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Fuzzy Model of the Fly Electroretinogram

Dorina E. Creanga

Univ. "Al. I. Cuza", Faculty of Physics, Bd. Copou, 11A, 6600-Iasi, Romania,
e-mail: mdor@uaic.ro

Abstract: The fly visual system was investigated by means of electroretinographic method and various results were obtained when the illumination parameters have been changed within certain value ranges. The "black box" approach was applied in order to model the visual system on the basis of Sugeno's fuzzy algorithm. The input parameters, characterizing the light beam exciting the eye were: the intensity, the wavelength and flickering frequency while the output parameter was the ratio between the amplitudes of the main electroretinographic response components. A couple of "if-then" rules were proposed and suitable verbal values were used in order to get, for the output parameter, values concordant with the experimental evidences recorded by electrophysiological study of the visual system. Convenient manners of generalization the numerous electroretinographic data can be obtain by means of such fuzzy modeling.
Key words: fuzzy algorithm, fly electroretinogram

1. Introduction

The complex systems from nature, either physical or biological systems are often evolving on the basis of complicated laws, which are difficult to approximate in the classical mathematics. Since the 70^{th} years one opined (Zadeh, 1968) that "most realistic problems tend to be complex and many complex problems are either algorithmically insoluble or, if solvable in principle, are computationally unfeasible". Though not very popular, qualitative modeling seems quite suitable for the description of such complex systems behavior, especially where uncertainty is obviously involved. A sort of qualitative models is that based on fuzzy logic and they are actually expected to express a non-linear process better than a classical quantitative method can do. Fuzzy modeling deals with the idea to find a set of local input-output relations able to describe complex processes in unpredictable systems. One of the most simple fuzzy models is that based on a fuzzy partition of the input space. The aim of this paper is to apply such a fuzzy model for describing the visual analyzer in the invertebrates, (the fly compound eye visual pattern). Due to its anatomical and physiological peculiarities the insect visual system represents a very convenient material for the study of the visual information processing in the living world. Characterized by an intermediate grade of complexity, the organization of the dipteran visual system is somewhat parallel to that of the vertebrate visual analyzer while its set of neurons is more limited and easier to identify (Hardie, 1986). The numerical results obtained by electroretinographic investigations in the case of the fruitfly, *Drosophila melanogaster* when the illumination parameters were varying within certain ranges, suggested the

utilization of the tools offered by the fuzzy logic in order to get a suitable generalization based on verbal variables.

2. Phenomenological Background

The visual system is specialized in processing optical information carried by a photons flow or, even by a single photon, as some evidence (Hardie & Minke, 1995) indicated. Photoreceptor cells are absorbing the light stimuli at the level of their membranes, where photopigment molecules are localized. The biochemical reactions initialized as a consequence of light absorption in the photosensitive molecules, induce biophysical changes of membranes structures, mainly ion channel permeability modifications. Then, the ion concentrations and the electrical charges of membrane faces change too so that the membrane potential modifies and an action potential is generated. This electrical signal is further processed by the optical ganglionaris cells and propagates towards the central nervous system. Using intracellular microelectrodes and the patch clamp technique, the action potentials at different levels of the optical pathway can be recorded directly (Hardie et al, 1979, Hardie, 1979, Jarvilehto & Zettler, 1973). But the bioelectrogenesis phenomenon can also be detected at the extracellular level, by measurements carried out at the eye surface, since all the tissues are able to conduct electrical impulses. The electroretinogram (ERG), is the result of extra-corneal electric activity projection. It contains information from both photoreceptor and ganglion cells. The study of dipteran visual system by means of ERG was carried out by many physiologists (Meffert & Smola, 1976, Hardie, 1995, Skingsley et al, 1995) since these invertebrate color vision is considered an interesting alternative to the vertebrate one. More, the electro-physiological investigations are somewhat easier and more convenient for long *in vivo* recordings,

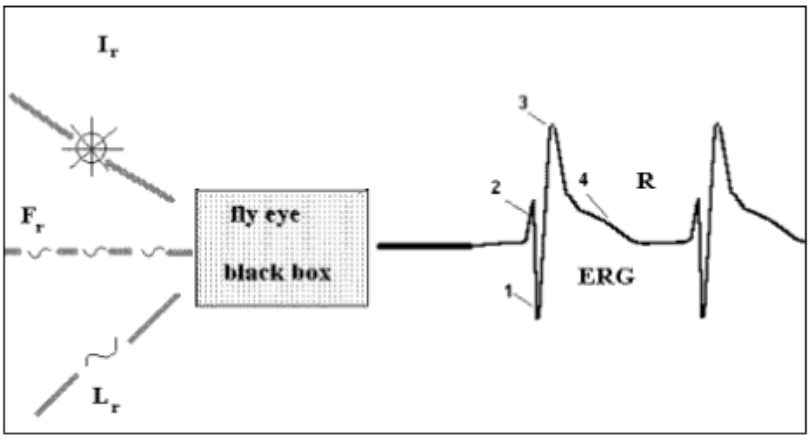

Fig. 1 – The ERG (electroretinographic) response of the fly eye stimulate by the flickering light beam in the "black box" approach. 1- the pre-potential, 2 – the hyperpolarization component named lamina-on-transient, 3 – the receptor potential (the main depolarisation component), 4 – the post-potential

being non-invasive. In the contrast to the vertebrate electroretinogram where the main component is a hyperpolarization of the photoreceptor cells, in the fly electroretinogram the principal amplitude is given by the depolarization of the two types of photoreceptor cells: six peripheral cells, noted usually R1-6 and two central, overlapped cells, noted R7-8. The first type of light receptors is specialized in small wavelength radiation reception while the second type in high wavelengths light reception. The peripheral receptors, connected to the first optical ganglionaris-lamina, represent a high sensitivity optical pattern, specialized in low intensity light reception. The central receptors, by-passing lamina and making synapse directly to the second order ganglionaris-medulla, represent rather a high acuity visual pattern, specialized in high intensity light processing (Stavenga & Hardie, 1989). So, for different combinations of light intensity and spectral composition, the contribution of a certain type of photoreceptors to the ERG depolarization component (named the receptor potential), is different, i.e. for different light intensities and spectral compositions, the receptor potential may have different values. In the ERG recording (Fig.1) this component represents a large duration and a high amplitude maximum of the electrical response obtained between the measuring electrode, placed onto the compound eye corneal and the reference electrode, slightly inserted in the fly thorax.

In the electroretinogram, the receptor potential is following a short duration hyperpolarization component (appearing as a minimum value of the recorded potential) named lamina-on-transient because it is assigned mainly to the lamina ganglionaris cells. There, the processing of the signal delivered by the peripheral photoreceptors yields a hyperpolarization of the L1 and L2 large monopolar cells membranes, as the intracellular recordings revealed (Stavenga & Hardie, 1989). Analogous to the vertebrates electroretinogram interpretation proposed by Granit (Gremy & Perrin, 1976), the ERG components in the dipteran are supposed to be not necessarily the result of consecutive bioelectrogenesis phenomena, but of some quasi-simultaneous membrane electrical potential changes, overlapping to give the extra-corneal electric activity recorded on the eye surface. For different values of the light intensity and spectral composition the lamina-on-transient component can also appear as having different amplitude values. Suitable electrical devices were designed to obtain fly electroretinograms both for unique light stimuli excitation (for instance a rectangular stimulus having one second duration) and for flashing light excitation (stimuli delivered with a frequency of 10-100 Hz, for instance). In the last case, the rapid lamina-on-transient component is easier to record since it appears as having a higher stability. As the resting potential is influenced by the variation of the illumination parameters, it is not recommended to work with the absolute values of the ERG components but with their ratio, which is obviously non-dimensional. Generally it was noticed that the receptor potential amplitude is larger than that of the lamina-on-transient ERG component, especially when the light intensity is not very high. Also, the receptor potential is increasing relatively to the lamina-on-transient when the light intensity increases, especially in the range of high intensity values and for large wavelengths. Speck and his collaborators

(Speck et al, 1984) showed that the ratio between the ERG main component amplitudes is slightly dependent on the light intensity and spectral composition. It was revealed (Cosens & Spatz, 1978) the influence of the light flashing frequency on the ERG amplitudes: to the increase of the light flickering frequency, the receptor potential decreases more rapidly than the hyperpolarization ERG component. In other terms, the fusion frequency for the receptor potential is lower than for the lamina-on-transient component.

Generally it was noticed that:

-(i) The receptor potential amplitude is lower than that of the lamina-on-transient ERG component, except the light intensity is not very high and flickering frequency is not very low;

-(ii) The receptor potential is increased relatively to the lamina-on-transient when the light intensity increases, especially in the range of high intensity values and for large wavelengths;

-(iii) The ratio between the ERG main component amplitudes (receptor potential/lamina-on-transient) is slightly dependent on the light intensity for both large and small wavelengths, in a linear manner (small positive slope);

-(iv) To the increase of the flickering frequency, the receptor potential is decreasing more rapidly than the hyperpolarization ERG component, for large and small wavelengths; in other terms, the fusion frequency for the receptor potential is lower than for the lamina-on-transient component;

-(v) Lamina-on-transient is diminishing slower than the receptor potential when the flickering frequency is enhancing, both for large and small wavelengths, following a curve which can be approximated with a straight line mainly for medium light intensity and moderate flickering frequency.

Our experimental recordings, carried out on *Drosophila melanogaster* (wild type, red eyed and white-eyed mutants) revealed also co-operative effects of the light intensity and spectral composition as well as the existence of the critical frequency range corresponding to a differentiated lamina-on-transient component behavior. As previously noticed in the literature no differences between male and female fly ERG appeared but individual photoreception peculiarities can be, sometimes, quite remarkable.

In the present paper a generalization of such experimental evidences, reproduced also within the framework of the experimental studies carried out by the author of this article, is intended.

3. The "Three Inputs-One Output" Fuzzy Model

Fuzzy modeling seems to be the most important issue in the fuzzy theory (Sugeno & Yasukawa, 1973). In order to construct a fuzzy model of the type “three inputs-one output”, first three variables are chosen to form the input vector (usually some parameters that can be measured or estimated within suitable value ranges). Then a system parameter is identified so that it represents the system answer to the

variations of the input vector components; it is the variable of the consequence -the output (Sugeno & Tanaka, 1991, Sugeno & Kang, 1988, Takagi & Sugeno, 1984). The input variables or the variables of the premise are usually noted $x_1, x_2, ..., x_k$ (in our case k=3). They are crisp variables as well as the output variable, $\boldsymbol{y}$ (the variable of the consequence).

The fuzzy model consists of a number of "if-then" rules or fuzzy implications, having for example, the next format:

$$\text{R: If } x_1 \textit{ is } A_1 \text{ and } \ldots \; x_k \textit{ is } A_k \text{ then } y = f(x_1,...,x_k)$$

The membership functions $A_1,...,A_k$ represent a fuzzy set, a fuzzy sub-space in which the implication $\boldsymbol{R}$ can be applied for reasoning. Adopting a linear function "*f*", in the consequence, then the implication can be written as:

$$\text{R: If } x_1 \textit{ is } A_1 \text{ and} \ldots x_k \textit{ is } A_k \text{ then } y = p_1 x_1 + ... + p_k x_k$$

Having *n* implications, $\boldsymbol{R_i}$ *(i=1, ..., n),* we have also *n* forms for *y* (y^i):

$$y^i = p_1{}^i x_1{}^i + ... + p_k{}^i x_k{}^i$$

and the final output y^* is given as an weighted average:

$$y^* = \frac{\sum_i w^i y^i}{\sum_i w^i}$$

the weights being concordant with the AND logic. This is, w^i is the truth value of the proposition $y=y^i$:

$$w^i = \left| y = y^i \right| = \left| (x_1{}^i \, is A_1{}^i \, and ... x_k{}^i \, is A_k{}^i) \right| \wedge \left| R^i \right| = (A_1{}^i (x_1{}^i) \wedge ... (A_k{}^i (x_k{}^i)) \wedge \left| R^i \right|$$

and $\wedge$ stands for the minimum operation. For simplicity, usually one can assume

$$\left| R_i \right| = 1$$

Verbal values are assigned to the membership functions, such as "small", "big", small$_1$", "small$_2$", etc. meaning that linguistic conditions are formulated and this way a generalization of numerous numerical results is easier. In the case of the model "three output-one input", known as Sugeno's fuzzy algorithm (Sugeno & Tanaka, 1991), we are in the framework of a "black box" approach, for a certain system what is describable by three premise variables and a single consequence variable. So, using observation based on knowledge and/or experience as well as numerical data, the three premise variables x_1, x_2, x_3 can be identified together with the consequence variable *y*. Then, several "if-then" rules can be formulated by means of convenient verbal values $A_1{}^i,...,A_k{}^i$ *(i=1,...,n; n*–the number of fuzzy

implications or rules) and adequate set of consequence parameters $p_1^{\,i},...,p_k^{\,i}$ is established. For example we can state two rules:

$\boldsymbol{R^1}$: If $x_1^{\,1}$ is medium and $x_2^{\,1}$ is medium and $x_3^{\,1}$ is superior

$$\text{then } y^1 = 0.2x_1^{\,1} + 0.3x_2^{\,1} + 0.1x_3^{\,1}$$

$\boldsymbol{R^2}$: If $x_1^{\,2}$ is inferior and $x_2^{\,2}$ is inferior and $x_3^{\,2}$ is medium

$$\text{then: } y^2 = 0.2x_1^{\,2} + 0.3x_2^{\,2} + x_3^{\,2}$$

where, for instance, inferior (I) means 0.25, medium (M) means 0.5 and superior (S) means 0.75. Is obvious that we have the correspondence:

$A_1^{\,1} \rightarrow$ medium, $A_1^{\,2} \rightarrow$ medium, $A_1^{\,3} \rightarrow$ superior, $A_2^{\,1} \rightarrow$ inferior, $A_2^{\,3} \rightarrow$ medium

$$\text{and } p_1^1 \Rightarrow 0.2;\ p_1^2 \Rightarrow 0.3;\ p_1^3 \Rightarrow 0.1;\ p_2^1 \Rightarrow 0.1;\ p_2^2 \Rightarrow 0.1;\ p_2^3 \Rightarrow 1$$

The output is:

$$y^* = \frac{\sum_i y^i w^i}{\sum_i w^i} = \frac{y^1 w^1 + y^2 w^2}{w^1 + w^2}$$

$$\text{and } w^1 = A_1^{\,1}(x_1^{\,1}) \wedge A_1^{\,2}(x_1^{\,2}) \wedge A_1^{\,3}(x_1^{\,3}) = 0.50$$

$$w^2 = A_2^{\,1}(x_2^{\,1}) \wedge A_2^{\,2}(x_2^{\,2}) \wedge A_2^{\,3}(x_2^{\,3}) = 0.250$$

$$y^1 = 0.2.0.5 + 0.3.0.5 + 0.1.0.75 = 0.125$$

$$y^2 = 0.1.0.25 + 0.1.0.25 + 0.75 = 1.25$$

$$y^* = \frac{0.50.0.125 + 0.25.1.25}{0.50 + 0.25} = 0.25$$

When a fuzzy algorithm is supposed to fit the observed data, then, generally, there are several ways to define the membership functions and the consequence parameters. If the aim is to optimize the fuzzy model in order to get the better approximation of the observed data, then a selection criterion is necessary (Takagi & Sugeno, 1984 have suggested the minimization of the mean square error). In our paper the aim is to get a generalization of the various numerical data obtained in the case of some electrophysiological measurements where many variations can occur when passing from an individual to another. On the other hand, similar

values for the ERG parameters possibly appear when the illumination parameters take values in different ranges.

4. Electroretinographic Data Approach by Fuzzy Modeling

In our view the fruitfly visual system is consistent with the "black box" that we investigated experimentally by recording the ERG for different ranges of the next three illumination variables (the input variables):

-the light beam intensity ***(x_1);***

-the light beam spectral composition, i.e. the wavelength ***(x_2);***

-the frequency of the light stimuli application (the flashing frequency ***(x_3)).***

We have chosen as the "black box" output parameter the half of the ratio between the receptor potential amplitude and the amplitude of the component lamina-on-transient, measured from the resting potential line, this is:

R = (1/2)(receptor potential amplitude/lamina-on-transient amplitude)

The crisp variables used by us were associated with reference values:

-the light beam intensity $\boldsymbol{I_m}=10^{14}$ photons/cm^{2}s (the intensity able to evoke the eye maximal response in the case of such fly species);

-the light wavelength, $\boldsymbol{L_m}$=700 nm (the maximal value of the fly eye spectral sensitivity within the visible range);

-the maximal frequency of the light stimuli application, $\boldsymbol{F_m}$=100Hz (where the ERG structure is no longer the standard one because the receptor potential is no more distinguishable). The reference values definitions are also governed by a certain degree of uncertainty, due to the individual variations within a certain fly population, even raised in controlled standardized conditions. So, the three-dimensional input vector is ($\boldsymbol{I_r}$, $\boldsymbol{L_r}$, $\boldsymbol{F_r}$) where:

$$I_r = \frac{I}{I_m}, L_r = \frac{L}{L_m}, F_r = \frac{F}{F_m}$$

The verbal values assigned to the input parameters are given below:

inferior → *I* → 0; medium-inferior → *MI* → 0.25; medium → *M* → 0.5; medium-superior → *MS* → 0.75; superior → *S* → 1.

Analyzing the numerical cases obtained in the ERG measurements we proposed a simplified output calculation on the basis of a conditioned weighted sum (Albino et al, 1995):

C1: If ***L*** is relatively small (blue excitation light), i.e. $\boldsymbol{L_r}$ is medium

$$\text{then } R = 0.3I_r + 0.5L_r - 0.2F_r$$

C2: If ***L*** is large (orange light) i.e. $\boldsymbol{L_r}$ is medium-superior

$$\text{then } R = 0.4I_r + 0.4L_r - 0.2F_r$$

This way, in the first place it is underlined the importance of the light wavelength for a possible raw classification of the experimental results. In the second place it is emphasized the fact that the dependence of $\boldsymbol{R}$ upon $\boldsymbol{I_r}$ and $\boldsymbol{L_r}$ is opposite to the $\boldsymbol{R}$ dependence upon $\boldsymbol{F_r}$**.** In the next figures (Figs. 2-3) are given the $\boldsymbol{R}$ values for medium $\boldsymbol{L_r}$ and respectively medium-superior $\boldsymbol{L_r}$.

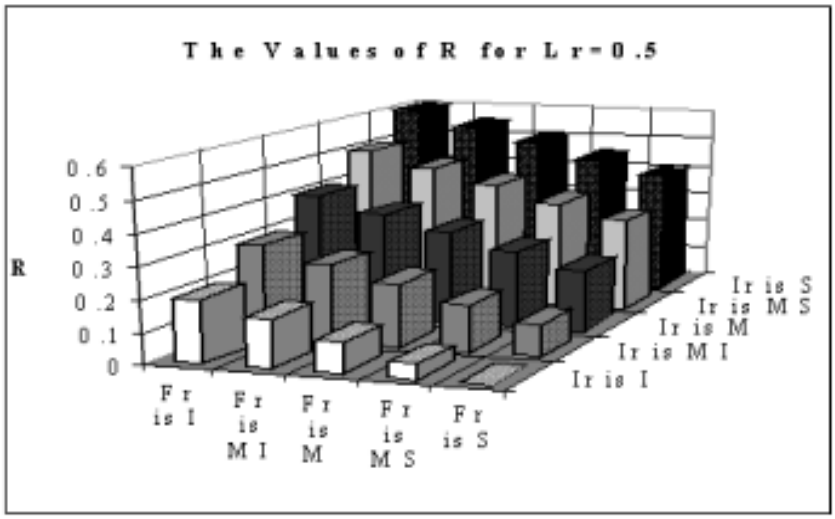

Fig. 2 – The values of the consequence variable, R, for blue excitation light

The zero values must be understand in the sense of the inferior limit towards the input parameters tend, in the mathematical view. From the physical viewpoint $I_r=0$ means a small number of exciting photons while $F_r=0$ means a very low flickering frequency.

The intracellular recordings showed that a membrane response could be obtained even for single photon action: there are the so-called bumps. It is obvious that R has generally values smaller than 0.5, in agreement with the experimental data, i.e. the receptor potential amplitude is smaller than the amplitude of the lamina-on-transient. Some exceptions are noticed for high intensity orange light at low flickering frequencies and even for blue light for high intensity and low flickering frequency. In such cases the importance of the light intensity is the dominant. It is also visible that for medium L_r values (blue light) and extreme values of I_r the *R-values* are, all the time, smaller than for medium superior L_r values (orange light).

The validity of the fuzzy model application is proved by the decreasing of the *R-values* for the increasing of the F_r values (for every I_r value) and by the increasing of *R*-values for the increasing of I_r values (for every F_r value). For all the I_r and F_r values R is smaller for medium L_r than for medium superior L_r**.**

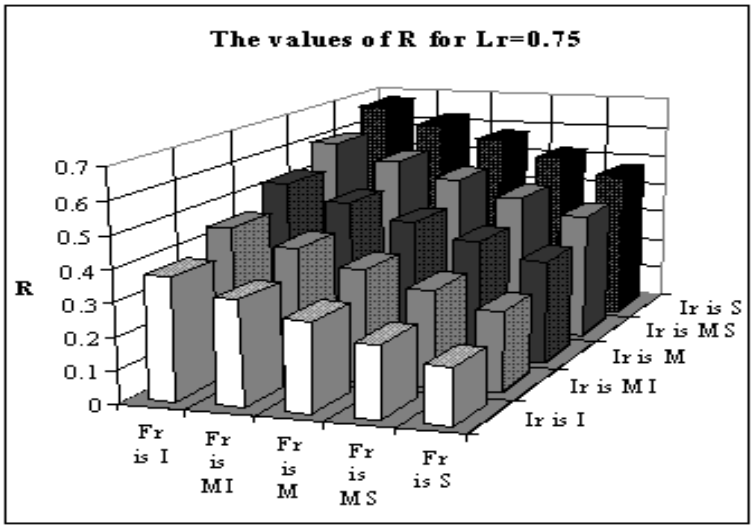

Fig. 3 – The values of the consequence variable, for orange excitation light

5. Conclusions

Working with the "three input, one output" fuzzy model, the electroretinographic experimental data for the *Drosophila melanogaster* fly have been generalized in a suitable manner. As the proposed "if-then" rules are taking into account the two important wavelength ranges where the two types of photoreceptor cells have different spectral sensitivities, the graphic comparison of the output ERG parameter values obtained by the fuzzy modeling revealed a good concordance with the literature data. This means, the ERG parameter, *R*, decreases when the flickering frequency is enhanced and increases when the light intensity is enhanced but, in the same time the values corresponding to small wavelength light excitation are different from those corresponding to high wavelength light (at the same intensity and flickering frequency). The limits of the model application are related mainly to some special value ranges of the input parameters. It needs to be further developed for non-linear approaches.

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