ERG Signal Modeling Based on the Retinal Model

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Abstract: ERG signal represents the responses of the each layer of retina for the visual stimulus and accumulated responses according to the signal processing occurring in the retina. By investigating the reaction types of each wave of the ERG, various kinds of information for the diagnosis and the signal processing mechanisms in the retina can be obtained. In this paper, the ERG signal is generated by simulating of the volume conductor field of response of each retina layer and summing of them algebraically. The retina model used for simulation is Shah's Computer Retina model which is one of the most reliable models recently developed. The generated ERG is compared with the typical ERG and shows a very close similarity. By changing the parameters of the retina model, the diagnostic investigation is performed with the variation of the ERG waveform.

1. Introduction

To investigate the retina mechanism, researches at the cellular level have been performed by physiologists. The methodology of such researches is fairly concrete but is very local and anatomical. So, it is difficult to clarify the visual information processing mechanism occurring in the overall retina. But the ERG analysis method gives non-invasive measures to examine a series of signal processing mechanism in the retina. Because the ERG wave represents a global retinal response as a consequence of superposition of volume conductor potentials caused by each retinal layer source, we can examine the signal processing mechanism of each layer by analyzing the ERG waveform. Furthermore, by stimulating a limited local part of the retina, it is possible to investigate the specific part of a retina.

A simple model was proposed to simulate the ERG by Krakau[1]. The model is a mosaic model which has two-layer retinal structure and dipole origins of a retina source origin. But, while Krakau did not consider the realistic structural influences in modeling, Doslak modelled the ERG in the global inhomogenous volume conductor which consists of several homogenous volume conductors in eye structure. The experiment results showed the similarity in comparing with the **"b wave"** measured at the projecting frontal part of a rabbit eye[2]. And in recent years, the three-dimensional extension of Doslak's ERG model, using the symmetry of the eye, has been proposed. But such existing ERG models are developed in the basis of the geometric structure and characteristics of several structural media of the eye and retina, which is signal generating source, was modeled as a simple dipole layer. So, it is not pertinent to research the complex signal processing mechanisms occurring in retina in relation to them. Hence, we propose a new ERG signal generating method by using the existing developed retina model. The ERG signal generating method using the retinal model can be applied to the assessment and verification of the retina model, and it is helpful to develop a more concise and realistic retina model by offering important information. It is then possible to examine the global retina mechanism and clinically, it can be used to detect the retinal abnormality and to diagnose retina diseases by examining the waveform of ERG signal according to the parameter variations of retina model.

In simulation, Shah's Computer Retina model, which is most similar to real biological early vision system and is verified with the data obtained by an experiment on a living creature, is used among the various retina models developed so far. While existing ERG models are made by modeling the dipole sources in volume conductor, in this paper, the ERG signal is simulated by summing the volume conductor potentials which are calculated from the responses of each layer obtained from the selected retinal model. The simulated ERG and a typical ERG are compared and clinical investigation is performed with the variation of the ERG waveform by changing the parameters of the retinal model.

2. Overview of ERG characteristics

The structure of a vertebrate retina is shown in Fig. 1. The light stimulus passes through the ganglion cell layer and arrives at the photoreceptor layer at the back of the retina. The light stimulus arriving in the photoreceptor layer is transduced to electrical signals and propagates through a horizontal cell, a bipolar cell, and an amacrine cell layer while generating the signal processing mechanisms at the each layer. A typical ERG obtained when a light stimulus is applied to a vertebrate retina is shown in Fig. 2, and **a, b, c, d wave** appears commonly in all vertebrates including human. When the light stimulates the eye, the **a** wave, which is small negative with a short latent period, appears first and then the positive large **b** wave appears. Following the **b** wave, a slow positive **c** wave emerges, which begins slowly and lasts long. Among the ERG waves, **a** wave is generated at the outer segment of the photoreceptor cell layer and **c** wave represents itself as potential differences at the pigment epithelium located after the photoreceptor cell

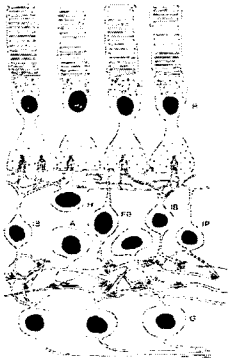

Fig. 1. Retina structure

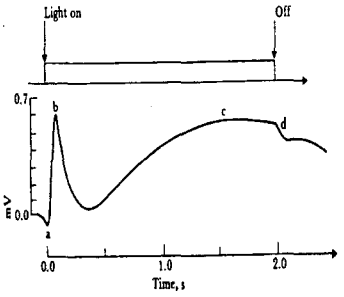

Fig. 2. Vertebrate ERG

layer. Most of the **b** wave is generated initially by variation of transmembrane of glial cell(muller cell) and bipolar cell, and part of it is the result of the influence of the ganglion cell layer. Even though the light stimulus is stopped, **off-effect d** wave appears because the transmembrane potential of the photoreceptor and bipolar cell is changed. The ERG signal reflects the electrical activity of cells in each retina layer like this, but the retina mechanism has not been explained in detail by mathematical model so far.

3. Selection of Retina model

3.1 Comparison of the existing retina models

To get a retina model that can be used to simulate ERG signal, various electrical retina models are compared and analyzed. The key point in comparing the models is the question of how much signal processing mechanism of retina is formulated in detail on the basis of transmission characteristics of anatomic physiology? , ie. whether it is formulated to model the whole layer or a part layer of the retina between photoreceptor and ganglion cell, and whether it can be used to simulate the secondary signal like a ERG. Among the models of modeling the whole visual signal processing mechanisms for each layer of the retina, we considered the models which consider the input and output transfer characteristic of retina by light stimulation of variable patterns more than by simple light stimulation. Therefore selected models are compressed into models of Gaudiano, Oguztoreli, Tzanakou, Curlander and S.Shah and the characteristics of each model are shown in the Table 1. In the model of Shah, because it contains not only the most features of existing models but also more parameters related in the ERG signal generation in consequence and results from the simulation of various retina signal processing mechanisms for several stimulus signal are compared with the real physiological data and the similarity is verified, Shah' model is adopted to basic model of ERG generating simulation.

Table 1. Comparison of retina model's physiological phenomena

Feature of model		Cu.	G.	O.	Tz.	Sa.
LTI(Linear Time-Invariant) system model			●			
Foveal modeling		●	●	●	●	●
Log-polar mapping						●
Time lag		●				●
Ⓟ	Ⓟ←Ⓗ feedback	●	●	●	●	●
	Ⓟ←Ⓑ feedback	●		●	●	●
	static local nonlinear transduction function					●
	cone coupling (gap junction)	●	●	●		●
	pigment bleaching			●		●
	cone cell RF-size adaptation with illumination			●		●
Ⓗ	Ⓗ←Ⓑ feedback	●	●	●		●
	lateral inhibition	●	●	●		●
	Ⓗ coupling (gap junction)	●	●			●
	Ⓗ RF-size adaptation with illumination					●
Ⓑ	center-surround mechanism(ON-OFF)	●	●			●
	lateral inhibition	●	●	●		
	midget and diffuse type cell					●
	Difference operator modeling					●
Ⓐ	amacrine modeling			●	●	
	lateral inhibition			●		
Ⓘ	interplexiform modeling					●
Ⓖ	X and Y type cell		●		●	
	M and P type cell					●

Ⓟ:Photoreceptor cell Ⓗ:Horizontal cell Ⓑ:Bipolar cell
Ⓐ:Amacrine cell Ⓘ:Interplexiform cell Ⓖ:Ganglion cell
Cu. : Curlander model G. : Gaudiano model O. : Oguztoreli model
Tz. : Tzanakou model Sa. : Shah model

3.2 Computer Retina model of Shah

"Computer Retina" model of Shah is modeled processing of achromatic visual information accepted by the cone cell in the primate retina. Among the mechanisms of Shah's model, equations of photoreceptor cell , horizontal cell, midget bipolar cell and diffuse bipolar cell layer which were used for generating ERG signal are like follows[4].

a. Cone cell output

$$cone\ [r,t] = v_r[r,t] * G(r;\sigma_{cone}\ [r,t])\,K(t;\tau_{cone}) - k_{hc}\ horz\ [r,t] \quad (1)$$

b.Horizontal cell output

$$horz\ [r,t] = cone\ [r,t] * G(r;\sigma_{horz}\ [r,t])\,K(t,\tau_{horz}) \quad (2)$$

c. Midget bipolar cell output

$$BP_{midget}\ [r,t] = BP_{sat}\ (k_{cb}\ cone\ [r,t] - k_{hb}\ horz\ [r,t]) * K(t,\tau_{midget}) \quad (3)$$

$$BP_{sat}\ (x) = \frac{1}{\pi}\tan^{-1}\left(\frac{x}{k_{BP_{midget}}}\right)$$

d. Diffuse bipolar cell output

$$BP_{diffuse}\ [r,t] = BP_{sat}\ (k_{cb}\ center\ [r,t] - k_{hb}\ surround\ [r,t]) * K(t;\tau_{diffuse}) \quad (4)$$

$$center\ [r,t] = \sum_{3\times3} cone\ [r,t]$$

$$surround\ [r,t] = \sum_{3\times3} horz\ [r,t-\tau_{delay}\ ] * G(r;3\sigma_{horz}\ [r,t])$$

$$BP_{sat}\ (x) = \frac{1}{\pi}\tan^{-1}\left(\frac{x}{k_{BP_{diffuse}}}\right)$$

4. ERG simulation using Shah's model

4.1 Design of simulation process

The output potentials at each layer - photoreceptor cell , horizontal cell, and (midget, diffuse) bipolar cell layer – for full-field flash are calculated. The experiment with the full-field flash was performed by Normann, Werblin,

and Schnapf et al. to investigate the temporal response characteristics of the retina and a uniform background light is flashed at constant intervals to examine the response of each cell in retina. Parameter values of the retina model produced by Shah are accepted as they are, and instead of a local light stimulus a full-field light stimulus on the local part of retina is used to simulate. The Simulation result is compared to real biological data and its similarity is verified, but notable features of Shah's model like an adaptation, change of receptive field according to light intensity etc., are excluded in simulation. The response of each layer for only limited light intensity needed to evoke an ERG is simulated. The response time delay of each layer is set to 1ms , which is unit step, and by varying the unit delay time at each layer different results are obtained. In Fig. 3, simulation flowchart is shown.

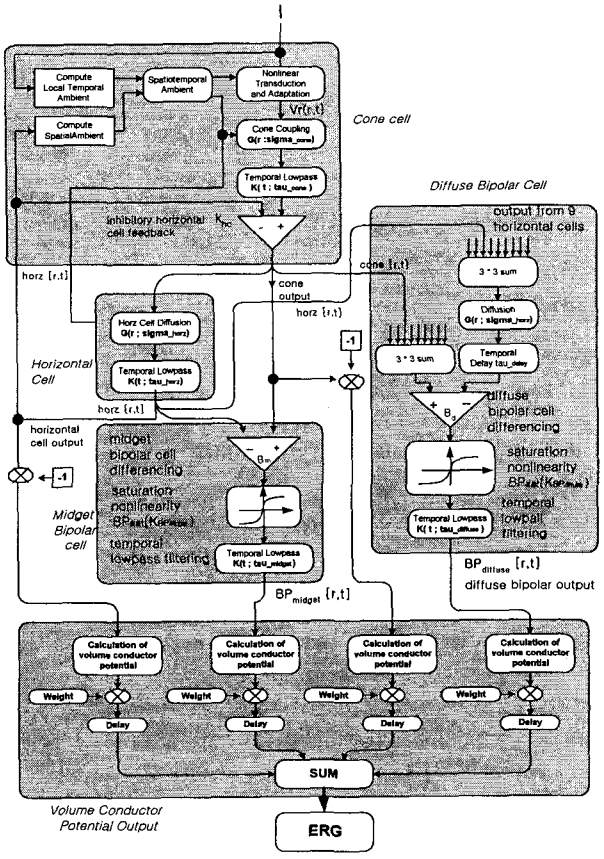

Fig. 3. ERG generating simulation flowchart

In the first block of Fig. 3, nonlinear transform process, by which light stimulus is transformed to electrical signal in the retina, cone coupling by the influences of gap junctions, integration time in cone, and inhibition function by the negative feedback signals of the horizontal cell layer are modeled. As a negative feedback inhibition signal, a pre-step output of the horizontal cell layer is applied and according to the extent of the delay time several pre-steps output of it is used. In this case only 1 pre-step output of it is used. In the second block, a diffusion process by the gap junction of horizontal cells and the influence of delay time because of it are calculated and the influence of the integration time in horizontal cell layer is also done. In the third and fourth block, the mechanisms of midget bipolar and diffuse bipolar cell are calculated and especially center-surround antagonistic phenomena, saturation nonlinearity of bipolar cell, and influence of time delay between center and surround are modeled. The time delay between center and surround is set to 3 steps(3 ms) and horizontal cell output, which is 3 step(3 ms) time-lagged compared to the output of the photoreceptor cell layer, is used as a surround input of the bipolar cell. But it is variable according to consideration of how much is the influence of the time delay at the terminal of diffuse bipolar cell. A "-1" is multiplied at each output of photoreceptor cell and horizontal cell. It is the cause of the reversion of output polarity of these cells. Because they are simulated as responding by depolarizing, but hyperpolarizing in reality. Because these outputs generated from the four blocks are considered as intracellular potentials of photoreceptors, horizontal, midget bipolar, and diffuse bipolar cell. To generate the ERG signal from them, the volume conductor potentials of each intracullular potential are calculated and then their weighting and time delay is adjusted.

4.2 Calculation of volume conductor potential

While the output potentials at each layer of the Shah's model are intracellular potentials in the retina neurons, the ERG signal is a volume conductor potential measured at the some distant ERG electrode located at cornea. Electrodes placed within such a volume conductor measure the net electric potential field(related to the current flow field), volume coductor potentials, which are produced by the summation of all action sources[3].

The equation of the volume conductor potential in volume conductor, which has action potential sources like a circular cylindrical fiber of finite extent similar to nerve fiber shown in Fig. 4 is deduced like a follows[5,6].

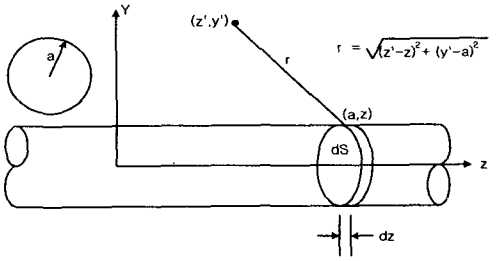

Fig. 4. Nerve fib

$$V_E(z',y') = K'K''\left[\frac{\partial V_m(z)}{\partial z}\frac{1}{r}\Big|_{S1} + \int_{-\infty}^{\infty}\frac{\partial^2 V_m(z)}{\partial z^2}\frac{1}{r}dz - \frac{\partial V_m(z)}{\partial z}\frac{1}{r}\Big|_{S2}\right]$$

Here, $$\frac{K'}{r} = \frac{K'}{\sqrt{(z'-z)^2 + \frac{\sigma_z}{\sigma_y}y'^2}} = W(z,z',y') \qquad (5)$$

$K' = \frac{A}{4\pi\sigma_y}$, A : scale factor

$K''\frac{\partial^2 V_m(z)}{\partial z^2} = I_m(z)$: transmembrane current

with $K'' = \frac{\pi a^2 \sigma_i}{4}$

σ_i : intracellular conductivity

a : fiber diameter

The formula assumes line source model, cylindrical anisotropy, and constant cross section. $V_m(z)$ is easily converted to $V_m(t)$ if we first assume that an action potential travels at a constant velocity along fiber and that temporal and spatial events can there be interchanged. The influences of fiber section of the fiber ends are not considered here because of fiber continuity in the retina. After the volume conductor potential for each region of the retina is obtained, pertinent weightings and delays are considered for each of them and we obtain the final ERG signal which is algebraically summed. In setting the weighting and delay, there seems to be several bases like a number of cells in each layer, the output magnitude of different kinds of cell, etc. But the validity of these is not verified so far. So there is no alternative but to adjust them empirically.

5. Results

The input light stimulus used in generating the ERG signal is a full-field flashing light which is mostly used in clinic, and it is simple to simulate. With the impulse-type pulse wave, which is very short and has 3 ms time constants, we simulate the ERG as a result of stimulating the local region of the retina. The simulated ERG is shown in Fig. 5, where a small negative **a** wave appears at first, followed by a rather large positive **b** wave. It is very similar to binocular ERG of a normal patient in Fig. 6. To verify whether or not the waves shown in Fig. 6 are really **a** and **b** waves in the ERG, while excluding each source of response in turn, the ERG generating simulation is performed. In Fig. 7, 8 the results of the ERG simulation, except for the influence of photoreceptor cell and bipolar cell layer, are shown in order. We can find that **a** wave disappears in Fig. 7 and **b** wave in Fig. 8. In a real clinical ERG experiment the **b** wave can be removed exclusively using chemicals,but it is impossible to remove only the **a** wave. If we remove process of photoreceptor cell layer there is no following process in retina so there are no waves shown in the ERG. Only in this paper the response of photoreceptor is excluded in the calculation of volume conductor potential after gaining the intracellular potential of each cell to know the relationship between response of photoreceptor cell layer and **a** wave in the ERG. When we exclude the influence of the horizontal cell layer, there are no spatial variations compared to Fig. 5. Therefore the **a** and **b** waves in the ERG are simulated correctly, and we verify there is no relationship between the **a**, **b** waves and the horizontal cell response.

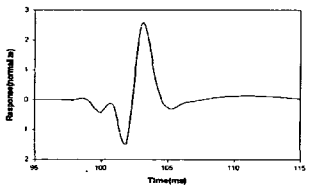

Fig. 5. Simulated ERG

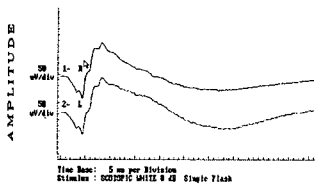

Fig. 6. ERG of normal patient

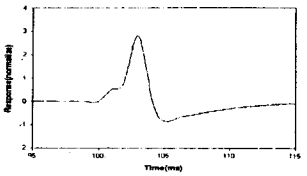

Fig. 7. ERG except for cone response

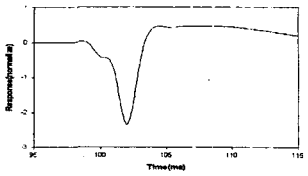

Fig. 8. ERG except for bipolar response

6. Conclusion

Through the ERG simulation it is verified that Shah's "Computer retina model" is reliable model and so by simulating the ERG signal with the retina model, the validity and assessment of the retina model used can be done. By comparing the typical ERG with the simulated ERG, it is possible to determine parameter values of retina model and as the results of it, it is helpful to develop a more precise and reliable retina model. The results are also meaningful in clinic. Besides, we can verify the theoretical background basis that it is possible to detect abnormality of special layer of retina by examining the ERG waveform using the retina model, it can be applied to diagnosis of retina diseases. The delay time between each of the components ERG waves represents important evidence of retinal abnormality in clinic and in this research effectiveness of the retina model is also assumed to be high.

In this paper, we show the only qualitative results of ERG model and it shows the variations of ERG waveform according to the mechanisms in the retina but it is not used for applications which needs quantitative results. So, with the use of retina model it is necessary to develop the ERG model reflected the influences of structures and media characteristics of retina.

Acknowledgment

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Reference

[1] C.E.T.Krakau, "On the potential field of the rabbit electroretinogram," Acta Ophthal., vol. 36, pp. 183-207, 1958.

[2] M.J.Doslak, R.P.Plonsey, and C.W.Thomas, "The effects of variations of the conducting media inhomogeneities on the electroretonogram", IEEE Bimed. Eng., vol. 27, 1980.

[3] G.S.Brindley, "The effect on the frog's electroretinogram of varying the amount of retina illuminated," J.Physiol., vol. 134, pp. 333-359, 1956

[4] S.Shah and M.D.Levin, "Visual information processing in primate cone pathways-part I:a model," IEEE Trans. Syst., Man, Cybern., vol. 26, pp.259-274, April 1996.

[5] J.Duchene and J.Y.Hogel, "A model of EMG generation," IEEE Biomed. Eng., vol. 47, pp. 192-201, Feb. 2000.

[6] R.Plonsey, "The active fiber in a volume Conductor," IEEE Biomed. Eng., vol. 21, pp. 371-381, Sep. 1974.