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Computational Estimation of Threshold Currents for Electrophosphenes

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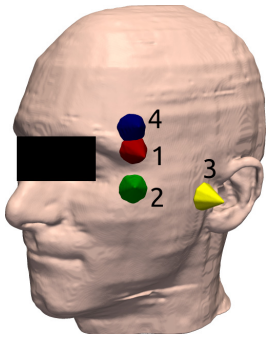
***Abstract*—Electrophosphenes are subjective sensations of light that are generated through electric stimulation at frequencies lower than 100 Hz. During electrical stimulation, an electric current flows through the human body between stimulation electrodes. Part of the current passes through the eye, where the current can activate or alter the function of retina, which results in the perception of electrophosphenes. Human exposure limits in international guidelines for the electric field in the central nervous system are set with the objective of preventing the generation of phosphenes. However, while it is possible to measure thresholds for phosphenes in terms of the applied electrode current, there is no straightforward way for determining the local threshold current density on the retina from measured data. In this study, current distributions induced by electrode setups of a previous experimental study are analyzed computationally in four anatomical human models. Computed results together with experimental data are used for determining local electrophosphene thresholds. At the frequency of highest sensitivity, 20 Hz, the threshold in terms of the maximum radial current density on the retina appears not to be less than 10–30 mA m^{-1}, where the variation is mainly caused by uncertainty due to electrode positioning. The threshold in terms of the total current that flows through the eyeball is 2–4 μA. These thresholds are comparable with those previously determined for magnetically induced phosphenes.**

I. Introduction

Phosphenes are subjective visual sensations that are generated within the eye and brain rather than by light from outside entering the eye [1]. Phosphenes can be elicited by various forms of mechanical, electric, or magnetic stimulation of the retina and brain. Among the effects of low-frequency electromagnetic fields on humans, phosphenes are thought to have the lowest stimulation threshold [2], [3]. Therefore, human exposure limits in international guidelines and standards for low frequency electromagnetic fields [4], [5] have been set with the objective of preventing the generation of phosphenes.

Knowledge on thresholds for eliciting phosphenes is largely based on experimental data on human volunteers. It is known, for example, that the thresholds are frequency dependent; the lowest threshold occurs at around 20 Hz, and it increases at lower and higher frequencies. However, experiments do not provide information about the distribution of the current around and within the retina, where the phosphenes are thought to originate from. This is because the human body is electrically heterogeneous, so the current inside the body follows a complex path that can only be determined using computational methods. Information on local retinal phosphene thresholds would allow comparison between different experimental studies and strengthening the scientific basis of exposure guidelines and standards.



Electrode placement	Electrodes	
	first	second
A(left)	1(left)	3(right)
A(right)	1(right)	3(left)
B(left)	1(left)	2(right)
B(right)	1(right)	2(left)
C	4(left)	4(right)

Fig. 1. Locations of the electrodes for the left side of the DUKE model and a list of the five electrode placements studied. Electrodes 1 and 4 are located approximately 1 cm and 3 cm superior to the outer edge of the eye, respectively, electrode 2 is located 1 cm inferior to the outer edge of the eye, and electrode 3 is located anterior to the ear. Electrode placements A(left), B(left), and C were studied experimentally by Adrian [6].

The goal of this study is to investigate the thresholds for phosphenes in terms of local retinal currents. For that purpose, we replicate computationally the experimental setup of the study of Adrian [6], who generated phosphenes in human subjects through stimulation by low-frequency currents, and investigated the threshold current required for eliciting phosphenes as a function of frequency. The estimated thresholds are compared with our previous study [7], in which we did a similar analysis for magnetically induced phosphenes using experimental data from the study of Lövsund *et al* [8].

II. Models and Methods

A. Experimental Setup and its Numerical Model

Adrian [6] generated phosphenes using stimulation electrodes that were placed near the eyes, and electric currents with varying frequency and intensity were input into the electrodes. He studied a total of three electrode placements, which are described in Fig. 1. The exact electrode positions in Fig. 1 have been selected by subjective judgment of the authors based on brief descriptions given in Adrian's work [6]. The effects of variations in electrode positioning are studied in Section III-B. Most experiments in [6] were performed with the standard electrode placement A(left), and some results

were also shown for placements B(left) and C. In addition to the three placements investigated by Adrian, in this study, we also study 'contralateral' electrode placements A(right) and B(right), which should ideally result in the same, but mirrored, current distributions as placements A(left) and B(left).

Adrian [6] used circular silver electrodes with a radius of 1.75 cm that were attached to the head using conductive cream. In this work, the electrodes are cone-shaped and are assumed to consist entirely of conductive cream. The base of the cone is a circle with a diameter of 2 cm, and the height of the cone is 2 cm. A pointwise current source or sink is placed at the tip of the cone. As the type of the cream was not described in [6], the conductivity of the electrodes has been chosen as 0.3 S m^{-1}, which is the conductivity of a 0.03 M saline solution [9].

B. Numerical Anatomical Models

Four anatomical models of the head are used. They are DUKE and ELLA [10] and TARO and HANAKO [11]. The models are based on MR images of healthy volunteers, and they consist of 3D heterogeneous representations of realistic individual anatomies. The eyes of the models have been modified to include sclera and retina, as described in [7]. All tissue conductivities are assumed to be linear, isotropic, and nondispersive in the studied frequency range (< 100 Hz). The conductivities of lens, cornea, sclera and vitreous humour have been obtained from [12]. The retina is assumed to have a conductivity of 0.7 S m^{-1} (blood), which falls between the conductivities of sclera (0.56 S m^{-1}) and vitreous humour (1.55 S m^{-1}). The conductivity of the cerebrospinal fluid (CSF) is assumed to be 1.8 S m^{-1} [13]. Other tissue conductivities are based on the data of Gabriel [14]. It should be noted that the CSF and vitreous humour have a significantly higher conductivity than other tissues such as fat (0.04 S m^{-1}), muscle (0.35 S m^{-1}), or brain tissues (0.06–0.10 S m^{-1}).

C. Computational Method

The computational method is identical to that used in our previous study [7]. Because the frequencies are low, the displacement current and induced magnetic field can be ignored. Therefore, the electric field can be determined by solving an elliptic partial-difference equation for the electric scalar potential. The equation is solved using an in-house code that utilizes the finite-element method, as described in [15]. The finite-element method uses piecewise linear basis functions in a cubical mesh with a uniform side length of 0.5 mm. The number of unknowns is about 40 million, depending on the size of the anatomical model.

D. Analysis of the Currents

Electrical stimulation experiments suggest that the retina is most sensitive to currents in the radial direction [16]. Therefore, in the following, computed results are presented in terms of the radial component of the current density on the retina and the total current that flows through the eyeball.

The radial component of the current density on the retina is approximated by treating each eye as a sphere, and transforming the Cartesian field to spherical coordinates with the origin at the centre of the eye, after which the maximum radial current density on the retina is determined. The total current that flows through the eyeballs is approximated by integrating the radial component of the current density over the surface of the eye.

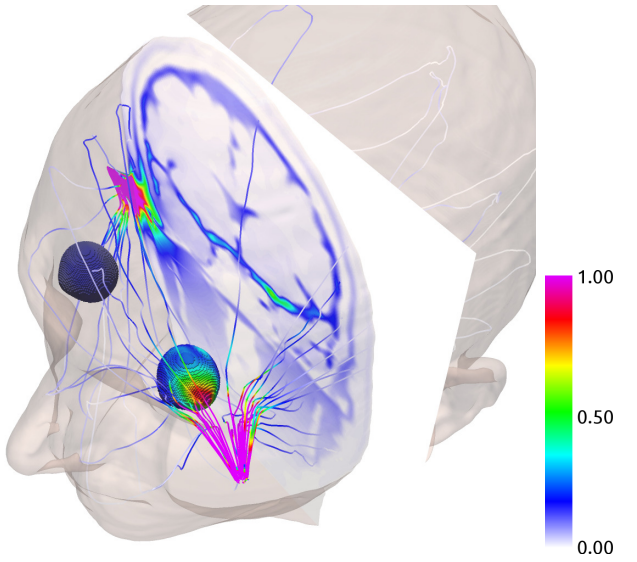


Fig. 2. Direction and magnitude of the current density for the DUKE model for electrode placement A(left), i.e., the current flows from the left eye to the right ear. The current density has been normalized by the maximum current density on the retina.

TABLE I
MAXIMUM RADIAL CURRENT DENSITY ON THE RETINA AND TOTAL CURRENT FLOWING THROUGH THE EYEBALL (MEAN ± S.D.). THE TOTAL CURRENT FED INTO THE ELECTRODES IS 10 μA. IPSILATERAL EYE IS THE ONE THAT IS ADJACENT TO ELECTRODE 1.

Electrode placement	Ipsilateral eye		Contralateral eye	
	Max. J_r (mA m^{-1})	Eye I (μA)	Max. J_r (mA m^{-1})	Eye I (μA)
A	19.1 ± 2.5	2.6 ± 0.3	1.8 ± 0.4	0.5 ± 0.1
B	19.3 ± 2.5	2.7 ± 0.3	22.9 ± 7.4	3.0 ± 0.6
C	7.3 ± 2.0	1.4 ± 0.2	-	-

III. RESULTS

In the following, all numerical values are r.m.s. values. Mean values and standard deviations have been calculated over a total of eight cases (four anatomical models and left and right electrode placements).

A. Calculated Currents

Fig. 2 shows the computed current density in the DUKE model for electrode placement A(left). It can be seen that the current density on the surface eyeball is highest on the side of the eyeball that is closest to the stimulating electrode.

Fig. 3 shows the distribution of the current density on each retina of the DUKE model for three electrode placements. The highest current density is found at the extreme periphery of the retina in the direction closest to the stimulating electrode. The direction of the current density is radial in points where the current density is the strongest.

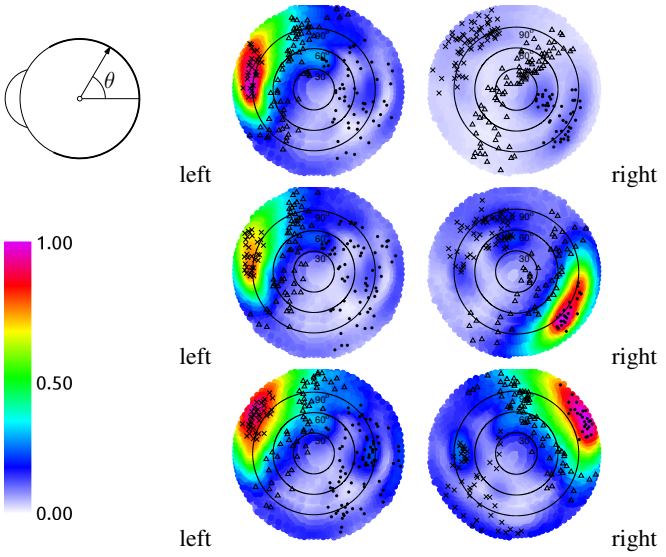


Fig. 3. Magnitude of the retinal current density on the left and right retinas of the DUKE model. From top to bottom: electrode placements A(left), B(left) and C. The linear rainbow scale has been normalized by the maximum retinal current density for each electrode placement. The markers show which component of the current is dominant (at least two times greater than the other). The placement of the markers has been chosen randomly such that the markers are distributed more densely in regions with a higher magnitude of current density. Crosses and dots = in and out directions of the radial component, triangles = tangential component. The model is facing in the same direction as the reader.

The maximum current densities and total eye currents are listed in Table I. In the table, the total current fed into the electrodes is 10 μA, which is the lowest measured phosphene threshold at 18–22 Hz, when taking into account transient phenomena caused by eye movement and blinking [6]. It seems that electrode placements A and B result in almost equal currents around the eyes, while electrode placement C gives a significantly lower current.

B. Effects of Electrode Location

Table II shows how the computed currents are affected by small changes in electrode positioning for electrode placement A. It appears that shifting the location of the electrodes by 1 cm can alter the maximum retinal current density by up to $\pm$50%. Variations in the total eye current are somewhat smaller, about $\pm$30%. However, current density on the contralateral retina stays constant regardless of small changes in electrode positioning. For reproducibility of experimental setups, it would therefore be advantageous that the electrodes be located as far away from the eyes as possible.

IV. Discussion

Using experimental data for phosphene thresholds in terms of the applied electrode current from [6] for all three electrode placements together with the results in Table I, one can estimate the phosphene thresholds in terms of the maximum retinal current density and total eye current. These estimated thresholds are shown Figs. 4 and 5, respectively. The figures do not take into account measurement uncertainty or inter-subject variation [6]. For comparison, the figures also show

TABLE II
Current density (mean $\pm$ S.D.) for electrode placement A when the position of electrode 1 is displaced in the vertical direction. The total current fed into the electrodes is 10 μA. Ipsilateral eye is the one that is adjacent to electrode 1.

	Ipsilateral eye		Contralateral eye	
Height of electrode 1	Max. J_r (mA m^{-1})	Eye I (μA)	Max. J_r (mA m^{-1})	Eye I (μA)
$-$1.0 cm	28.1 $\pm$ 3.8	3.4 $\pm$ 0.6	1.8 $\pm$ 0.4	0.5 $\pm$ 0.1
$-$0.5 cm	25.0 $\pm$ 2.1	3.1 $\pm$ 0.5	1.8 $\pm$ 0.4	0.5 $\pm$ 0.1
0.0 cm	19.1 $\pm$ 2.5	2.6 $\pm$ 0.3	1.8 $\pm$ 0.4	0.5 $\pm$ 0.1
+0.5 cm	14.2 $\pm$ 1.9	2.2 $\pm$ 0.2	1.8 $\pm$ 0.4	0.5 $\pm$ 0.1
+1.0 cm	10.3 $\pm$ 2.1	1.8 $\pm$ 0.2	1.8 $\pm$ 0.4	0.5 $\pm$ 0.1

previously estimated thresholds for magnetophosphenes from [7] for two background luminance levels. In [7], the thresholds were determining using similar methods as in this paper but from experimental data on magnetophosphenes [8].

From Fig. 4, the threshold current density appears to be of the same order of magnitude as with magnetophosphenes at around 20 Hz. However, there is a wide range of uncertainty caused by electrode positioning. In Fig. 5, which shows the threshold in terms of the total eye current, the variation range is narrower due to smaller impact of electrode positioning, and the threshold currents agree with those for magnetophosphenes around 20 Hz. Unlike in Fig. 4, all three electrode placements provide almost similar thresholds. In both figures, the threshold for electrophosphenes increases more rapidly than that for magnetophosphenes at frequencies higher and lower than 20 Hz, which could partly be explained by differences in experimental setups in [6] and [8]. However, even in identical exposure conditions, as studied by Lövsund *et al* [17], the electrophosphene threshold rises more rapidly than the magnetophosphene threshold at frequencies lower and higher than 20–30 Hz.

In the study of Adrian [6], the measurements were performed in a 'moderately lit room', and the eyes were closed for measurements to avoid blinking. It is mentioned that the lowest threshold electrode current at 20 Hz decreases to about 10 μA if blinking and eye movement is allowed. From Table II, the corresponding local thresholds are 10–30 mA m^{-1} and 2–4 μA. Assuming that blinking was allowed in [8], comparable thresholds at 20 Hz for magnetophosphenes would be about 15 mA m^{-1} and 4 μA in a background luminance of 130 cd m^{-2} [7].

During the experiments of Adrian [6], phosphenes were observed in the periphery of the visual field (but which periphery is not mentioned), and there was an absence of perceived phosphenes at the centre of the visual field. This agrees with the locations of peak current densities studied herein; the peak current density was found at the periphery of the retina, and the magnitude of the current density was low at the posterior pole, i.e., at the centre of the visual field. For magnetophosphenes (Fig. 6), the distribution of the current on the retinas was spread more evenly over the periphery of the retina than for electrophosphenes. It can be hypothesized whether different retinal current distributions

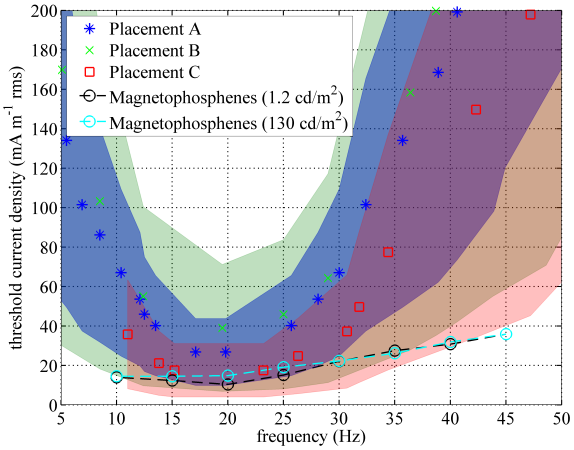


Fig. 4. Estimated phosphene threshold in terms of the maximum retinal current density. Areas shaded with blue, green, and red show the variation ranges due to standard deviation and an additional ±50% variation from electrode positioning for electrode placements A, B, and C, respectively. The curves for magnetophosphenes are based on estimated thresholds from [7].

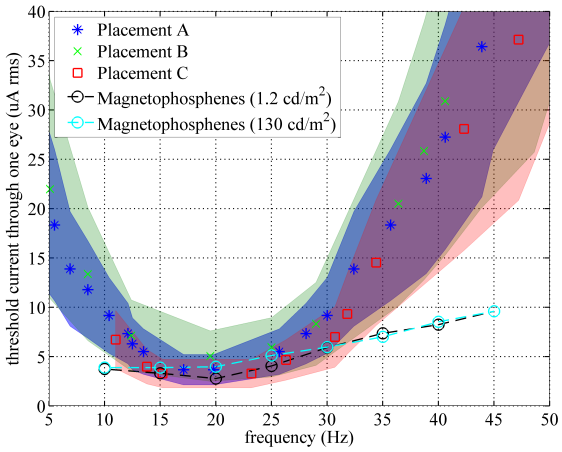


Fig. 5. Estimated phosphene threshold in terms of the total current flowing through one eye. Notation is similar to Fig. 4, but the variation from electrode positioning is ±30%.

could explain some of the differences in frequency response and reported differences in the 'nature' and position of electro- and magnetophosphenes [17].

V. Conclusions

Computational methods and anatomically realistic models were used together with previous experimental data to analyze retinal threshold currents for inducing electrophosphenes. It was found that threshold currents for electrically induced phosphenes are comparable to those for magnetically induced phosphenes at the frequency of highest sensitivity (20 Hz). However, the frequency responses and distributions of the current density on the retina were different for the two types of phosphenes. It was also found that if the stimulation electrodes

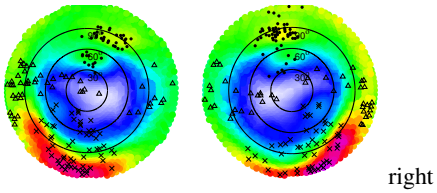


Fig. 6. Current density on the retinas of the DUKE model for the experimental setup for eliciting magnetophosphenes (from [7]).

are located close to the eyes, it is difficult to analyze the thresholds accurately, as positioning of the electrodes has a great impact on the retinal current density.

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