Computational Modelling of Retinal Electric Stimulation

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Electrode Placement

- Vitreous Humour
- Ganglion Cells
- Bipolar Cells
- Photoreceptors
- RPE
- Choroid
- Sclera
Electrode Placement

Epiretinal

Vitreous Humour

Ganglion Cells

Bipolar Cells

Photoreceptors

RPE

Choroid

Sclera
Electrode Placement

Vitreous Humour

Ganglion Cells

Bipolar Cells

Photoreceptors

RPE

Choroid

Sclera

Suprachoroidal
To understand how to safely deliver electric charge in a vision implant ...

... in order to achieve a desired pattern of spatio-temporal neural activation in the retina.
Current Flow in a Volumetric Conductor

\[ \nabla \cdot (-\sigma \nabla V) = 0 \]

\[ J = -\sigma \nabla V \]

\( \sigma \): electrical conductivity (S/m)

\( V \): electric potential (V)

\( J \): Current density (A/m\(^2\))
Simulating Multi-Electrode Arrays

3D Retinal Structure
Modelling Neural Excitation of the Retina

Modelling Neural Excitation of the Retina

Retinal Ganglion Cell

Axon

Soma

Dendrites

Compartmental Model

Vi

Ve
Modelling Neural Excitation of the Retina

extracellular domain

intracellular domain
Continuum Equivalent

\[ C_m \frac{\partial V_m}{\partial t} + J_{ion} = g_r (V_i - V_r) \]

\[ \nabla.(-\sigma_e \nabla V_e) = \beta g_r (V_i - V_r) \]

\[ J_{ion} = g_Na m^3 h (V_m - V_{Na}) + g_Ca c^3 (V_m - V_{Ca}) \]

\[ + g_K n^4 (V_m - V_K) + g_{Ka} a^3 (V_m - V_K) \]

\[ + g_{KCa} (V_m - V_K) + g_L (V_m - V_L) \]

Gating variables \((m, h, c, n, a\) and \(h_A\))

(Fohlmeister & Miller, 1997)
Optimising Ionic Models to Data

Potential Missing Current:

\[ i_h = g_h \cdot y^2 \cdot (E_m - E_h) \]
A Modified Retinal Ganglion Cell Model

\[
\frac{dV_m}{dt} = -\frac{1}{C_m} (J_{\text{ion}} + J_{\text{mis}})
\]

Fohlmeister-Miller RGC Model (1997):

\[
J_{\text{ion}} = I_{Na} + I_{Ca} + I_{K} + I_{KCa} + I_{KA}
\]

Hyperpolarization-activated current:

\[
i_h = g_h \cdot y^2 \cdot (E_m - E_h)
\]

\[
\frac{dy}{dt} = \alpha_y \cdot (1 - y) - \beta_y \cdot y
\]

\[
\alpha_y = k_\alpha \cdot e^{S_\alpha(E_m - E_{50,\alpha})}
\]

\[
\beta_y = \frac{k_\beta \cdot (E_m - E_{50,\beta})}{1 - e^{S_\beta(E_m - E_{50,\beta})}}
\]

Voltage responses of \(i_h\) in hyperpolarized RGCs
Whole-Cell Patch RGC Data

- 120 pA
- 60 pA
- -120 pA
- -180 pA
All cell types modeled possess a receptive field from which inputs are converged.
• Retinal model with two hex electrodes, each consisting of a single active electrode and six returns.
• Injecting current I into the vitreous fluid and retinal neurons.
• Pulling current I through the six guard electrodes.
• Active RGC layer with remaining passive retinal layers below
Epiretinal imbalanced stimulation

50 µA

20 µA

1 ms / phase

30 mV

2 ms

mV

-60

-40

-20

0

20

30 mV
Twinhex suprachoroidal stimulation

200 µA

120 µA

1 ms / phase

2 ms

30 mV

mV

-60

-40

-20

0

20

40
Threshold comparison (model & data)

Threshold comparison (model & data)

Three stimulation scenarios

- One guard active
- Two guards active
- Six guards active
Continuum Modelling of the Retinal Network

1. Extracellular Space
2. RGC
3. Deeper Cells
4. Synapses
### Model Architecture

<table>
<thead>
<tr>
<th>Retinal ganglion cell</th>
<th>Modified Fohlmeister, 97</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta \left( C_m \frac{\partial V_m}{\partial t} + J_{ion} + i_{sn} \right) = g_r (V_r - V_i)$</td>
<td></td>
</tr>
</tbody>
</table>

- $C_m$: membrane capacitance (1\(\mu\)F/cm\(^2\))
- $\beta$: surface to volume ratio of GCL (m\(^{-1}\))
- $J_{ion}$: sum of ionic currents (A/m\(^2\))
- $i_{sn}$: sum of synaptic currents (A/m\(^2\))
- $g_r$: resistive tie (S/m\(^2\))
- $V_r$: resting potential (V)
- $V_m$: transmembrane potential (V)
- $V_i$: intracellular potential (V)

![Diagram of Retinal Ganglion Cell](image1)

**Graph:**

- Time (ms) vs. Membrane Potential (mV)
- Graph shows the membrane potential over time for two different points, P1 and P2, at t = 4ms.
Model Architecture

### Bipolar & Amacrine cells

\[ C_m \frac{\partial V_m}{\partial t} + \frac{V_m - V_r}{R_m} = g_r (V_r - V_i) \]

*R_m* specific membrane resistance (\( \Omega \cdot \text{m}^2 \))

### Synapses

\[ \frac{dP_{sn}}{dt} = \frac{p_\infty - P_{sn}(t)}{\tau_{sn}} \]

\[ P_{sn} \text{ synaptic gating parameter} \]

\[ p_\infty \text{ synaptic transfer function} \]

\[ V_{pre} \text{ averaged presynaptic potential} \]
Simulated Network Response

RGC

Synaptic currents

BC & AC
\[ I = g \ pq(V_m - V_r) \]

\[ \frac{dp}{dt} = \alpha_p(1 - p) - \beta_p p \]

\[ \alpha, \beta_p = \frac{k}{1 + e^{s(V_m - E_{50})}} \]

Horizontal Cell

![Horizontal Cell](image_url)

![Graphs](image_url)
Generic Ionic Model Optimisation

SAC

OFF Cone BC
All cell types modeled possess a receptive field from which inputs are converged.
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