about the patient will be retrieved from the disk and displayed on the screen. If the information is correct press [ENTER]; otherwise, press [ESCAPE] and select

the patient again or insert a new disk. Any new tests performed on a patient with a record in the system will be included with the old tests.

After the general information about the patient has been gathered or retrieved from a previous record, 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] ELECTROOCULOGRAM
[U] USER DEFINED TEST
[Q] QUIT

Select the test to perform using the letter enclosed in the square brackets or the up and down cursors.

The steps required to perform a test using the MFTS2 system are summarized below:

1.- Calibrate the MFTS2 system.
2.- Select the type of test you are going to perform.
3.- Enter the patient's general information.
4.- Turn on the LKC system and initialize it for the test you are going to perform if the stimulus is controlled by the LKC.
5.- Dark adapt the patient.
6.- Dilate the patients pupils (if required by the protocol).
7.- Connect the electrodes to the patient and the system.
8.- Adjust the filter settings in the GRASS machine and select the pushbuttons in the Pushbutton Electrode Selector panel.
9.- Follow the instructions on the MFTS2 system to perform the test.

3.2.1 SINGLE FLASH RECORDING (ERG):

If Single Flash Recording (ERG) is chosen the LKC Ganzfeld unit will be used as a stimulating device. Turn on the LKC system to control the Ganzfeld unit. Select ERG recording and follow the instructions in the LKC system until you reach the ERG-display screen. At this point the LKC is ready to be used for ERG testing. The Single Flash Recording (ERG) option on the MFTS2 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 the type of protocol to be used by entering the number enclosed in the square brackets or use the up and down cursor keys.

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

The Massof protocol allows the user to run through white filter, single flash, scotopic stimulus starting at a the lowest possible intensity to the maximum intensity in steps of 2 dB. This protocol is used for the Naka-Rushton function.

A user defined protocol is also available in which the user can manually type in the desired stimulus.

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.

Steps required to perform an ERG recording on the MFTS2 system:

1.- Use F4 and F5 to select the stimulus. F5 will select the next stimulus and F4 is used to go back to a previous stimulus. The stimulus is displayed on the top of the display screen. If User Defined Protocol is selected, F4 and F5 will prompt the user for the stimulus to be used. The user must enter the stimulus intensity, filter, etc. It is important to enter the correct stimulus in order identify the data when creating a report or viewing the data in the future.

STIMULUS=> *Enter the stimulus to be used for this recording.*

STIMULUS=> **10 dB Scotopic Single Flash, White** [ENTER]

2.- Observe the patient's unstimulated ERG signal (baseline) by pressing F2. This function is useful to observe if the patient is ready for the recording. The signal should be steady before recording.

3.- Once the stimulus is selected and the patient has a steady baseline the test can be performed. To record a test press F1. A new screen will be displayed with the special function keys to adjust the stimulus in the LKC system. Remember that the Ganzfeld unit, used as a stimulus, cannot be directly controlled with

the MFTS2 program. Therefore, the user must set the Ganzfeld unit to the correct stimulus. Once the stimulus is adjusted in the LKC system press the [RCRD] key in the LKC keyboard and the ERG will be recorded.

4.- After the test is recorded it will be displayed on the ERG-display screen. If the recording looks good it can be stored on disk by pressing F3. Otherwise, the measurement can be performed again by pressing the F1 function key.

F7 can be used to change the duration of the recording. The default value is 250 msec. However, if with 250 msec the ERG does not reach steady state the recording time can be prolonged to 500 msec. Press F7 to change the recording duration, then select "a" or "b" for 250 or 500 mSec respectively.

5.- Once the ERG tests are finished you must exit the program by selecting F6. At this point the user can select another test to perform on the patient or exit to the main menu. IT IS VERY IMPORTANT TO GO BACK TO THE MAIN MENU AFTER THE TESTS ARE COMPLETED WITHOUT TAKING THE FLOPPY DISK OUT FROM THE COMPUTER. Otherwise, some vital information will not be recorded in the disk.

3.2.2 AVERAGE RECORDING ERG or VER:

This option is used to perform average recordings of ERG's or VER's. A menu with the possible stimulating devices is presented so the user can select the stimulating device that is going to be used in the recording:

[0] LKC GANZFELD
[1] NICOLET CHECKERBOARD
[2] LKC CHECKERBOARD

*** SELECT STIMULUS ***

Select the device that is going to be used to produce the stimulus by typing the number enclosed in the square brackets or using the up and down cursor keys.

If the LKC GANZFELD is going to be used as a stimulating device, the LKC system must be turned on and ERG recording selected. Follow the instructions in the LKC system until the ERG-display screen is reached. At this point the LKC system is ready to begin testing.

The MFTS2 system will ask the user for the flash intensity and frequency of the stimulus, the number of channels that are going to be used for the recording and the number of recordings to be averaged:

Enter Intensity: *Enter the flash Intensity in dB (0-48)*
Enter Frequency (Hz): *Enter the flash Frequency in Hz*
Enter Number of Channels: *Enter the Number of channels (1-2)*
Enter Number of Frames to be Averaged: *Enter the Number of Frames (1-30)*

Enter Intensity: **12** [ENTER]
Enter Frequency (Hz): **1** [ENTER]
Enter Number of Channels: **2** [ENTER]
Enter Number of Frames to be Averaged: **15** [ENTER]

Once the information above is entered the MFTS2 system will remind the user to set the LKC Ganzfeld unit to the correct stimulus. Average recording must be selected in the LKC, in order for the LKC system to create a continuous stimulus. After the LKC Ganzfeld is adjusted press [RCRD] on the LKC keyboard and the test will begin.

If the pattern monitors are going to be used as stimulating devices (LKC or NICOLET checkerboard), the following menu is presented for the user to select the stimulus size:

[0] 32x32 Reversal Checkerboard
[1] 16x16 Reversal Checkerboard
[2] 8x8 Reversal Checkerboard
[3] 4x4 Reversal Checkerboard

*** SELECT STIMULUS ***

Enter 0-3 to select the checkerboard size or use the up and down cursor keys. The user must also enter the frequency of the stimulus and the number of frames to be averaged.

If the LKC pattern monitor is used turn on the LKC system and adjust the stimulus to the appropriate value. Select average recording in the LKC for the system to produce a continuous stimulus. Turn on the Trigger Box which is connected to the LKC screen. After the stimulus is adjusted to the desired value, the trigger box on and the patient ready, press [RCRD] on the LKC keyboard.

If, on the other hand, the Nicolet pattern monitor is used, the LKC system is not required. Turn on the Nicolet monitor and adjust the stimulus to the desired size. Once the stimulus is set and the patient ready press [ENTER] on the XT computer keyboard.

After the test is performed the display screen will show the recording and the following menu will be displayed on the bottom of the screen:

F1:Filter F2:Move F3:Scale F4:Store F5:Repeat F6:Next F7:Quit

Select the desired action by presing the function keys F1-F7.

F1: is used to filter the recording. This option will ask the user for the low and high pass frequency of the filter.

F2: is used to move the recording up and down on the display screen.

F3: is used to change the scale of the vertical axis of the display.

F4: is used to store the recording on the disk.

F5: is used to repeat the last recording. The last stimulus will be used. With this option the user does not have to enter all the stimulus information.

F6: is used to go on to another stimulus.

F7: is used to exit the average recording test.

IT IS VERY IMPORTANT TO EXIT THE TEST USING THE F7:QUIT OPTION AND RETURN TO THE MAIN MENU AFTER THE TEST IS COMPLEAT OTHERWISE, SOME IMPORTANT INFORMATION WILL NOT GET RECORDED ON THE DISK.

3.3 REPORT

After data has been gathered and stored on disk the MFTS2 system can be used to create a printed report or to view the data. Insert the disk containing the patients data into drive A. Select REPORT at the MFTS2 main menu. A list with the name of the patients that have data on the disk in drive A will be displayed in the computer screen. Use the up and down cursor keys to highlight the patient for which you desire to create a report and press [ENTER] to select the patient. An example of the selection of the screen to select the patient is shown below:

FILE	NAME	TEST
1:	CASTRO, JUAN	ERG
2:	SMITH, JOHN	ERG,VER

TOTAL FILES: 2

Action keys:

Up, Down cursor keys : Highlight patient.
[ENTER] key : View information and data for highlighted patient.
[Esc] key : Exit to main menu.

After the patient is selected from the database on drive A, the general information about the patient will be displayed on the screen. The stimulus of the recordings will also be displayed. Use the up and down cursor keys to highlight the stimulus you desire to view. Press [ENTER] to view the highlighted data. Use the [Pg Dn] key to select other groups of data from the same patient, [Pg Up] key to return to a previous screen containing data from the patient or [Esc] key to select a different patient.

Example of the screen to select the stimulus to view.

PATIENT: JUAN CASTRO BIRTHRATE: 09/14/63 SEX: M
ADDRESS: TELEPHONE:

DIAGNOSIS:

COMMENTS:

FILE	TEST	DATE	STIMULUS	LABEL
CASJU-1.RB	ERG	10/13/89	36 db Scotopic Single flash White	R
CASJU-1.LB	ERG	10/13/89	36 db Scotopic Single flash White	L
CASJU-2.RB	ERG	10/13/89	20 db Scotopic Single flash White	R
CASJU-2.LB	ERG	10/13/89	20 db Scotopic Single flash White	L

Action keys:

Up, Down cursor keys : Highlight data.
[Pg Dn], [Pg Up] keys: Select other screens of data from the selected patient.
[ENTER] key : View highlighted data.
[Esc] key : Select a new patient.

After the record to view is selected, the recording will be displayed on the screen. The bottom of the screen will display the following menu:

F1:Flt F2:Mv F3:Scl F4:Prnt F5:Lst F6:Cnt F7:Nxt F8:Crs

Use function keys F1-F8 to perform the desired action.

F1: FILTER: This option is used to filter the recording displayed on the screen. Press [F1], select the waveform to be filtered and enter the filter cutoff frequencies.

[F1]: *Example of the filter function:*

Which waveform? *Enter the number of the waveform that you want to filter, out of the waveforms displayed on the screen.*
Enter Low Cutoff frequency (0-500 Hz): *Enter the low cutoff frequency of the filter. Press [ENTER]*
Enter high Cutoff frequency (0-500 Hz): *Enter the high cutoff frequency of the filter. Press [ENTER]*

F2: MOVE: This option can be used to move the waveforms displayed on the screen in the vertical direction. Press [F2], select the waveform to move, press [Esc] when finished.

[F2]: *Example of the move waveform function:*

Which one do you want to move: *Enter the number of the waveform that you wish to move.*

F3: SCALE: Use this option to change the vertical scale. Press [F3] and enter the new length in microvolts per division.

[F3]: *Example of the change vertical scale function:*

Enter new scale: *Enter new length of division in* μv.

F4: LIST: This option is used to go back to the selection of patients from the database. Data from a different patient can be selected using this option.

F5: PRINT: This option is used to create a printed report on the Dataproducts serial printer. Make sure the serial cable from the XT computer is connected to the Dataproducts printer. Then press [F5] to create a printed report.

F6: CONTINUE: This option can be used to view several records from the selected patient at the same time (up to a maximum of four). Press [F6] and select the record to view.

F7: NEXT: This option is used to view another set of records from the selected patient deleting the previous viewed records from the screen. Press [F7] and select the record to view.

F8: CURSORS: This option will display two cursors for each of the waves displayed on the screen. The top of the screen will display the coordinates of the cursor positions. The cursors should be positioned in the trough and peak positions of the waveforms. Press [F8]. Select the waveform for which you want to move the cursors by entering the number of the waveform (1,2,3 or 4). The bottom of the screen will indicate the waveform for which the cursors are active. *Cursor of waveform 1* indicates that the cursors of waveform labeled 1 are active. If you press [2] the bottom of the screen will indicate: *Cursor of waveform 2* and you can position the cursors for waveform labeled two. Enter [a] or [b] to select the trough or peak cursor. Enter [a] and use the left and right cursor keys to position the trough cursor. Enter [b] to position the peak cursor. Enter [c] to turn the cursors off. Enter [Esc] to exit the cursor positioning option.

If the cursors are turned on, the printed report will calculate and report the Peak-Trough amplitude and the implicit time (time of the peak).

[F8]: *Example of placing cursors on the waveforms:*

Cursor of waveform 1; a:Trough cursor b:Peak cursor c:cursor off

Action keys:

1,2,3 or 4: Select the waveform for which you desire to position the cursors.
a or b: Select the Trough or Peak cursor respectively.
left and right cursor keys: Move the cursor left and right respectively:
c: Delete the cursors.
[Esc]: Exit cursor positioning.

REFERENCES

1. M.A. Johnson, S. Marcus, M.J. Elman, T.J McPhee, "Neovascularization in Central Retinal Vein Occlusion: Electroretinographic Findings", Arch Ophthalmol, vol 106, March 1988.

2. Z. Li, "Visual System Modeling and System Response Analysis", Masters Thesis, New Jersey Institute of Technology, Newark, NJ 07102, 1989.

3. A.U. Meyer, et al, "Clinical Electrophysiology of the Eye: Physiological Modeling and Parameter Estimation", 1989 IEEE International Conference on Systems, Man and Cybernetics, IEEE Catalog No. 89CH2809-2, pp. 687-692, 1989.

4. K.G. Lu, "Contrast Sensitivity Measurement Via Evoked Potential", Masters Thesis, New Jersey Institute of Technology, Newark, NJ 07102, 1988.

5. Y.H. Hsiao, "A Parameter Identification System for the Human Electroretinogram", Masters Thesis, NJIT, Newark, NJ 07102, 1985.

6. R.H. Mashland, "The Functional Architecture of The Retina", Scientific American, 255, 1986.

7. F.H. Adler, "Adler's Physiology of The Eye", The CV Mosby Company, Saint Louis, MO, 1975.

8. D.A. Baylor, "Photoreceptor Signals and Vision", Investigative Ophthalmology & Visual Science, January 1987.

9. K.T. Brown, "The electroretinogram: Its components and their origin", Vision research, 8, p 633, 1968.

10. D.C. Hood, D.G. Birch, "The Relationship Between Models of Receptor Activity and the A-Wave Of The Human ERG", Clin. Vision Sci. Vol 5, No. 3, pp. 293-297, 1990.

11. R.D. Penn, W.A. Hagins, "Kinetics Of The Photocurrent Of Retinal Rods", Biophysical Journal, Vol 12, pp. 1973-1094, 1972.

12. D.A. Baylor, B.J. Nunn, J.L. Schnapf, "The Photocurrent, Noise And Spectral Sensitivity Of Rods Of The Monkey Macaca Fascicularis", J Physiol 357, pp. 575-607, 1984.

13. D.C. Hood, D.G. Birch, "The A-Wave of the Human Electroretinogram and Rod Receptor Function", Investigative Ophthalmology & Visual Science, Vol. 31, No. 10, pp. 2070-2080, 1990.

14. B.G. Fuortes, A.L. Hodgkin, "Changes in Time Scale and Sensitivity in the Ommatidia of Limulus", J. Physiol, No. 172, pp 239-263, 1964.

15. K.I. Naka, W.A. Rushton, "S-Potentials from Colour Units in the Retina of Fish", J. Physiology, 185, pag 536, 1966.

16. R.W. Massof, L. Wu, "Properties of Electroretinographic Intensity Response Functions In Retinitis Pigmentosa", Doc. Ophthalmol 57, pag 279, 1982.

17. L. Wu ,R.W. Massof ,S.J. Starr, "Computer Assisted Analysis of Clinical Electroretinographic Intensity-Response functions", Doc Ophthalmol, No 37, pp. 231-239, 1983.

18. M.A. Johnson, et al, "Pattern-Evoked Potentials and Optic Nerve Fiber Loss in Monocular Laser-Induced Glaucoma", Investigative Ophthalmology & Visual Science, Vol 30, No 5, pp 897-907, May 1989.

19. J.J. Castro, "Multi Function Test System Version 2 Manual", Electrophysiology Laboratory, Eye Institute of New Jersey, 15 South 9th Street, Newark, NJ 07107, 1990.

20. M.S. Caceci, W.P. Cacheris, "Fitting Curves to Data", BYTE Magazine, May 1984.

21. G.V. Reklaitis, A. Ravindran, K.M. Ragsdell, "Engineering Optimization, Methods and Applications", Wiley-Interscience Publication, 1983.