In Silico Development of 3-Dimensionel Retina Model and Monophasic Stimulation Environment

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Abstract

Degenerative retinal diseases could cause loss of vision completely. The progress in certain technological fields and multidisciplinary studies conducted with collaboration from different branches of science makes vision restoration possible with visual prosthesis. Visual prosthesis concept uses electrical stimulation of retinal tissue. Computational modeling of retina tissue in silico provides optimization of stimulation parameters and advantages in terms of both financial and time issues. In this study, 3 dimensional retina is modelled and the effects of monophasic electrical stimulation is investigated under stationary conditions. The solution is made using Finite Element Method (FEM). It is concluded that electric field distribution is much more near stimulation electrode than periphery retina. With the needed improvements in the model, it could be used efficiently for time dependent and parameter based investigations.

Key words: Epiretinal prosthesis, electrical stimulation, finite element analysis, monophasic stimulation, visual prosthesis.

1. Introduction

Efforts for the restoration of the diseases related with loss of vision and blindness affecting much more people day by day has increased with the developing technology in recent years. Factors resulted from the impairment in retina layers and aging lead to loss of vision. Age-related Macular Degeneration (AMD) and Retinitis Pigmentosa (RP) are the most frequently encountered two diseases leading to blindness in the world [1]. AMD damages retinal pigment epithelium (RPE) layer in the eye and leads to tunnel-like vision just before complete blindness and affects 30% of population which is above 70 years of age [2-4]. RP impairs photoreceptor layer. After retinal photoreceptor layer is impaired, it leads to fully blindness over time.

This study aims to develop 3 dimensional retina stimulation environment and simulate epiretinal stimulation with monophasic pulses under quasi static conditions. Dimensions of retina tissue is determined in compliance with real one. Stimulation and return electrodes are positioned on the tissue. Potential difference of 1, 2, 3 V is applied to the stimulation electrodes and then electric field distribution around the tissue is investigated.

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2. Materials and Method

2.1. Visual Prosthesis Concept

It has been stated that more than 40 millions of people have been affected from loss of vision all over the world, it is expected that AMD which is the leading reason of loss of vision in developed countries will affect more than 4 millions of people in USA until 2020 [5]. Although there is not any research which have been carried out yet on the diseases causing loss of sight in Turkey, it is reported that more than %30 of cases seen is associated with these two diseases [4]. Because these diseases cannot be treated, restorative treatments with multi-disciplinary studies are focused. When even diseases become serious, it is known that some inner layers of the retina remain intact for years. Visual prosthesis bypasses the parts which lost their functionality in visual pathway and aims to regenerate the visual perception in the form of little light spots called phosphenes using the functional layers left. Studies on the visual prosthesis dates back to old times [6-9], so Brindley showed that visual perception could be obtained using the electrical stimulation in 1960s.State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results [1].

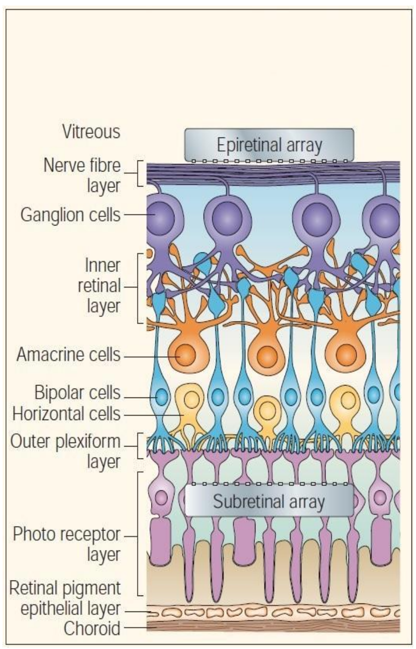

Figure 1. Layers of cross sectional retina [20]

Visual prosthesis could be classified as retinal prosthesis, cortical prosthesis and optic nerve prosthesis [3, 10]. Retinal prosthesis covers the restorative studies related with impairments in retinal layers, presented in Figure 1. Retinal prosthesis are divided into subretinal and epiretinal prostheses. Non-retinal prosthesis aims to provide the visual restoration by using outer parts of visual pathway, which includes optic nerve and cortical prosthesis. Subretinal implants are placed into impaired photoreceptor region between RPE and bipolar cell layer. Although being close to nerve cells remained intact has advantages such as requiring less energy for stimulation, it has a set of disadvantages such as very limited space capacity for units like power supply and processor, possibility of affecting the tissues thermally and difficulty of surgical operation [11]. Some studies conducted, the current required to be applied for providing the visual perception is tried to be provided with set of micro-photodiode placed into the photoreceptor region. Because current obtained from micro-photodiodes remain too low to produce enough amplitude, systems developed recently are externally supplied with a wire or wirelessly. The implant with 1500 micro-photodiode and 16 stimulation electrode supplied by means of a cable from external power supply was placed into 12 human subjects. Test results showed that patients detected the lines with correct orientation, letter U was stated correctly in four directions (20/24), from 62 cm distance 8.5 cm sized letters were recognized [12, 13]. A device which contains a set of micro photodiode supplied by a laser was placed into 14 human subjects. The highest visual acuity obtained from tests was determined as 20/1000 (logMAR: 1.69) [10]. A device which is developed by Retina Implant AG and made up from titanium-nitrite (TiN) and containing 16 electrodes, sized 50 mm and covering 280 mm area, and having 1550 microphotodiodes have implanted into 12 patients without any problems. The experiments conducted have showed promising results in terms of letter separation and object localization [14, 15].

Epi-retinal prosthesis are placed in such a way that it will contact with nerve fibers forming ganglion cells. Although fully intraocular device is aimed in the design of systems, some units are still in extra ocular region. In epiretinal prosthesis, it is essential that image taken from out of the eye with a camera is turned into electrical pattern by a processor and then retinal nerve cells are stimulated electrically by means of stimulation electrodes. The systems developed recently have included an electrode array placed on retinal layer, wireless data/power transfer unit, processor, power supply in outer region and a miniature camera. Argus I and Argus II are the devices having the longest surveillance period among the epiretinal implants which have been developed so far. 500 um diameter sized Argus I device has 16 electrodes. Results obtained from experiments with 3 human subjects showed objective and subjective visual perception findings such as the ability of distinguishing directions of moving objects, changing current levels and the ability of distinguishing brighter and duller perceptions [2, 16]. Argus II model which was placed in 32 human subjects in five countries is consisted of camera fixed to a glass, a processor used for digitization and filtering, an inductive coil link used for transferring data and power with units located in intraocular region and electrode array having 60 stimulation electrodes. In the experiments, better visual acuity result, letter detection which passed successfully to a large extent with 22 patients, correct detection of nearly all letters in the alphabet with 6 patients were seen [17, 18]. Epiret3 and Intelligent Medical Implants AG are two of the leading epiretinal implant systems developed by other groups. It was reported that visual perception was provided in the studies conducted with human subjects [19]. Epiretinal implants have optimal heat dissipation and thus have low possibility of thermal damage to tissues. While epiretinal implants have advantages such as using higher stimulation currents, occupying smaller space within eye, easy updating of the extraocular units such as processor and camera, causing less damage to tissues surgically; spontaneous stimulation of axons of ganglion cells is an important deficit.

In cortical prosthesis, visual cortex is directly stimulated, thus it may be a cure for loss of vision with high damage level. Nevertheless, since tissues in which surgical intervention will be performed are close to the brain, cortical prosthesis carries the biggest risk compared to other prosthesis types. Nervous code complexity poses an important problem in visual cortex. The retina and optic nerve which is the more anterior site in the visual pathway are less complex than visual cortex, and have also less neural code complexity [20].

In optic nerve prosthesis, electrical stimulation of optic nerve which is composed from the outputs of ganglion cells, nerve fibers, provides a basis. Therefore, this type of prosthesis may be used in patients whose ganglion cell region has not been damaged. In the experiments on this prosthesis type, the system including spiral-cuff electrodes was placed into two human subjects and the ability of recognizing simple patterns and distinguishing the objects were observed [21].

2.2. 3-Dimensional retina model

The simplified model geometry consists 6 mm x 6 mm x 250 µm domain. Dimensions of the retina are determined as width of 6 mm and height of 250 µm in harmony with real one. It is assumed that retina is homogeneous and isotropic. Ground and stimulation electrodes are placed on retina close each other to generate activation region between them.

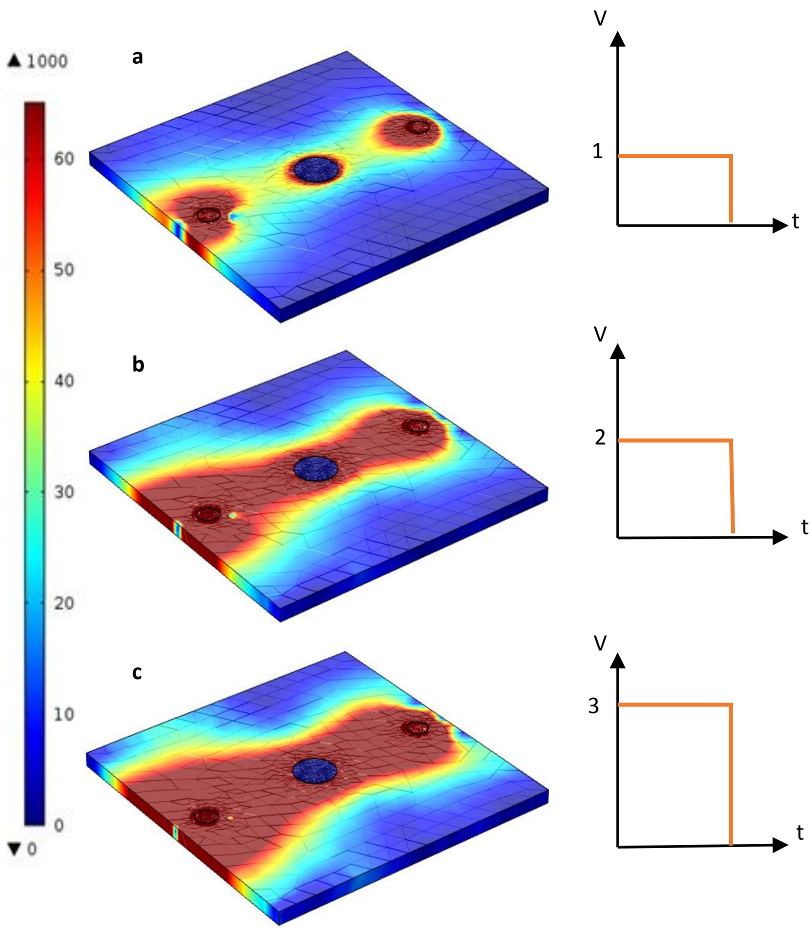

Figure 3. Electric field distribution over retina depending on applied potential difference, (a) applied potential difference is 1 V, (b) applied potential difference is 2 V, (c) applied potential difference is 3 V.

4. Discussion

Electrical stimulation initiates with the depolarization of the membranes of cells which are stimulated. This occurs with depolarization provided with ionic current flow between at least two electrodes which are close to the cells. It is seen that as the potential difference increases the maximum electric field intensity also increases. Additionally, the region of electric field enlarges. This means that nerve cells in deep regions of the tissue could be stimulated with the increasing stimulation amplitude. Similarly, periphery retina regions could also be stimulated to activate remaining nerve cells. In comply with the bipolar electrode configuration concept, an activation region is created between electrodes, which provides efficient stimulation.

An indispensable requirement of implantable stimulation electrodes is the ability of delivering both safe and efficient current. The implant, a microelectrode array (MEA), is placed to the retinal tissue to stimulate the retina ganglion cell layer or photoreceptor cell layer depending on the region it is placed. Stimulation has to be within allowable limits to avoid thermal damage to the tissues and electrode corrosion. In this point it is seen that development of realistic simulation models provides great benefits. Simulation models are useful to test whether the system are within safe limits, or not. Thus, the system can be revised if necessary in design phase by saving high amount of time and money.

Conclusions

Recently, visual prosthesis concept has gained enormous interest. In literature it could be seen that visual perception, called phosphene, can be obtained using electrical stimulation of remaining nerve cells through visual pathway. There are a number of physiological and biological causes that should be taken into consideration to reach visual restoration. Researches using realistic simulation models save both time and unnecessary expenses. In this point, simulation studies have a critical importance.

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