Virtual electrode design for increasing spatial resolution in retinal prosthesis

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Retinal prostheses systems are currently used to restore partial vision to patients blinded by degenerative diseases by electrically stimulating surviving retinal cells. To obtain likely maximum resolution, electrode size is minimised, allowing for a large quantity on an array and localised stimulation regions. Besides the small size leading to fabrication difficulties and higher electrochemical charge density, there are challenges associated with the number of drivers needed for a large electrode count as well as the strategies to deliver sufficient power to these drivers wirelessly. In hopes to increase electrode resolution while avoiding these issues, the authors propose a new ‘virtual electrode’ design to increase locations of likely stimulation. Passive metallisation strategically placed between disk electrodes, combined with alternating surrounding stimuli, channel current into a location between electrodes, producing a virtual stimulation site. A computational study was conducted to optimise the passive metal element geometry, quantify the expected current density output, and simulate retinal ganglion cell activity due to virtual electrode stimulation. Results show that this procedure leads to array geometry that focuses injected current and achieves retinal ganglion cell stimulation in a region beneath the ‘virtual electrode,’ creating an alternate stimulation site without additional drivers.

1. Introduction: Most of the currently implemented epi-retinal prosthesis systems utilise arrays of surface electrodes placed against the retina. These electrically stimulate the neural tissue based on modulated input from an external camera [1]. This has produced encouraging results, allowing blind patients who have degenerative diseases to regain some visual perception [2, 3]. However, the resolution is not yet sufficient to accomplish important tasks, such as facial recognition, and it is widely believed that a larger number of electrodes would likely provide a more useful vision in this regard [4, 5]. There are restrictions on how many electrodes can be placed on these arrays and how small they can be. More importantly, there are significant limitations on how many electrodes can be driven by separate drivers and the power required by attempting to increase the electrode count through simply increasing the number of physical electrodes. Further, to fit a large number of electrodes, the size of the electrodes and the space between them needs to decrease. This leads to further constraints, since the smaller size has been shown to increase the impedance at the electrode surface, which increases the amount of charge density and the risk of damaging tissue and/or the electrodes themselves [5, 6]. Closer spatial proximity of electrodes also weakens the focus of stimuli, as charge injection from surrounding electrodes can affect the response beneath any individual electrode when they are concurrently utilised. This can lead to a large stimulation range and discredits the logic for increasing the number of electrodes [7].

Alternative stimulation strategies have been studied to create virtual stimulation sites beneath these electrode arrays, channelling current to locations in between electrodes [8–11]. This bypasses concerns with building arrays with many small electrodes, and allows for currently implanted designs to continue to be used while providing higher resolution of stimulus locations. Computational and experimental studies have shown that using simultaneous monopolar stimulation of adjacent electrodes increases the field between them, and can theoretically be used to stimulate these regions [9–11]. Choosing different ground locations to channel current is another option [10, 12].

While these methods have been shown to increase the fields between electrodes and can cause stimulation, they do not create a focused current injection that would be expected if another

electrode was placed in the centre virtual location. This work introduces a design for a virtual electrode configuration that channels current to the centre of the array, producing as high of a current density beneath the virtual electrode as is seen under a firing electrode, while ensuring that the tissue beneath the electrodes does not respond to the injected current. This is accomplished through the usage of short pulses applied to perpendicular pairs of bipolar electrodes, and strategically placed passive metal elements for channeling the current to a specific location in the centre of each set of four electrodes. Applying this electrode configuration can significantly increase the number of acting ‘electrodes’ on an array. This can lead to improved array design, providing a means for increasing the resolution and for selectively stimulating cells within a small radius of tissue.

2. Virtual electrode methodology: The virtual electrode phenomenon is produced using a purposely designed configuration of passive metal elements placed in between active disk electrodes, in conjunction with a judicious choice of signal timing and shape of the adjacent electrodes. The design proposed in this work is shown in Fig. 1. This is accomplished through the use of time-offset pulses, as in [8, 9], applying pulses with a short enough of a pulse width that they are uninfluential on the tissue, but offset in time so that they create a wider pulse in the location between the electrodes. As described as well in [8, 9], applying a short stimulus to two adjacent electrodes, having one stimulus be delayed by the width of the stimuli, produces a stimulus of twice the width in the centre. If this pulse width is too narrow to elicit neural response, then the centre location could be the sole location of neural stimulation. Differently from previous attempts at this strategy, bipolar stimulation is used rather than monopolar, using the diagonal, perpendicular pairs of electrodes in any given set of four electrodes for the two stimuli. A narrow anodic stimulus is applied to one pair, then immediately following it an identical stimulus is applied to the second pair.

This systematic current injection used in conjunction with the designed passive metal elements focus the current even further in order to produce sufficient charge density to cause a stimulus site in the centre of the structure. The passive metal elements provide

Fig. 1 Virtual electrode system: alternating pulses are applied to electrode pairs 1 and 2, with a pulse width of t , creating a pulse width of $2t$ in the centre. Passive metal elements are incorporated to further focus the current

a highly conductive path from the positive electrode to the negative, forcing more of the current into this specific location. Incorporating a gap between the pieces of metal in the centre of the four electrodes provides capacitive pathways for the current, creating a high current density location in this centre location. The initial idea for this methodology was based on the observation of current traveling through adjacent electrodes and then into the tissue when electrodes are placed in close proximity, since the electrodes nearby form a more conductive path to the current return than the tissue.

3. Electrode array model and tools: For the purposes of designing the electrode configuration and simulating various geometries, a computational model was constructed with a size of $300 \times 300 \times 150$ voxels for use with our multi-resolution and multi-scale admittance method (AM), described in [13, 14]. Each voxel is cubic with a width of $10 \mu\text{m}$ and is given an integer value, each integer representing a different tissue or material resistive properties. An insulated 2×2 electrode array was incorporated into the model, comprised of disk electrodes with a diameter of $200 \mu\text{m}$ and a pitch of $400 \mu\text{m}$, placed flush against the retina tissue. The electrode dimensions and placement were based on the retinal prosthesis system reported in [1].

The electrode array is placed flush with the retinal surface. The retina was described using multiple layers, with the resistivity varying every $20 \mu\text{m}$ beneath the surface of the array corresponding to published measurements of rat retina [15]. The relative permittivity of all of the retinal tissue was varied based on the width of the time step used for the bipolar stimulation, ranging from 4700 to 8200. The tissue surrounding the electrode array was given the properties of vitreous humour, with a relative permittivity of 98 [16].

The AM was used to compute resulting voltages due to defined current source(s). This method first meshes the model, combining voxels at locations further from boundaries and current source locations in order to decrease the number of nodes. Next, the meshed discretised model is used to build a circuit network based on the resistivity and permittivity values, describing each edge of a voxel as a resistance and capacitance. An admittance matrix is populated with the resulting admittance values seen at each node (G). By defining a current vector (I) that defines the initial current at each node, allowing for current sources to be defined, the resulting voltages throughout the model (V) can be solved for using the linear equation $GV = I$. These voltages may then be used to solve for the electric field magnitude in any direction by taking the ratio of the voltage drop between adjacent nodes and the distance between them. The current density may then also be considered by scaling the magnitude of the electric field at each voxel by the conductivity of the tissue the voxel represents [13, 14].

4. Passive metal element design: The AM was used to optimise the geometry of the passive metal elements placed in between the electrodes. The metal geometries were designed to be $10 \mu\text{m}$ thick, placed flush with the surface of the array without any sources connected. Simulations were run, applying a total of four anodic pulses, as shown in Fig. 1, with a pulse width of $10 \mu\text{s}$. Many different configurations were considered: it was found that having the metal surrounding the firing and return electrodes produced a higher density of current in the centre and, as described in the later section, is most effective in causing neural activation in regions proximal to the centre of the set of electrodes. By narrowing the metal elements, the amount of current that passed across proximate elements was decreased, channelling more current towards the centre. Three notable patterns describing this conclusion are shown in Fig. 2a, with each subsequent pattern having a narrower geometry. Normalised current density accumulated after these four time steps at a slice $30 \mu\text{m}$ into the retinal tissue is given in Fig. 2b. Fig. 2c provides linear plots of these slices, quantifying the difference between the accumulated current density through the electrodes and through the virtual electrode. All plots were normalised to the maximum current density magnitude in order to provide a comparison of the effective current channelling between the different configurations.

5. Neural activation modelling: The resulting accumulated current density analysis showed an interesting ability for this system to channel current towards the centre of a square electrode configuration. However, the current density beneath the firing electrodes, built over the time of multiple pulses, remained at a similar magnitude to that under the virtual electrode location. The ability for this stimulation mechanism to be useful depends on the underlying retinal cells responding to the longer pulse width in the centre, and not to the shorter pulses beneath the firing electrode locations. Thus, a further pulse was conducted to simulate the response of retinal ganglion cells (RGCs). A multi-scale approach was taken, applying the voltage results from the AM simulations to a model of a RGC. The cell was placed in multiple locations, using an otherwise identical model. Since the admittance mesh is a lumped representation of the underlying neural cells, this multi-scale process sufficiently models the impedance of each individual cell. This approach allows for a comparative study of the stimulation threshold for cells in different locations beneath the electrode array.

A RGC model was built from the morphology extracted from a connectome dataset built on high-resolution transmission electron microscopy images [17]. The RGC considered includes a cell body and the dendritic branches. The morphology was imported into NEURON software [18], in which it was split into compartments of tapered cylinders, each described electrically as a cable model. The active properties of the membrane were described using the

Fig. 2 Three notable patterns of electrode and passive metal element and linear plots of normalised current density
a Electrode and passive metal element pattern
b Normalised accumulated current density after four time steps (two pulses applied to each pair), taken 30 μm into the retinal tissue for each pattern
c Linear plots of normalised current density comparing magnitude between firing electrodes and the virtual electrode (location given by white dotted lines in (*b*))

passive properties and five-ionic current model as described by Fohlmeister and Miller [19]. The ionic gating rate constants and ionic channel conductances were given identical values to measurements given in [20]. The ability of this cellular morphology to behave as observed experimentally with these active properties applied was simulated by clamping the membrane to various current magnitudes, and comparing the resulting spiking to the results given in [19].

This RGC was duplicated to create two models. The coordinates of the RGC's were translated in order to be centred 30 μm into the admittance model described in the previous sections of this Letter, with one cell being beneath one of the firing electrodes and another beneath the virtual electrode. Only the model with the electrode configuration shown in Fig. 1 was considered since it resulted in the most focused current density in the virtual electrode location. The placement of the cells within the admittance model is shown in Fig. 3. The voltages throughout the admittance model that resulted from the current density analysis were interpolated, providing a potential at each compartment of these two RGC models. These voltages were then applied as extracellular voltages, by placing voltage sources in series with the membrane circuit at each compartment [21].

Simulations were then run, analysing the cellular response to the voltages resulting from previous AM simulations. The input voltages were linearly scaled in NEURON until activation of both cells was observed. For this initial simulation with a pulse width of 10 μs , a larger magnitude of 1670 μA was required for the cell beneath the firing electrode to activate, while only 700 μA were required for the cell beneath the virtual electrode location. As expected, the shorter pulse width applied to the firing electrode required a much higher magnitude to cause stimulation than the wider pulse width in the centre of the electrodes.

The AM simulations were repeated for different pulse widths, varying from 10 to 100 μs , modifying the permittivity values appropriately for each case. The magnitude of the interpolated extracellular voltages was again scaled until activation was observed to compute the stimulation threshold. Results of the threshold calculations are given in Figs. 3 and 4, indicating that this configuration can provide a virtual electrode stimulus regardless of the pulse width.

At these current thresholds, the charge density and charge per phase beneath the firing electrodes were computed to analyse potential safety implications, as these parameters have been shown as cofactors in potential neural tissue damage using disk electrodes

Fig. 3 Placement of the cells within the admittance model

a Three-dimensional rendering of ganglion cells beneath virtual electrode and firing electrode, coloured according to membrane voltage 1.75 ms after 50 μ s-wide 250 μ A pulse applied, showing only activation in virtual location
b Membrane voltage over time for the same stimulus

Fig. 4 Minimum current magnitude necessary to be applied to the electrodes in the AM model in order to stimulate an RGC beneath a firing electrode and the virtual electrode for varying pulse width

[22]. The charge per phase was calculated by multiplying the current waveform width by the magnitude of the pulse at the threshold. The charge density per phase was then calculated by dividing the charge per phase by the area of the electrode. All current threshold and pulse width combinations presented in this Letter were well within the boundaries for safe stimulation as proposed in [22].

6. Conclusions: An electrode configuration for surface electrode arrays used in retinal prostheses systems was designed in order to provide an extra virtual stimulation site in the centre of sets of electrodes. Through a computational study, the method of using alternating short pulses applied to perpendicular bipolar electrodes, with focusing passive metal elements, was shown to have the ability to create virtual electrodes. This could have significant implications for future implanted surface electrode arrays, being able to provide a finer resolution of selectively stimulated retinal cells without the necessity for more feed points, or drivers.

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8 References

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