"Mathematical Modeling Of Retinal Cells."

The Appendices are derived from references [1]–[14] and constitute summarized equations and parameters used for modeling.

Appendix A
Mathematical Model Of Rod Cells [1]–[3]

Membrane potential (V [mV])

$$I_{\mathrm{ALL}} = I_{\mathrm{photo}} + I_{\mathrm{h}} + I_{\mathrm{Kv}} + I_{\mathrm{Ca}} + I_{\mathrm{Cl(Ca)}} + I_{\mathrm{K(Ca)}} + I_{\mathrm{L}} + I_{\mathrm{ex}} + I_{\mathrm{ex2}}$$

$$C_m \frac{dV}{dt} = -I_{\mathrm{ALL}} (V(0) = -36.186)$$

$$C_m = 0.02 \text{ [nF]}$$

Photocurrent (I_{photo} [pA]) (Baylor & Nunn, 1986 [2]; Forti et al., 1989 [3])

$$\frac{dRh}{dt} = J_{\mathrm{hv}} - \alpha_1 \cdot Rh + \alpha_2 \cdot Rh_{\mathrm{i}},\ Rh(0) = 0$$

$$\frac{dRh_i}{dt} = \alpha_1 \cdot\ Rh - (\alpha_2 + \alpha_3) \cdot Rh_{\mathrm{i}},\ Rh_{\mathrm{i}}(0) = 0$$

$$\frac{dTr}{dt} = \varepsilon \cdot Rh \cdot (T_{\mathrm{tot}} - Tr) - \beta_1 \cdot Tr + \tau_2 \cdot PDE - \tau_1 \cdot Tr \cdot (PDE_{\mathrm{tot}} - PDE),\ Tr(0) = 0$$

$$\frac{dPDE}{dt} = \tau_1 \cdot Tr \cdot (PDE_{\mathrm{tot}} - PDE) - \tau_2 \cdot PDE \quad (PDE(0) = 0)$$

$$\frac{d[Ca^{2+}]}{dt} = b \cdot J - \gamma_{\mathrm{Ca}} \cdot ([Ca^{2+}] - Ca_0) - k_1 \cdot (e_{\mathrm{T}} - [Cab]) \cdot [Ca^{2+}] + k_2 \cdot [Cab] \quad (Ca^{2+}](0) = 0.3)$$

$$\frac{d[Cab]}{dt} = k_1 \cdot (e_{\mathrm{T}} - [Cab]) \cdot [Ca^{2+}] - k_2 \cdot [Cab]$$

$$([Cab](0) = 34.88)$$

$$\frac{dcGMP}{dt} = \frac{A_{\max}}{1.0 + ([Ca^{2+}]/Kc)^4} - cGMP \cdot (\overline{V} + \alpha \cdot PDE) \quad (cGMP(0) = 2.0)$$

$$J = \frac{J_{\max} \cdot (cGMP)^3}{(cGMP^3 + 10^3)}$$

$$I_{\mathrm{photo}} = -J \left[1.0 - \exp\left(\frac{V - 8.5}{17.0}\right)\right]$$

Hyperpolarization-activated current (I_{h} [pA])

$$\alpha_{\mathrm{h}} = \frac{8}{\exp\left(\frac{V+78}{14}\right) + 1}, \qquad \beta_{\mathrm{h}} = \frac{18}{\exp\left(-\frac{V+8}{19} + 1\right)}$$

$$\frac{d}{dt}\begin{bmatrix} C_1 \\ C_2 \\ O_1 \\ O_2 \\ O_3 \end{bmatrix} = \mathbb{A} \times \begin{bmatrix} C_1 \\ C_2 \\ O_1 \\ O_2 \\ O_3 \end{bmatrix},$$

$$\mathbb{A} = \begin{bmatrix} -4\alpha_{\mathrm{h}} & \beta_{\mathrm{h}} & 0 & 0 & 0 \\ 4\alpha_{\mathrm{h}} & -3(\alpha_{\mathrm{h}} + \beta_{\mathrm{h}}) & 2\beta_{\mathrm{h}} & 0 & 0 \\ 0 & 3\alpha_{\mathrm{h}} & -(2\alpha_{\mathrm{h}} + 2\beta_{\mathrm{h}}) & 3\beta_{\mathrm{h}} & 0 \\ 0 & 0 & 2\alpha_{\mathrm{h}} & -(\alpha_{\mathrm{h}} + 3\beta_{\mathrm{h}}) & 4\beta_{\mathrm{h}} \\ 0 & 0 & 0 & \alpha_{\mathrm{h}} & -4\beta_{\mathrm{h}} \end{bmatrix}$$

$$(C_1(0) = 0.646, \quad C_2(0) = 0.298, \quad O_1(0) = 0.0517,$$

$$O_2(0) = 0.00398, \quad O_3(0) = 0.000115),$$

$$I_h = \overline{g}_{\mathrm{h}} \cdot (O_1 + O_2 + O_3)(V - E_{\mathrm{h}}),$$

$$\overline{g}_{\mathrm{h}} = 3.0 \text{ [nS]}, \quad E_{\mathrm{h}} = -32 \text{ [mV]}$$

Delayed rectifier current (I_{Kv} [pA])

$$\alpha_{m_{\mathrm{Kv}}} = \frac{5(100 - V)}{\exp\left(\frac{100-V}{42}\right) - 1},\ \beta_{m_{\mathrm{Kv}}} = 9\ \exp\left(-\frac{(V - 20)}{40}\right)$$

$$\alpha_{h_{\mathrm{Kv}}} = 0.15 \exp\left(-\frac{V}{22}\right),\ \beta_{h_{\mathrm{Kv}}} = \frac{0.4125}{\exp\left(\frac{10-V}{7}\right) + 1}$$

$$\frac{dm_{\mathrm{Kv}}}{dt} = \alpha_{m_{\mathrm{Kv}}} \cdot (1 - m_{\mathrm{Kv}}) - \beta_{m_{\mathrm{Kv}}} \cdot m_{\mathrm{Kv}} (m_{\mathrm{Kv}}(0) = 0.430)$$

$$\frac{dh_{\mathrm{Kv}}}{dt} = \alpha_{h_{\mathrm{Kv}}} \cdot (1 - h_{\mathrm{Kv}}) - \beta_{h_{\mathrm{Kv}}} \cdot h_{\mathrm{Kv}} (h_{\mathrm{Kv}}(0) = 0.999)$$

$$I_{\mathrm{Kv}} = \overline{g}_{\mathrm{Kv}} \cdot m_{\mathrm{Kv}}^3 \cdot h_{\mathrm{Kv}} \cdot (V - E_{\mathrm{K}})$$

$$\overline{g}_{\mathrm{Kv}} = 2.0 \text{ [nS]}, \quad E_{\mathrm{k}} = -74 \text{[mV]}$$

Calcium current $(I_{\rm Ca}\,[\rm pA])$

$$\alpha_{m_{\rm Ca}} = \frac{3(80-V)}{\exp\left(\frac{80-V}{25}\right)-1}, \quad \beta_{m_{\rm Ca}} = \frac{10}{1+\exp\left(\frac{V+38}{7}\right)}$$

$$h_{\rm Ca} = \frac{\exp\left(\frac{40-V}{18}\right)}{1+\exp\left(\frac{40-V}{18}\right)}$$

$$\frac{dm_{\rm Ca}}{dt} = \alpha_{m_{\rm Ca}}\cdot(1-m_{\rm Ca}) - \beta_{m_{\rm Ca}}\cdot m_{\rm Ca}$$
$$m_{\rm Ca}(0) = 0.436$$

$$I_{\rm Ca} = \overline{g}_{\rm Ca}\cdot m_{\rm Ca}^4\cdot h_{\rm Ca}\cdot(V-E_{\rm Ca})$$

$$\overline{g}_{\rm Ca} = 0.7\,[\rm nS],\ E_{\rm Ca} = -12.5\log(\frac{[Ca]_{\rm s}}{[Ca]_0})$$
$$[Ca]_0 = 1600\,[\mu\rm M]$$

Calcium-activated chloride current $(I_{\rm Cl(Ca)}\,[\rm pA])$

$$m_{\rm Cl(Ca)} = \frac{1}{1+\exp\left(\frac{0.37-[Ca]_{\rm s}}{0.09}\right)}$$

$$I_{\rm Cl(Ca)} = \overline{g}_{\rm Ca(Cl)}\cdot m_{\rm Ca(Cl)}\cdot(V-E_{\rm Ca(Cl)})$$

$$\overline{g}_{\rm Ca(Cl)} = 2.0\,[\rm nS],\ E_{\rm Ca(Cl)} = -20\,[\rm mV]$$

Calcium-activated potassium current $(I_{\rm K(Ca)}\,[\rm pA])$

$$\alpha_{m_{\rm K(Ca)}} = \frac{15(80-V)}{\exp\left(\frac{80-V}{40}\right)-1},\ \beta_{m_{\rm K(Ca)}} = 20\ \exp\left(-\frac{V}{35}\right)$$
$$\frac{dm_{\rm K(Ca)}}{dt} = \alpha_{m_{\rm K(Ca)}}\cdot(1-m_{\rm K(Ca)}) - \beta_{m_{\rm K(Ca)}}\cdot m_{\rm K(Ca)}$$
$$m_{\rm K(Ca)}(0) = 0.642$$

$$m_{\rm K(Ca)_s} = \frac{[Ca]_{\rm s}}{[Ca]_{\rm s}+0.3}$$

$$I_{\rm K(Ca)} = \overline{g}_{\rm K(Ca)}\cdot m_{\rm K(Ca)}^2\cdot m_{\rm K(Ca)_s}\cdot(V-E_{\rm K})$$

$$\overline{g}_{\rm K(Ca)} = 5.0\,[\rm nS], E_{\rm K} = -74\,[\rm mV]$$

Leakage current $(I_{\rm L}\,[\rm pA])$

$$I_{\rm L} = g_{\rm L}\cdot(V-E_{\rm L})$$

$$g_{\rm L} = 0.35\,[\rm nS],\ E_{\rm L} = -77\,[\rm mV]$$

Intracellular calcium system $([Ca]_{\rm s}\,[\mu\rm M])$

$$\begin{aligned}\frac{d[Ca]_{\rm s}}{dt} = &-\frac{I_{\rm Ca}+I_{\rm ex}+I_{\rm ex2}}{2F\cdot V_1}\cdot 10^{-6} \\ &- D_{\rm Ca}\frac{S_1}{\delta\cdot V_1}([Ca]_{\rm s}-[Ca]_{\rm f}) \\ &- L_{\rm b1}[Ca]_{\rm s}(B_{\rm L}-[Cab]_{\rm ls}) + L_{\rm b2}[Cab]_{\rm ls} \\ &- H_{\rm b1}[Ca]_{\rm s}(B_{\rm H}-[Cab]_{\rm hs}) + H_{\rm b2}[Cab]_{\rm hs} \\ &[Ca]_{\rm s}(0) = 0.0966\end{aligned}$$

$$\begin{aligned}\frac{d[Ca]_{\rm f}}{dt} = &D_{\rm Ca}\frac{S_1}{\delta\cdot V_2}([Ca]_{\rm s}-[Ca]_{\rm F}) \\ &- L_{\rm b1}[Ca]_{\rm f}(B_{\rm L}-[Cab]_{\rm lf}) \\ &+ L_{\rm b2}[Cab]_{\rm lf} - H_{\rm b1}[Ca]_{\rm f}(B_{\rm H}-[Cab]_{\rm hf}) \\ &+ H_{\rm b2}[Cab]_{\rm hf} \\ &[Ca]_{\rm f}(0) = 0.0966\end{aligned}$$

$$\frac{d[Cab]_{\rm ls}}{dt} = L_{\rm b1}[Ca]_{\rm s}(B_{\rm L}-[Cab]_{\rm ls}) - L_{\rm b2}[Cab]_{\rm ls}$$
$$[Cab]_{\rm ls}(0) = 80.929$$

$$\frac{d[Cab]_{\rm hs}}{dt} = H_{\rm b1}[Ca]_{\rm s}(B_{\rm H}-[Cab]_{\rm hs}) - H_{\rm b2}[Cab]_{\rm hs}$$
$$[Cab]_{\rm hs}(0) = 29.068$$

$$\frac{d[Cab]_{\rm lf}}{dt} = L_{\rm b1}[Ca]_{\rm f}(B_{\rm L}-[Cab]_{\rm lf}) - L_{\rm b2}[Cab]_{\rm lf}$$
$$[Cab]_{\rm lf}(t=0) = 80.929$$

$$\frac{d[Cab]_{\rm hf}}{dt} = H_{\rm b1}[Ca]_{\rm f}(B_{\rm H}-[Cab]_{\rm hf}) - H_{\rm b2}[Cab]_{\rm hf}$$
$$[Cab]_{\rm hf}(0) = 29.068$$

$$I_{\rm ex} = J_{\rm ex}\ \exp\left(-\frac{(V+14)}{70}\right)\frac{[Ca]_{\rm s}-[Ca]_{\rm e}}{[Ca]_{\rm s}-[Ca]_{\rm e}+2.3},$$

$$I_{\rm ex2} = J_{\rm ex2}\frac{[Ca]_{\rm s}-[Ca]_{\rm e}}{[Ca]_{\rm s}-[Ca]_{\rm e}+0.5}$$

APPENDIX B
PARAMETER DESCRIPTIONS FOR ROD CELLS MODELLING [1], [3], [4]

α_1 = Rate constant of Rh* inactivation $(50\, s^{-1})$

α_2 = Rate constant of the reaction $Rh_{\mathrm{i}} \rightarrow$ Rh* $(0.0003\, s^{-1})$

α_3 = Rate constant of the decay of inactive rhodopsin $(0.03\, s^{-1})$

ε = Rate constant of T* activation $(0.5\, s^{-1}\mu\mathrm{M}^{-1})$

T_{Tot} = Total transducin $(1000\, \mu\mathrm{M})$

β_1 = Rate constant of T* inactivation $(2.5\, s^{-1})$

τ_1 = Rate constant of PDE activation $(0.2\, s^{-1}\mu\mathrm{M}^{-1})$

τ_2 = Rate constant of PDE inactivation $(5\, s^{-1})$

PDE_{Tot} = Phosphodiesterase $(100\, \mu\mathrm{M})$

γ_{Ca} = Rate constant of Ca^{2+} extrusion in the absence of Ca^{2+} buffers mediated by the $Na^{+} - Ca^{2+}$ exchanger $(50\, s^{-1})$

Ca_0 = Intracellular Ca^{2+} concentration at the steady state $(0.1\, \mu\mathrm{M})$

b = Proportionality constant between Ca^{2+} influx and photocurrent $(0.25\, \mu\mathrm{M}\, s^{-1}\, \mathrm{pA}^{-1})$

k_1, k_2 = 'on' and 'off' rate constants for the binding of Ca^{2+} to the buffer ($0.2\, s^{-1}\mu\mathrm{M}^{-1}$ and $0.8\, s^{-1}$), respectively

e_{T} = Low-affinity Ca^{2+} buffer concentration $(500\, \mu\mathrm{M})$

$\overline{V}$ = Cyclic GMP hydrolysis in dark $(0.4\, s^{-1})$

K_{c} = Maximal activity of guanylate cyclase $(100\, \mu\mathrm{M})$

$A_{\max}$ = Maximal activity of guanylate cyclase $(65.6\, \mu\mathrm{M}\, s^{-1})$

σ = Proportionality constant $(1.0\, s^{-1}\mu\mathrm{M}^{-1})$

$J_{\max}$ = Maximal cyclic GMP gated current inexcised patches (5040 pA)

F = Faraday constant, $(9.648 \times 10^{4}\, \mathrm{cmol}^{-1})$

V_1 = Volume of the submembrane area $(3.812\times10^{-13}\, \mathrm{dm}^3)$

V_2 = Volume of the deep intracellular area $(5.236 \times 10^{-13}\, \mathrm{dm}^3)$

δ = Distance between submembrane area and the deep intracellular area $(5.9 \times 10^{-5}\, \mathrm{dm})$

S_1 = Surface area of the submembrane and the deep intracellular area spherical boundary $(3.142 \times 10^{-8}\, \mathrm{dm}^2)$

$L_{\mathrm{b1}}, L_{\mathrm{b2}}$ = On and off rate constants for the binding of Ca to low-affinity buffer $(0.4\, s^{-1}\mu\mathrm{M}^{-1},\ 0.2\, s^{-1}\mu\mathrm{M}^{-1})$

$H_{\mathrm{b1}}, H_{\mathrm{b2}}$ = On and off rate constants for the binding of Ca to high-affinity buffer $(100\, s^{-1}\mu\mathrm{M}^{-1},\ 90\, s^{-1}\mu\mathrm{M}^{-1})$

B_{L} = Total low-affinity buffer concentration $(500\, \mu\mathrm{M})$

B_{H} = Total high-affinity buffer concentration $(200\, \mu\mathrm{M})$

J_{ex} = Maximum Na-Ca exchanger current $(20\, \mathrm{pA})$

J_{ex2} = Maximum Ca-ATPase exchanger current $(20\, \mathrm{pA})$

D_{Ca} = Ca diffusion coefficient $(6 \times 10^{-8}\, \mathrm{dm}^2\mathrm{s}^{-1})$

$[Ca]_{\mathrm{e}}$ = Minimum intracellular Ca^{2+} concentration $(0.01\, \mu\mathrm{M})$

APPENDIX C
MATHEMATICAL MODEL OF CONE CELLS [5]

Equation

Full model with rate-limiting of the catalysed step

$$\tau_L \frac{dV}{dt} = E - V(1 + G_f + G_i)$$

$$G_i = \frac{\overline{G}_i}{1 + z_i/K}$$

$$\tau_f \frac{dG_f}{dt} = F(V) - G_f$$

$$F(V) = \frac{\overline{G}_f}{1 + exp[(V - V_f/V_\varepsilon]}$$

$$(\frac{d}{dt} + \alpha)^{n-1} y_{n-1} = \alpha^{n-2} I(t)$$

$$\frac{dZ_1}{dt} = \alpha y_{n-1} - k_{12} Z_1 + k_{21} Z_2$$

$$\frac{dZ_2}{dt} = k_{12} Z_1 - (k_{21} + k_{23}) Z_2 + k_{32} Z_3$$

$$\frac{dZ_3}{dt} = k_{23} Z_2 - (k_{32}) + k_{34}) Z_3$$

$$A_{K21} = K_{12} = \overline{K}_{12} + V Z_2 \left[\frac{K_{12M} - \overline{K}_{12}}{K_{12M} - \overline{K}_{12} + V Z_2} \right]$$

Initial conditions for the integration were that for t $\leq$ 0 all concentrations, y_1 to y_{n-1} and Z_1, Z_3 were zero, and V(0) = V_D where V_D (the potential in darkness) satisfies

$$V_D\left[1+\frac{\overline{G}_f}{1+exp[(V_D-V_f/V_\epsilon]+\overline{G}_1}\right]=E$$

Appendix D
Parameter Descriptions For Cone Cells Modeling [5]

Circuit parameters

E = Approximate Value to give peak potential of -67 mV with dark resting potential of -42 mV (-72 [mV])

τ_L = Analysis in Baylor et al. 1974 [6]

$\overline{G}_f$ = To give 'sag' of 5 mV from peak to plateau (0.2)

$\overline{G}_i$ = To give -42 mV resting potential in darkness (0.7)

τ_f = From inspection of 'sag' time constant (67 [msec])

V_f = Half way between resting potential of -42 mV and E = -72 mV (-57 [mV])

V_E = Guess based on voltage dependence of other conductance change and synaptic mechanisms (4 [mV])

Parameters controlling time course of conductance change

n = Characteristics of linear response (6)

α = Characteristics of linear response (83 $\cdot$ 3 sec^{-1})

$\overline{K}_{12}$ = Characteristics of linear response (10 sec^{-1})

K_{12M} = Upper limit to $k_{12}$was chosen from trial solutions (250 sec^{-1})

K_{23} = Characteristics of falling phase (17 sec^{-1})

K_{34} = Characteristics of falling phase (1.3 sec^{-1})

K_{32} = Characteristics of falling phase (0.03 sec^{-1})

$A : \frac{K_{12}}{K_{21}}$ = From steady - state relation between potential and light intensity (6.76)

V = From steady - state relation between potential and light intensity (2.125 sec^{-2} or 0.05133 sec^{-2} $molecule^{-1}$ cone)

K = From steady - state relation between potential and light intensity (10 sec or 414 $\text{molecule}^{-1}\text{cone}^{-1}$)

Appendix E
Mathematical Model Of Bipolar Cells [7]

Delayed rectifying potassium current (I_{Kv} [pA])

$$\alpha_{m_{\mathrm{Kv}}}=\frac{400}{\exp\left(-\frac{(V-15)}{36}\right)+1}$$

$$\beta_{m_{\mathrm{Kv}}}=\exp\left(-\frac{V}{13}\right)$$

$$\frac{dm_{\mathrm{Kv}}}{dt}=\alpha_{m_{\mathrm{Kv}}}\cdot(1-m_{\mathrm{Kv}})-\beta_{m_{\mathrm{Kv}}}\cdot m_{\mathrm{Kv}}$$

$$\alpha_{h_{\mathrm{Kv}}}=0.003\ \exp\left(-\frac{V}{7}\right)$$

$$\beta_{h_{\mathrm{Kv}}}=\frac{80}{\exp\left(-\frac{(V+115)}{15}\right)+1}+0.02$$

$$\frac{dh_{\mathrm{Kv}}}{dt}=\alpha_{h_{\mathrm{Kv}}}\cdot(1-h_{\mathrm{Kv}})-\beta_{h_{\mathrm{Kv}}}\cdot h_{\mathrm{Kv}}$$

$$g_{\mathrm{Kv}}=\overline{g_{\mathrm{Kv}}}\cdot m_{\mathrm{Kv}}^3\cdot h_{\mathrm{Kv}}$$

$$I_{\mathrm{Kv}}=g_{\mathrm{Kv}}\cdot(V-E_{\mathrm{K}})$$

$$\overline{g_{\mathrm{Kv}}}=2.0\,[\mathrm{nS}],\quad E_{\mathrm{K}}=58\,[\mathrm{mV}]$$

Transient outward current (I_{A} [pA])

$$\alpha_{m_{\mathrm{A}}}=\frac{1200}{\exp\left(-\frac{(V-50)}{28}\right)+1}$$

$$\beta_{m_{\mathrm{A}}}=6\ \exp\left(-\frac{V}{10}\right)$$

$$\frac{dm_{\mathrm{A}}}{dt}=\alpha_{m_{\mathrm{A}}}\cdot(1-m_{\mathrm{A}})-\beta_{m_{\mathrm{A}}}\cdot m_{\mathrm{A}}$$

$$\alpha_{h_{\mathrm{A}}}=0.045\ \exp\left(-\frac{V}{13}\right)$$

$$\beta_{h_{\mathrm{A}}}=\frac{75}{\exp\left(-\frac{(V+50)}{15}\right)+1}$$

$$\frac{dh_{\mathrm{A}}}{dt} = \alpha_{h_{\mathrm{A}}} \cdot (1 - h_{\mathrm{A}}) - \beta_{h_{\mathrm{A}}} \cdot h_{\mathrm{A}}$$

$$g_{\mathrm{A}} = \overline{g_{\mathrm{A}}} \cdot m_{\mathrm{A}}^3 \cdot h_{\mathrm{A}}$$

$$I_{\mathrm{A}} = g_{\mathrm{A}} \cdot (V - E_{\mathrm{K}}), \quad \overline{g_{\mathrm{A}}} = 35\,[nS]$$

Hyperpolarization activated current $(I_{\mathrm{h}}\,[\mathrm{pA}])$

$$\alpha_{\mathrm{h}} = \frac{3}{\exp\left(\frac{(V+110)}{15}\right) + 1}, \quad \beta_{\mathrm{h}} = \frac{1.5}{\exp\left(-\frac{(V+115)}{15}\right) + 1}$$

$$M = [C_1\, C_2\, O_1\, O_2\, O_3]^t, \quad \frac{d}{dt}M = KM$$

$$K = \begin{bmatrix} 4\alpha_{\mathrm{h}} & -\beta_{\mathrm{h}} & 0 & 0 & 0 \\ 4\alpha_{\mathrm{h}} & 3\alpha_{\mathrm{h}} + \beta_{\mathrm{h}} & -2\beta_{\mathrm{h}} & 0 & 0 \\ 0 & -3\alpha_{\mathrm{h}} & 2\alpha_{\mathrm{h}} + 2\beta_{\mathrm{h}} & -3\beta_{\mathrm{h}} & 0 \\ 0 & 0 & -2\alpha_{\mathrm{h}} & \alpha_{\mathrm{h}} + 3\beta_{\mathrm{h}} & -4\beta_{\mathrm{h}} \\ 0 & 0 & 0 & -\alpha_{\mathrm{h}} & 4\beta_{\mathrm{h}} \end{bmatrix}$$

$$m_{\mathrm{h}} = O_1 + O_2 + O_3, \quad g_{\mathrm{h}} = \overline{g_{\mathrm{h}}} \cdot m_{\mathrm{h}},\; I_{\mathrm{h}} = g_{\mathrm{h}} \cdot (V - E_{\mathrm{h}})$$

$$\overline{g_h} = 0.975\,[\mathrm{nS}], \quad E_h = -17.7\,[\mathrm{mV}]$$

Calcium current $(I_{\mathrm{Ca}}\,[\mathrm{pA}])$

$$\alpha_{m_{\mathrm{Ca}}} = \frac{12000(120 - V)}{\exp\left(\frac{V-120}{25}\right) - 1}$$

$$\beta_{m_{\mathrm{Ca}}} = \frac{40000}{\exp\left(\frac{V+68}{25}\right) + 1}$$

$$\frac{dm_{\mathrm{Ca}}}{dt} = \alpha_{m_{\mathrm{Ca}}} \cdot (1 - m_{\mathrm{Ca}}) - \beta_{m_{\mathrm{Ca}}} \cdot m_{\mathrm{Ca}}$$

$$h_{\mathrm{Ca}} = \frac{\exp\left(-\frac{(V-50)}{11}\right)}{\exp\left(-\frac{(V-50)}{11}\right) + 1}$$

$$E_{\mathrm{Ca}} = 12.9\,\log\left(\frac{[Ca^{2+}]_0}{[Ca^{2+}]_{\mathrm{s}}}\right)$$

$$g_{\mathrm{Ca}} = \overline{g_{\mathrm{Ca}}} \cdot m_{\mathrm{Ca}}^4 \cdot h_{\mathrm{Ca}}$$

$$I_{\mathrm{Ca}} = g_{\mathrm{Ca}} \cdot (V - E_{\mathrm{Ca}})$$

$$\overline{g_{\mathrm{Ca}}} = 1.1\,[\mathrm{nS}]$$

$$[Ca^{2+}]_{\mathrm{o}} = 2500\,[\mu\mathrm{M}]$$

Ca-dependent K current $(I_{\mathrm{K(Ca)}}\,[\mathrm{pA}])$

$$\alpha_{m_{\mathrm{K(Ca)}}} = \frac{100 \cdot (230 - V)}{\exp\left(\frac{230-V}{52}\right) - 1}$$

$$\beta_{m_{\mathrm{K(Ca)}}} = 120\,\exp\left(-\frac{V}{95}\right)$$

$$\frac{dm_{\mathrm{K(Ca)}}}{dt} = \alpha_{m_{\mathrm{K(Ca)}}} \cdot (1 - m_{\mathrm{K(Ca)}}) - \beta_{m_{\mathrm{K(Ca)}}} \cdot m_{\mathrm{K(Ca)}}$$

$$m_{\mathrm{Kc1}} = \frac{[Ca^{2+}]_{\mathrm{s}}}{[Ca^{2+}]_{\mathrm{s}} + 0.2}$$

$$g_{\mathrm{K(Ca)}} = \overline{g_{\mathrm{K(Ca)}}} \cdot m_{\mathrm{K(Ca)}}^2 \cdot m_{\mathrm{Kc1}}$$

$$I_{\mathrm{K(Ca)}} = g_{\mathrm{K(Ca)}} \cdot (V - E_{\mathrm{K}})$$

$$\overline{g_{\mathrm{K(Ca)}}} = 8.5\,[\mathrm{nS}]$$

Leakage current $(I_{\mathrm{L}}\,[\mathrm{pA}])$

$$I_{\mathrm{L}} = g_{\mathrm{L}} \cdot (V - E_{\mathrm{L}})$$

$$g_{\mathrm{L}} = 0.23\,[\mathrm{nS}]$$

$$E_{\mathrm{L}} = \; - 21\,[\mathrm{mV}]$$

Membrane potential $(V\,[\mathrm{mV}])$

$$C\frac{dV}{dt} = \; - (I_{\mathrm{Kv}} + I_{\mathrm{A}} + I_{\mathrm{h}} + I_{\mathrm{Ca}} + I_{\mathrm{K(Ca)}} + I_{\mathrm{L}})$$

$$C = 0.02\,[\mathrm{pF}]$$

Appendix F
Mathematical Model Of Calcium Mechanism On Bipolar Cells [7]

Calcium concentration

$$\frac{d[Ca^{2+}]_{\rm s}}{dt} = -\frac{I_{\rm Ca}}{2F\cdot V_{\rm s}} - \frac{D_{\rm Ca}\cdot S_{\rm sd}}{V_{\rm s}\cdot d_{\rm sd}}\left([Ca^{2+}]_{\rm s} - [Ca^{2+}]_{\rm d}\right) - \frac{(I_{\rm ex}+I_{\rm ex2})}{2F\cdot V_{\rm s}} + \beta_{\rm bl}\cdot[Ca^{2+}]_{\rm bls} - \alpha_{\rm bl}\cdot[Ca^{2+}]_{\rm s}\cdot\left([Ca^{2+}]_{\rm b1max} - [Ca^{2+}]_{\rm bls}\right) + \beta_{\rm bh}\cdot[Ca^{2+}]_{\rm bhs} - \alpha_{\rm bh}\cdot[Ca^{2+}]_{\rm s}\cdot\left([Ca^{2+}]_{\rm bhmax} - [Ca^{2+}]_{\rm bhs}\right)$$

$$\frac{d[Ca^{2+}]_{\rm d}}{dt} = \frac{D_{\rm Ca}\cdot S_{\rm sd}}{V_{\rm d}\cdot d_{\rm sd}}([Ca^{2+}]_{\rm s} - [Ca^{2+}]_{\rm d}) + \beta_{\rm bl}\cdot[Ca^{2+}]_{\rm bld} - \alpha_{\rm bl}\cdot[Ca^{2+}]_{\rm d}\cdot\left([Ca^{2+}]_{\rm b1max} - [Ca^{2+}]_{\rm bld}\right) + \beta_{\rm bh}\cdot[Ca^{2+}]_{\rm bhd} - \alpha_{\rm bh}\cdot[Ca^{2+}]_{\rm d}\cdot\left([Ca^{2+}]_{\rm bhmax} - [Ca^{2+}]_{\rm bhd}\right)$$

Calcium buffer concentration

$$\frac{d[Ca^{2+}]_{\rm bls}}{dt} = \alpha_{\rm bl}\cdot[Ca^{2+}]_{\rm s}\cdot\left([Ca^{2+}]_{\rm blmax} - [Ca^{2+}]_{\rm bls}\right) + \beta_{\rm bl}\cdot[Ca^{2+}]_{\rm bls}$$

$$\frac{d[Ca^{2+}]_{\rm bhs}}{dt} = \alpha_{\rm bh}\cdot[Ca^{2+}]_{\rm s}\cdot\left([Ca^{2+}]_{\rm bhmax} - [Ca^{2+}]_{\rm bhs}\right) + \beta_{\rm bh}\cdot[Ca^{2+}]_{\rm bhs}$$

$$\frac{d[Ca^{2+}]_{\rm bld}}{dt} = \alpha_{\rm bl}\cdot[Ca^{2+}]_{\rm d}\cdot\left([Ca^{2+}]_{\rm blmax} - [Ca^{2+}]_{\rm bld}\right) + \beta_{\rm bl}\cdot[Ca^{2+}]_{\rm bld}$$

$$\frac{d[Ca^{2+}]_{\rm bhd}}{dt} = \alpha_{\rm bh}\cdot[Ca^{2+}]_{\rm d}\cdot\left([Ca^{2+}]_{\rm blmax} - [Ca^{2+}]_{\rm bhd}\right) + \beta_{\rm bh}\cdot[Ca^{2+}]_{\rm bhd}$$

Calcium pump and exchanger

$$I_{\rm ex} = \frac{J_{\rm ex}\cdot([Ca^{2+}]_{\rm s} - [Ca^{2+}]_{\rm min})}{[Ca^{2+}]_{\rm s} - [Ca^{2+}]_{\rm min} + 2.3}\cdot\exp\left(-\frac{(V+14)}{70}\right)$$

$$I_{\rm ex2} = \frac{J_{\rm ex2}\cdot([Ca^{2+}]_{\rm s} - [Ca^{2+}]_{\rm min})}{[Ca^{2+}]_{\rm s} - [Ca^{2+}]_{\rm min} + 0.5}$$

Appendix G
Parameter Descriptions Of Calcium Mechanism On Bipolar Cells [7]

$[Ca^{2+}]_{\rm s}$ = Intracellular calcium concentration just below the cellular membrane, $[\mu{\rm M}]$

$[Ca^{2+}]_{\rm d}$ = Intracellular calcium concentration just below the central space, $[\mu{\rm M}]$

$[Ca^{2+}]_{\rm bls}$ = Binding to low affinity internal buffers, $[\mu{\rm M}]$

$[Ca^{2+}]_{\rm bld}$ = Unbinding to low affinity internal buffers, $[\mu{\rm M}]$

$[Ca^{2+}]_{\rm bhs}$ = Binding to high affinity internal buffers, $[\mu{\rm M}]$

$[Ca^{2+}]_{\rm bhd}$ = Unbinding to high affinity internal buffers, $[\mu{\rm M}]$

F = Faraday constant, 9.649×10^5 cmol^{-1}

$D_{\rm Ca}$ = Ca diffusion coefficient, 6×10^{-8} dm^{2}sec^{-1}

$V_{\rm s}$ = Volume of the submembrane area, 1.692×10^{-13} dm^{-3}

$V_{\rm d}$ = Volume of the deep intracellular area, 7.356×10^{-13} dm^{-3}

$S_{\rm sd}$ = Surface area of the submembrane and the deep intracelluar area spherical boundary, 4×10^{-8} dm^{-2}

$d_{\rm sd}$ = Distance between submembrane area and the deep intracellular area, 5.9×10^5 dm

$[Ca^{2+}]_{\rm blmax}$ = Total low-affinity buffer concentration, $400\,\mu$M

$[Ca^{2+}]_{\rm bhmax}$ = Total high-affinity buffer concentration, $200\,\mu$M

$\alpha_{\rm bl}$, $\beta_{\rm bl}$ = On and off rate constants for the binding of Ca to low-affinity buffer, $0.4\,{\rm sec}^{-1}\,\mu{\rm M}^{-1}, 0.2\,sec^{-1}\,\mu{\rm M}^{-1}$

$\alpha_{\rm bh}$, $\beta_{\rm bh}$ = On and off rate constants for the binding of Ca to high-affinity buffer, $100\,{\rm sec}^{-1}\,\mu{\rm M}^{-1}, 90\,{\rm sec}^{-1}\,\mu{\rm M}^{-1}$

J_{ex} = Maximum Na-Ca exchanger current, $9\,\text{pA}$

J_{ex2} = Maximum Ca-ATPase exchanger current, $9.5\,\text{pA}$

$[Ca^{2+}]_{\text{min}}$ = Minimum intracellular Ca concentration for Ca extrusion, $0.05\,\mu$M

APPENDIX H
MATHEMATICAL MODEL OF AMACRINE CELLS [8]

Amacrine Cell current

C_m = 1 μF/cm^2

$\overline{g}_K$, $\overline{g}_{Na}$, $\overline{g}_L$ = Maximum Conductance, 0.4, 4, 0.4 [nS]

V_K, V_{Na}, V_L = Reversal Potential, -80, 40, -54 [mV]

$$I = C_m \frac{dV_m}{dt} + \overline{g}_K n^4 (V_m - V_K) + \overline{g}_{Na} m^4 h (V_m - V_{Na}) + \overline{g}_L (V_m - V_L)$$

$$\frac{dn}{dt} = \frac{\alpha_n}{5}(V_m)(1-n) - \frac{\beta_n}{5}(V_m)n$$
$$\frac{dm}{dt} = \alpha_m(V_m)(1-m) - \beta_m(V_m)m$$
$$\frac{dh}{dt} = \frac{\alpha_h}{3.5}(V_m)(1-h) - \frac{\beta_h}{3.5}(V_m)h$$

$$\alpha_n(V_m) = \frac{0.01(V_m+10)}{exp(\frac{V_m+10}{10})-1}, \alpha_m(V_m) = \frac{0.1(V_m+25)}{exp(\frac{V_m+25}{10})-1}$$

$$\alpha_h(V_m) = 0.07exp(\frac{V_m}{20}), \qquad \beta_n(V_m) = 0.125exp(\frac{V_m}{80})$$

$$\beta_m(V_m) = 4exp(\frac{V_m}{18}), \qquad \beta_h(V_m) = \frac{1}{exp(\frac{V_m+30}{10}+1)}$$

APPENDIX I
MATHEMATICAL MODEL OF GANGLION CELLS [9]–[11]

Ionic currents

In a single-compartment model, the five (plus leakage) ion currents, and the capacitative current may be summed according to Kirchoff's law:

$$I_{\text{stim}} = C_m \frac{dV}{dt} + \overline{g}_{\text{Na}} m^3 h (V - V_{\text{Na}}) + \overline{g}_{\text{Ca}} m_{\text{Ca}}^3 (V - V_{\text{Ca}}) + (\overline{g}_{\text{K}} n^4 + \overline{g}_{\text{A}} m_{\text{A}}^3 h_{\text{A}} + \overline{g}_{\text{K(Ca)}})(V - V_{\text{K}}) + \overline{g}_{\text{L}}(V - V_{\text{L}})$$

Of the reversal (equilibrium) potentials, only V_{Ca} was modeled as variable according to the Nernst equation, where

$$V_{Ca} = \frac{RT}{2F} \log \left(\frac{[Ca^{2+}]_{\text{e}}}{[Ca^{2+}]_{\text{i}}} \right),$$

and

$$\frac{d[Ca^{2+}]_{\text{i}}}{dt} = \frac{-3I_{\text{Ca}}}{2Fr} - \frac{([Ca^{2+}]_{\text{i}} - [Ca^{2+}]_{\text{res}})}{\tau_{\text{Ca}}}$$

(cf. Fohlmeister et al. 1990 [10]). The $g_{\text{K,Ca}}$ is ligand gated according to the equation

$$g_{\text{K,Ca}} = \overline{g}_{\text{K(Ca)}} \frac{([Ca^{2+}]_{\text{i}}/(Ca^{2+})_{\text{diss}})^2}{1 + ([Ca^{2+}]_{\text{i}}/(Ca^{2+})_{\text{diss}})^2}$$

State variables (m, h, c, n, a, and h_A) of the voltage-gated channels follow the first order kinetic equations of Hodgkin-Huxeley 1952 [11]

$$dx\,/\,dt = -(\alpha_x + \beta_x)\,x + \alpha_x$$

where x is generic for the individual state variables.

Na^+ channel

$$\alpha_m = \frac{-0.6(E+30)}{e^{-0.1(E+30)}-1}; \quad \beta_m = 20e^{-(E+55)/18}$$
$$\alpha_h = 0.4e^{-(E+50)/20}; \quad \beta_h = \frac{6}{e^{-0.1(E+20)}+1}$$

Ca^{2+} channel

$$\alpha_{m_{\text{Ca}}} = \frac{-0.3(E+13)}{e^{-0.1(E+13)}-1}; \quad \beta_{m_{\text{Ca}}} = 10e^{-(E+38)/18}$$

K^+ channel

$$\alpha_n = \frac{-0.02(E+40)}{e^{-0.1(E+40)}-1}; \quad \beta_n = 0.4e^{-(E+50)/80}$$

A channel

$$\alpha_{m_{\text{A}}} = \frac{-0.006(E+90)}{e^{-0.1(E+90)}-1}; \quad \beta_{m_{\text{A}}} = 0.1e^{-(E+30)/10}$$

$$\alpha_{h_{\text{A}}} = 0.04e^{-(E+70)/20}; \quad \beta_{h_{\text{A}}} = \frac{0.6}{e^{-0.1(E+40)}+1}$$

These constants operate in the first-order kinetic equation; $dx/dt = -(\alpha_x + \beta_x)x + \alpha_x$. Membrane potential is in mV; temperature was modeled at $-22\,^{\circ}$C

$$\begin{aligned} \overline{g}_{\text{Na}} &= 50mS/cm^2 & C_m &= 1\mu F/cm^2 \\ \overline{g}_{\text{Ca}} &= 2.2mS/cm^2 & V_{\text{Na}} &= 35mV \\ \overline{g}_{\text{K}} &= 12mS/cm^2 & V_{\text{K}} &= -75mV \\ \overline{g}_{\text{A}} &= 36mS/cm^2 & V_{\text{leakage}} &= -60\,to - 65mV \\ \overline{g}_{\text{K(Ca)}} &= 0.05mS/cm^2 & R_{\text{n}} &\cong 1\,G\Omega \end{aligned}$$

APPENDIX J
MATHEMATICAL MODEL FOR CHEMICAL SYNAPSE [12]

Synaptic current

$$I_{\mathrm{syn}}(t) = g_{max} S(t)(V(t) - E_{\mathrm{syn}})$$

where $S(t)$ is the solution to the following differential equation

$$\frac{dS(t)}{dt} = \frac{S_\infty - S(t)}{(1 - S_\infty)\tau} \quad and \quad S_\infty = \tanh\left(\frac{(V_{\mathrm{pre}} - V_{\mathrm{th}})_*}{V_{\mathrm{slope}}}\right)$$

---

where $(X)_*$ represents the following ramp-like function

$$(X)_* = \begin{cases} \text{if } X \leq 0 \text{ then} \begin{cases} -X & \text{if } X \leq 0 \\ 0 & \text{if } X > 0 \end{cases} \\ \\ \text{if } X \geq 0 \text{ then} \begin{cases} X & \text{if } X \geq 0 \\ 0 & \text{if } X < 0 \end{cases} \end{cases}$$

$S(t)$ = synaptic transfer function
g_{max} = maximum conductance, $2.56\,[\mathrm{nS}]$
E_{syn} = reversal potential, $0\,[\mathrm{mV}]$
τ = time constant, $10\,[\mathrm{ms}]$
V_{slope} = voltage sensitivity of the synapse, $10\,[\mathrm{pA}]$
V_{pre} = presynaptic membrane potential, $[\mathrm{mV}]$
V_{th} = voltage threshold to activate the synapse, $[\mathrm{mV}]$

APPENDIX K
MATHEMATICAL MODEL OF ELECTRICAL SYNAPSES [13], [14]

Experiments show that, to a good approximation, the magnitude of the current that flows through a gap junction is proportional to the magnitude of the difference of the voltages of the two cells, i.e., the gap junction acts like an ohmic resistor:

$$|I_{gap}| = g_c|\Delta V|$$

The sign of the current depends on which cell is being considered. For example, if $V_2 > V_1$ then a current of magnitude $g_c(V_2 - V_1)$ will flow from cell 2 to cell 1. For cell 1 this is an inward (negative) current while for cell 1 it is an outward (positive) current. If $V_2 < V_1$ the the currents will have the opposite signs. In either case, the appropriate way to put this in the the differential equations for the voltages of the two cells is as follows.

$$C_1 \frac{dV_1}{dt} = -I_{ion,1} + I_{app,1} + g_c(V_2 - V_1)$$

$$C_1 \frac{dV_2}{dt} = -I_{ion,2} + I_{app,2} + g_c(V_1 - V_2)$$

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