Medical Engineering & Physics 36 (2014) 1644–1655

Contents lists available at ScienceDirect

Medical Engineering & Physics

journal homepage: www.elsevier.com/locate/medengphy

Operational challenges of retinal prostheses

Erich W. Schmid[a,*], Wolfgang Fink[b,c], Robert Wilke[d]

[a] Institute of Theoretical Physics, Tübingen University, Auf der Morgenstelle 14, 72076 Tübingen, Germany
[b] Visual and Autonomous Exploration Systems Research Laboratory, Division of Physics, Mathematics and Astronomy, California Institute of Technology, Pasadena, CA 91125, USA
[c] Visual and Autonomous Exploration Systems Research Laboratory, Departments of Electrical & Computer Engineering, Biomedical Engineering, and Ophthalmology & Vision Science, University of Arizona, Tucson, AZ 85721, USA
[d] Krankenhaus Dresden-Friedrichstadt, Dresden, Germany

ARTICLE INFO

Article history:
Received 25 June 2013
Received in revised form 14 August 2014
Accepted 7 September 2014

In Memoriam Thomas A. Tombrello, Caltech's Robert H. Goddard Professor of Physics (1936–2014).

Keywords:
Retinal prosthesis
Epiretinal implant
Subretinal implant
Suprachoroidal implant
Electric stimulation
Phosphenes
Cross-talk
Field line bunching
Electric field profile
Electric current profile
Electric field shaping

ABSTRACT

Two computational models for research on retinal implants are presented. In the first model, the electric field produced by a multi-electrode array in a uniform retina is calculated. It is shown how cross talk of activated electrodes and the resulting bunching of field lines in monopole and dipole activation prevent high resolution imaging with retinal implants. Furthermore, it is demonstrated how sequential stimulation and multipolar stimulation may overcome this limitation. In the second model a target volume, i.e., a probe cylinder approximating a bipolar cell, in the retina is chosen, and the passive Heaviside cable equation is solved inside this target volume to calculate the depolarization of the cell membrane. The depolarization as a function of time indicates that shorter signals stimulate better as long as the current does not change sign during stimulation of the retina, i.e., mono-phasic stimulation. Both computational models are equally applicable to epiretinal, subretinal, and suprachoroidal vision implants.

1. Introduction

Since more than 15 years researchers are trying to restore vision to people suffering from macular degeneration or retinitis pigmentosa by implanting a multi-electrode array in epiretinal, subretinal, or suprachoroidal position [1–14] to stimulate the retina and thereby the visual pathway via electrical stimulation. Some early subretinal designs used photodiodes as power sources and failed for lack of power. Recent designs with energy supplied from external power sources report remarkable success [6,13]. Despite these reported successes, there remains the need for improvement.

Fig. 1 shows an image section taken from a newspaper with about 1500 pixels. Viewed from the right distance one clearly recognizes a former president of the United States. This is not trivial because there are more prerequisites that must be met before one can recognize the person: (1) every pixel must be confined to its location on a mesh without overlap with its neighbor, and (2) pixels must be tunable (i.e., adjustable grayscale) independently from each other.

To meet these prerequisites by electrical stimulation of the retina, the following challenges are expected: (a) phosphenes created by electrical stimulation may be bigger than the area allowed for one pixel; (b) neighboring phosphenes might influence each other via cross talk; and (c) it might be difficult to tune the brightness of pixels with the needed accuracy without increasing their size.

To date, retinal prostheses are still far away from producing a visual percept that is comparable in quality to the image shown in Fig. 1, despite the fact that the number of electrodes on the implanted electrode arrays is already comparable to the number of pixels in Fig. 1.

* Corresponding author. Tel.: +49 707163275.
E-mail address: erich.schmid@uni-tuebingen.de (E.W. Schmid).

http://dx.doi.org/10.1016/j.medengphy.2014.09.004
1350-4533/

Fig. 1. Image section with 1500 pixels, copied from a newspaper.

Fig. 2 shows the electric current lines (full lines, red) emerging from a single electrode placed in subretinal position. Equipotential lines are also shown (broken lines, blue). The vitreous has been removed and replaced by silicone oil with negligible electric conductivity. If the patient sees a phosphene: where does the electric signal enter into the visual pathway? The possibilities are:

Area A: The electric field is almost vertical and rather strong, the target volume is small. The primary targets are bipolar cells. One expects a low threshold and small phosphenes.

Area B: The electric field is almost horizontal. With monopole excitation, this area has the shape of a torus and is slightly larger than area A. Area B is ideal for electrodes operating as dipoles.

Area C: The electric field is almost horizontal and weak. The area is widespread. One expects interference of the electric signal with neural network processing in the ganglion cell and inner plexiform layer. Phosphenes are expected to have a size similar to the thickness of the retina (when their angular size is visualized by projecting from the plane of perception back to the retina).

For the design of a retinal prosthesis the interesting quality of a percept is its brightness and size, which are hard to measure in vitro or in animal experiments. Few measurements have been done

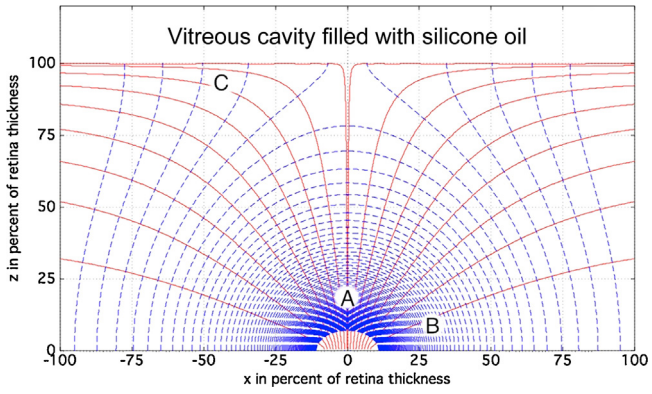

Fig. 2. One electrode in the center of a subretinal multi-electrode array is activated. The vitreous has been replaced by silicone oil of extremely small electric conductivity. Current lines are shown in red (full lines), equipotential lines in blue (broken lines). Areas where the electric signal might possibly enter into the visual pathway are indicated by A, B, and C (see text). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

on human test subjects [10,15–23]. Rather large phosphenes have been found in these investigations, potentially suggesting stimulation in area C. However, the answer is unknown, and thus all three possibilities need further investigations.

We present and discuss theoretical tools, which will be helpful in finding answers, either by proposing experiments, or by analyzing experimental results [24]. The emphasis is on their application to problems of electrical stimulation and imaging. Quasi-static electric fields generated by multi-electrode arrays in a model tissue and their resulting neural stimulation are calculated.

The electrical properties of nerve cells have been studied for many years. Starting from the pioneering work by Hodgkin and Huxley [30] cellular neurophysiology has rapidly developed and is well described in textbooks (e.g., Johnston and Wu [31]). The idea of a subretinal prosthesis is to replace lost rods and cones with an array of electrodes [3,4]. Such an electrode sends a weak electric current into the extra-cellular space of the retinal tissue. The electric field associated with this current can enter into the intracellular space of a retinal neuron via the residual conductivity of the cell membrane and via the membrane capacitance. This so-called passive process can become active in the way described by Hodgkin and Huxley: The stimulation signal carried by the current can thus enter into the visual pathway and lead to the perception of a phosphene. This process is termed electrical stimulation of the retina. The passive stimulation process is described by Heaviside's telegraph equation or more precisely, by the antenna version of that equation.

In the following, examples will be given for subretinal multi-electrode arrays. However, the computer codes are equally applicable to epiretinal and suprachoroidal array positions.

2. Model 1: calculation of the electric field of a subretinal electrode array

To study electrical stimulation, we need to know the stimulating electric field.

2.1. Continuum approximation of the retinal tissue

The retinal tissue consists of various types of cells with rather small clefts in between. The quasi-static electric current has to follow these extracellular clefts. We call it an *Ohmian current* in contrast to a *displacement current* that will be discussed in a follow-up publication [25].

In a *continuum approximation*, cells and clefts form an electric conductor with an average electric conductivity σ. There is an electric current density $\boldsymbol{j}(x,y,z,t)$ and an electric field $\boldsymbol{E}(x,y,z,t)$. The two are related via Ohm's law:

$$\boldsymbol{j}(x,y,z,t) = \sigma \boldsymbol{E}(x,y,z,t). \quad (1)$$

In a refined model, the electric conductivity σ would be a tensor with components depending on the space coordinates x,y,z. Unfortunately, very little information is available on the components of this tensor for the human retina. Therefore, and for simplicity, we replace the tensor by a scalar in Eq. (1). However, we allow for one refinement: there may be two horizontal layers with two different values of σ. This will afford us to study the effect of a thin layer of extracellular fluid between the multi-electrode array and the retina. It will also allow us to calculate the current field when the vitreous is replaced by silicone oil (Fig. 2).

2.2. The multi-electrode array

In most of our calculated examples the multi-electrode array will be flat, with flat 50 μm × 50 μm-electrodes spaced 70 μm