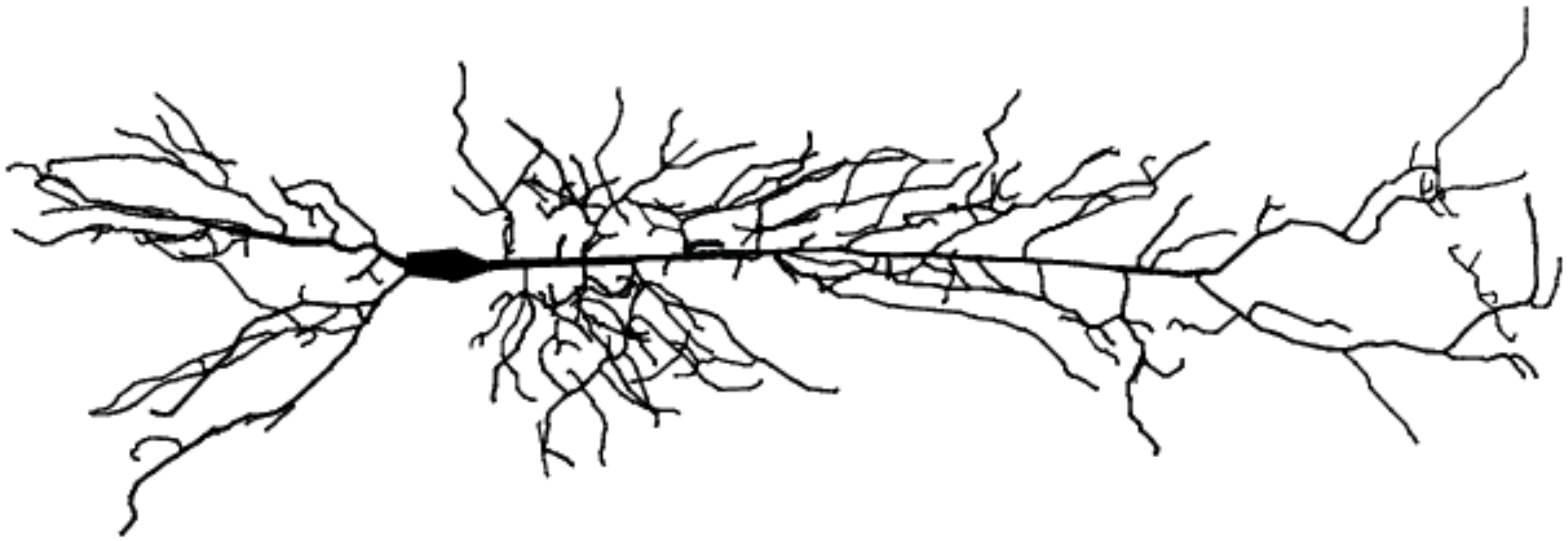
Dendrites, neurons and resonances



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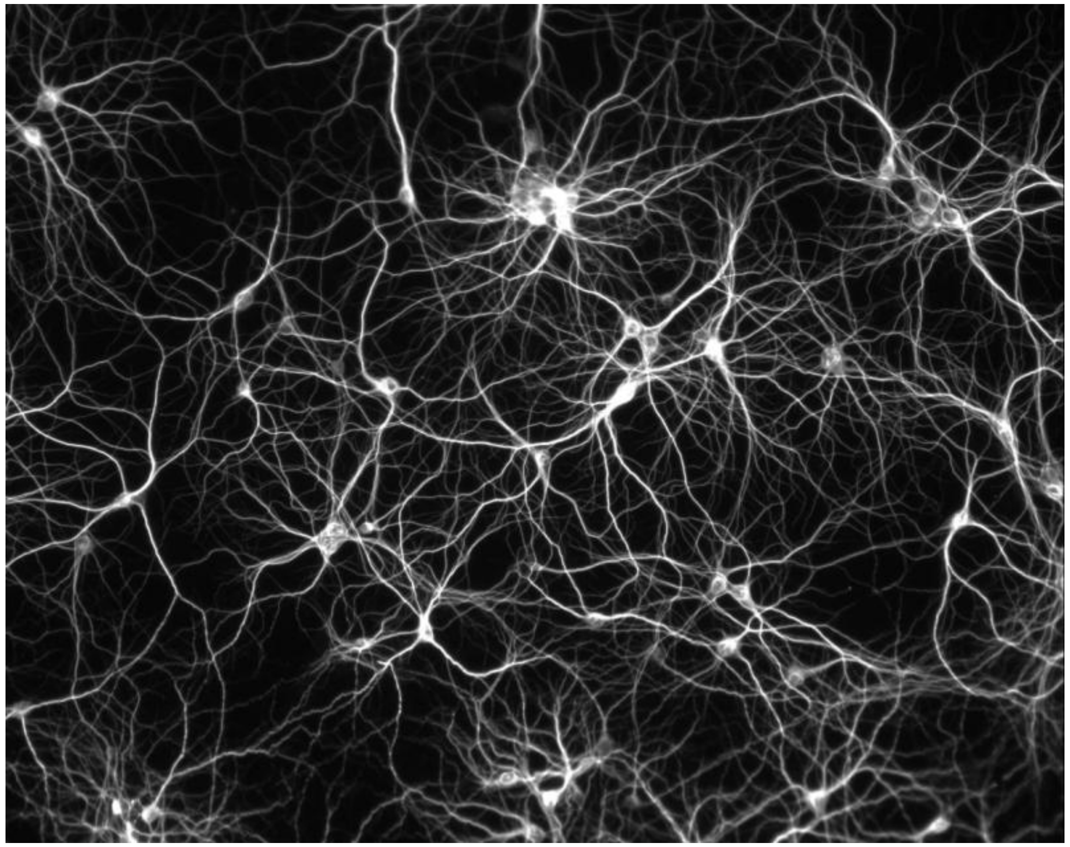
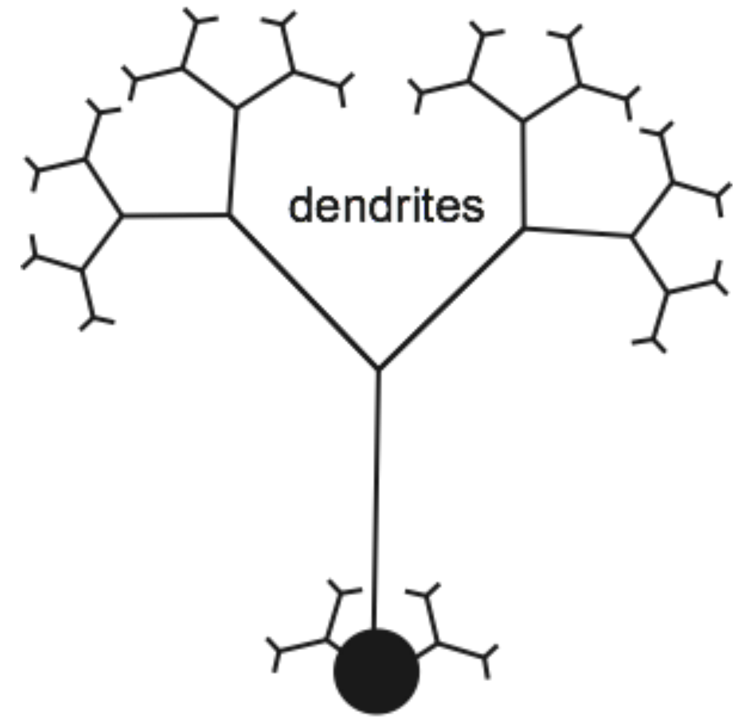
THE UNIVERSITY OF WARWICK

Neural networks



Non-isopotential structure

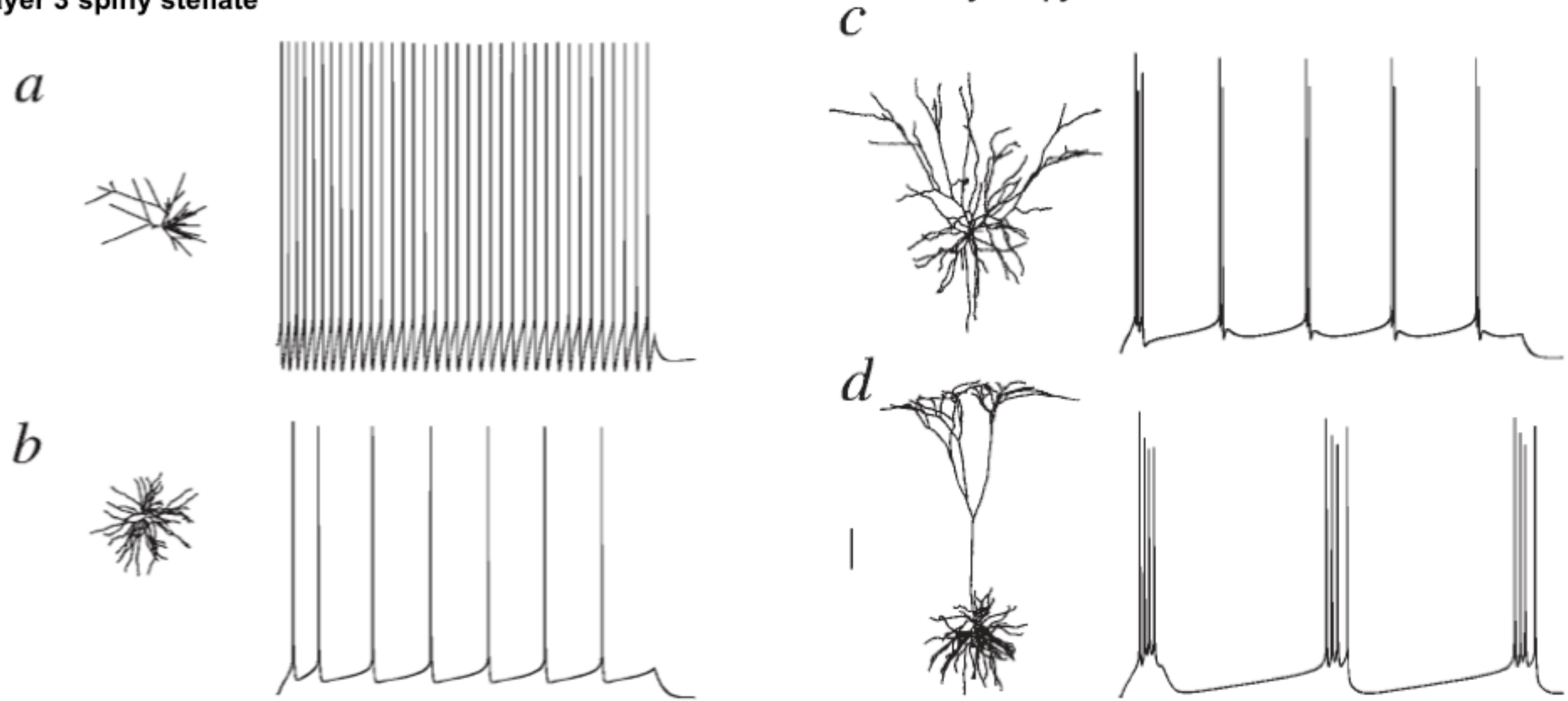


Isopotential soma

Distinct firing patterns

Layer 3 spiny stellate

Layer 3 pyramidal



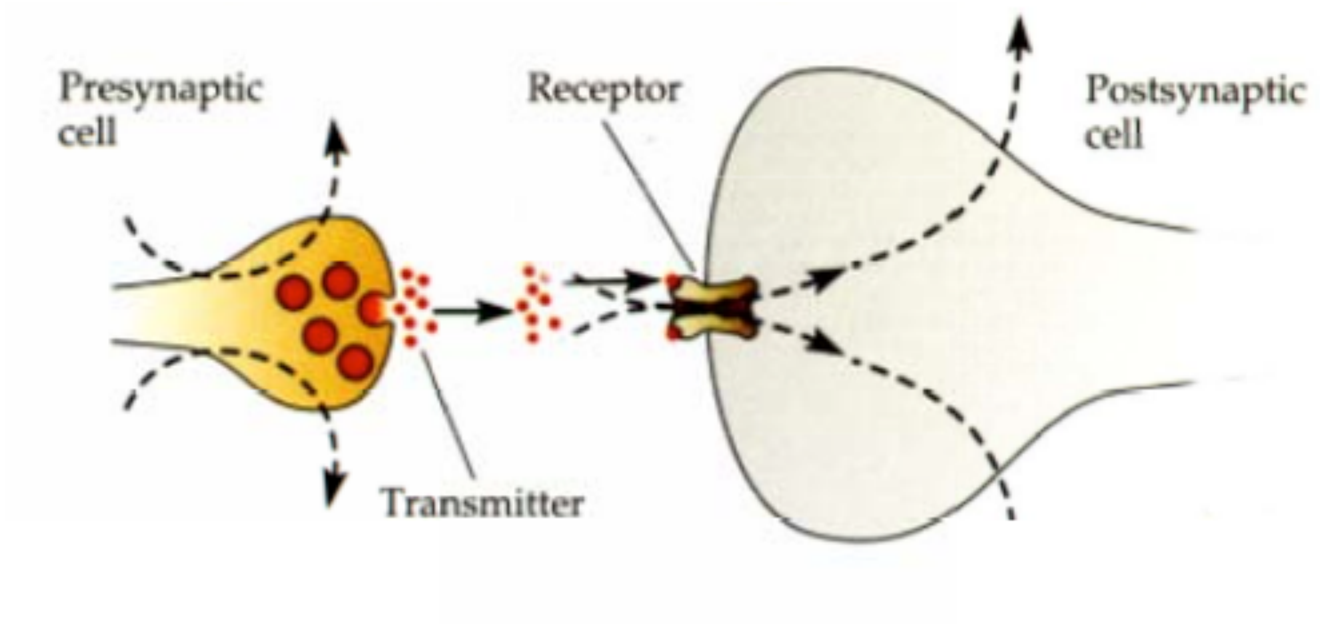
Layer 4 spiny stellate

Layer 5 pyramidal

From Mainen and Sejnowski, 1996

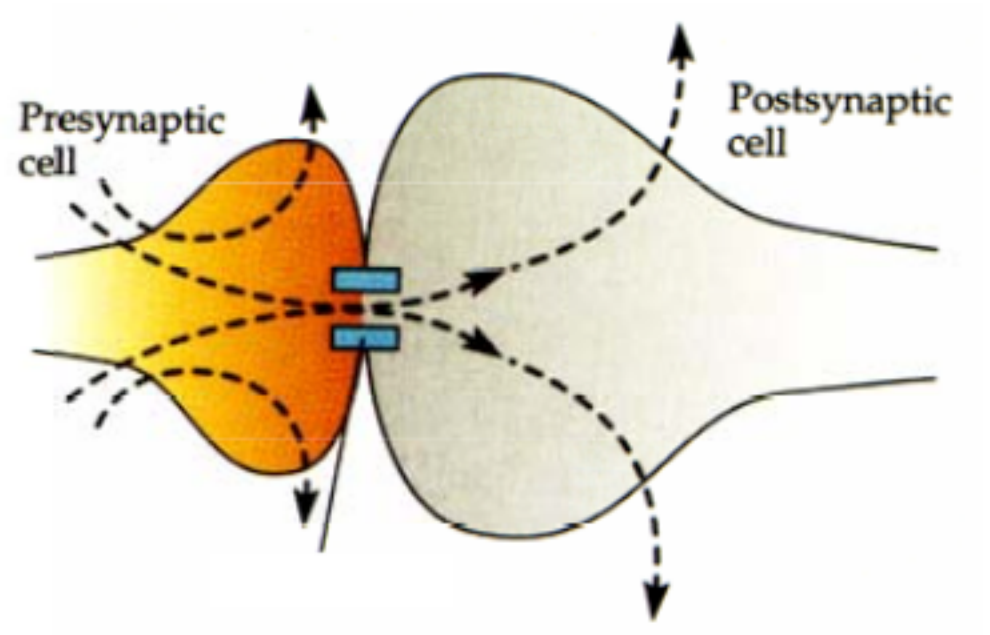
Synapses

with transmitter



chemical synapse

and without

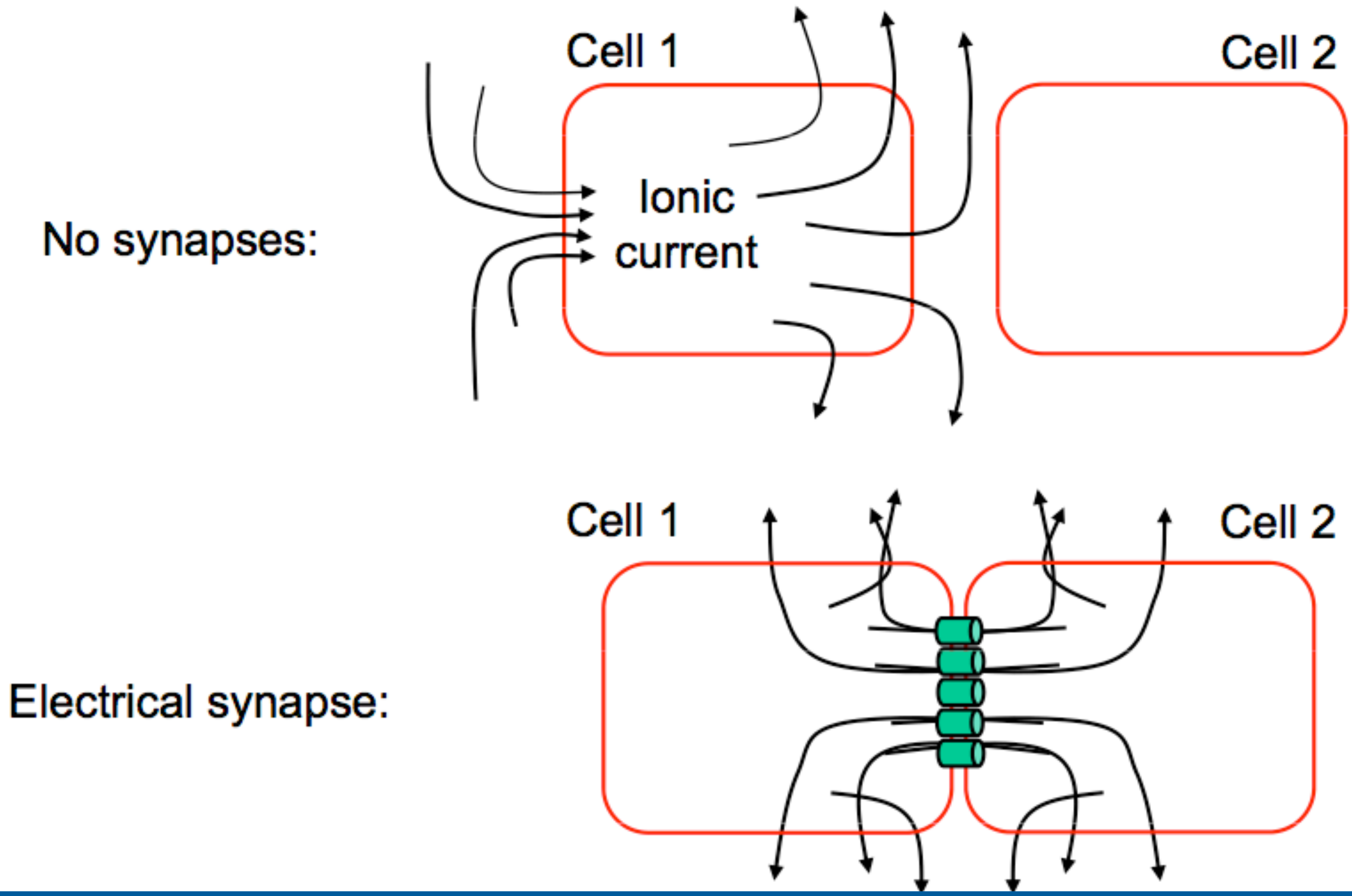


electrical synapse

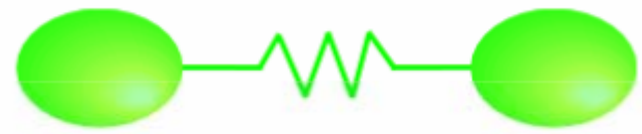
- An electrical synapse is a mechanical and electrically conductive link between two adjacent nerve cells.
- It is formed at a fine gap between the pre- and post-synaptic cells known as a gap junction.

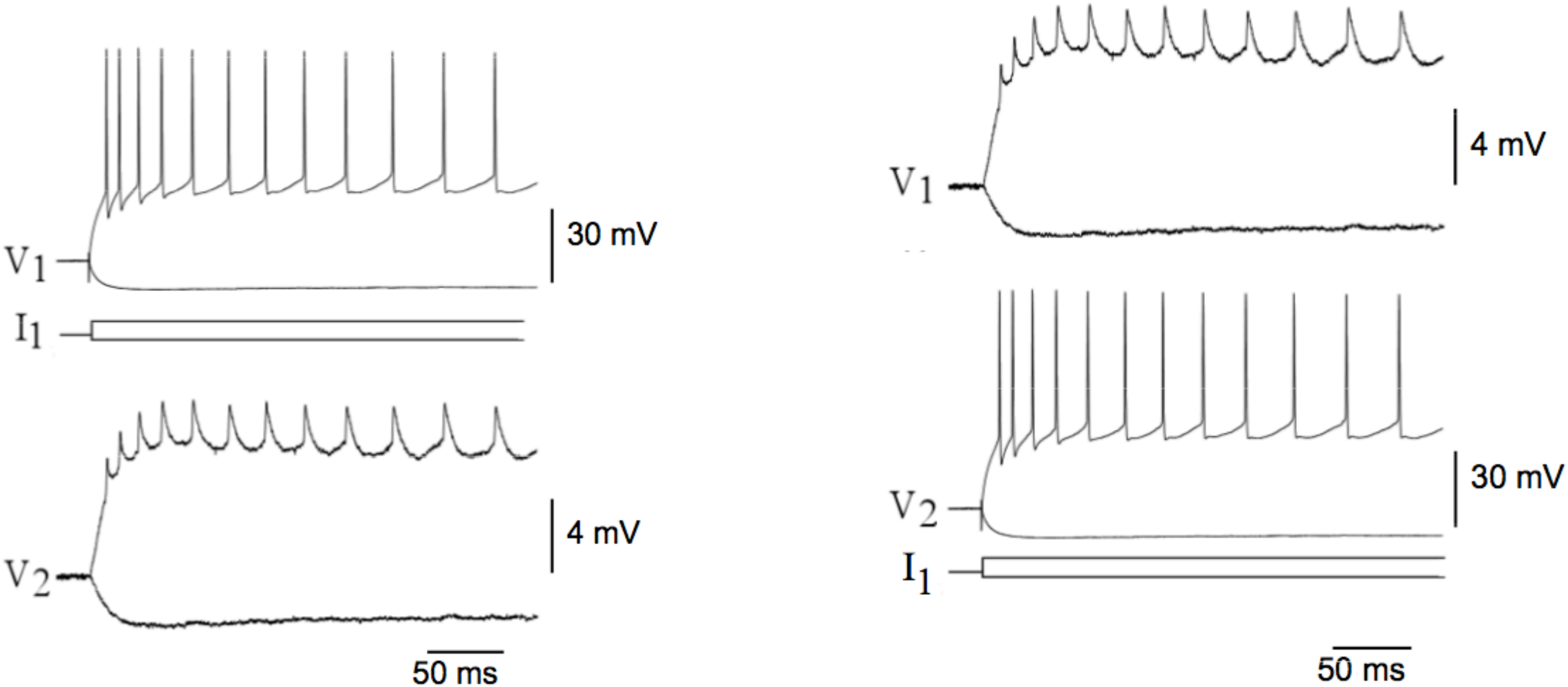
Electrical synapses

- The pore of a gap junction channel is much larger than the pores of the voltage-gated ion channels.
- A variety of substances (ions and even molecules) can simply diffuse between the cytoplasm of the pre- and post-synaptic neurons.



Most electrical synapses are bidirectional and symmetrical





Chemical vs Electrical synaptic transmission

chemical synapse

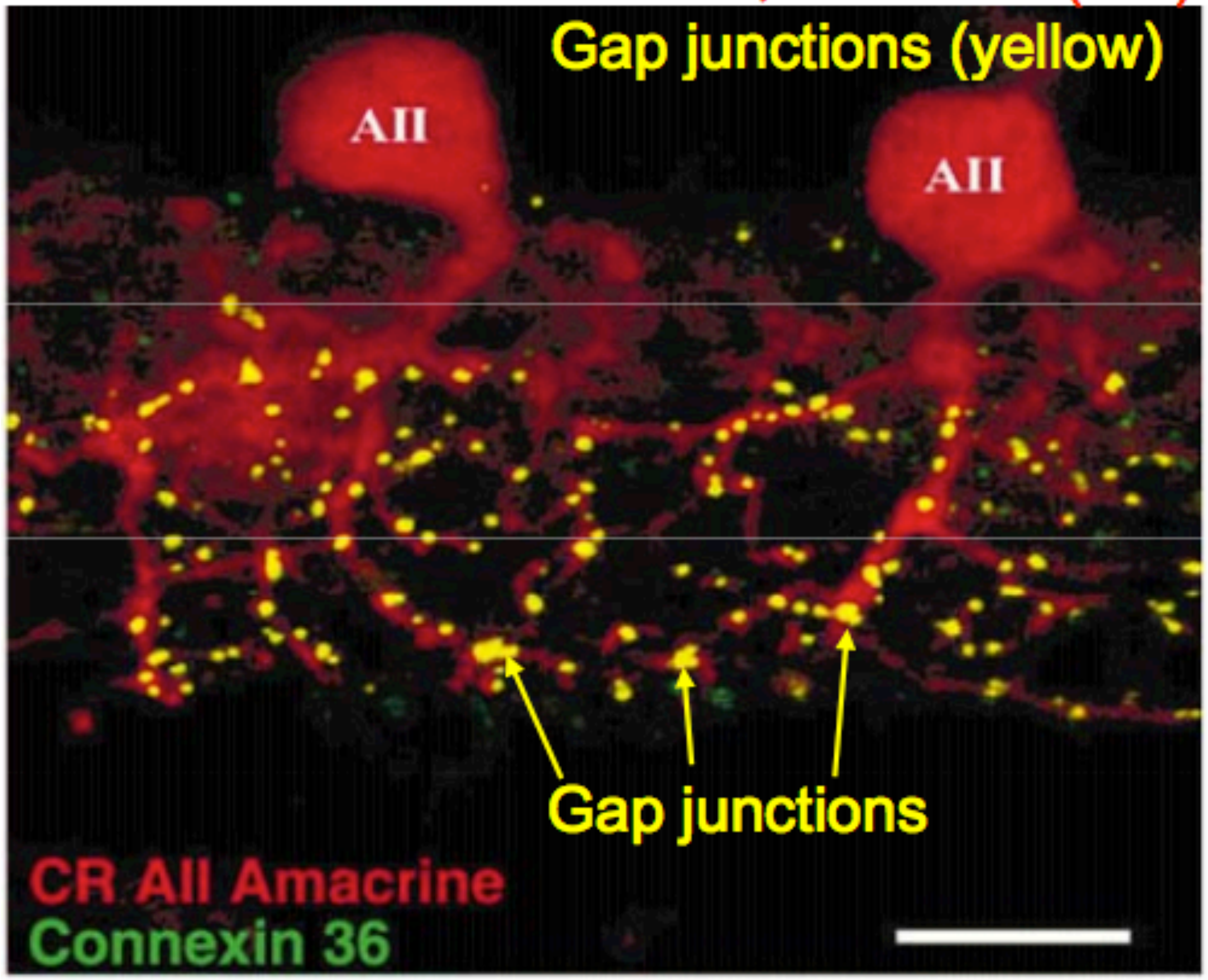
- Unidirectional communication
- Reliability varies
- Metabolically expensive
- Modifiable strength (LTP, LTD)

electrical synapse

- Bidirectional communication
- Very reliable transmission
- Metabolically inexpensive
- Modifiable strength (poorly understood)

Electrical synapses can pass sub-threshold signals and they activate faster than chemical synapses.

Electrical synapses are very common in the retina

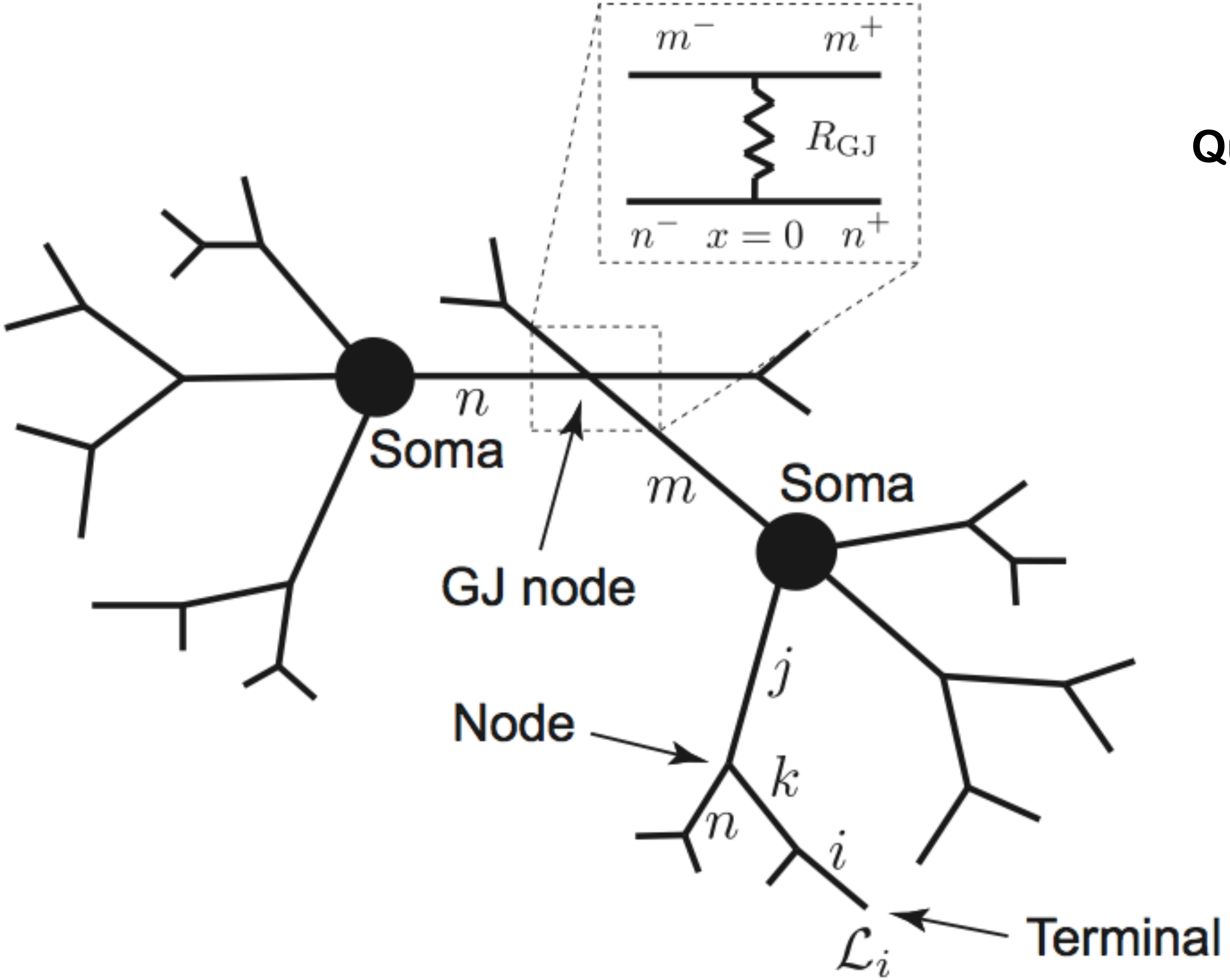


Mills et al., J Comp Neurol, 2001

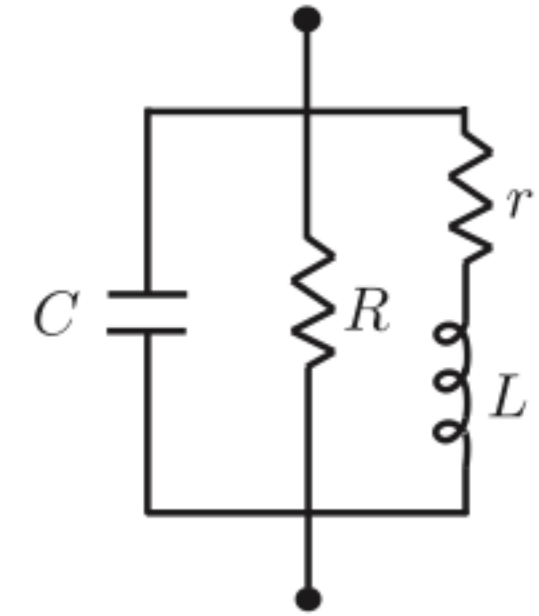
Elimination of electrical synapses from the brain by knocking out the Cx36 gene demonstrates:

- The mice are viable
- Retinal deficits (total night blindness)
- Impairment of fine motor control
- EEG abnormalities
- Impairment of complex motor learning tasks and object memory
- Deficits of circadian behaviour
- ...

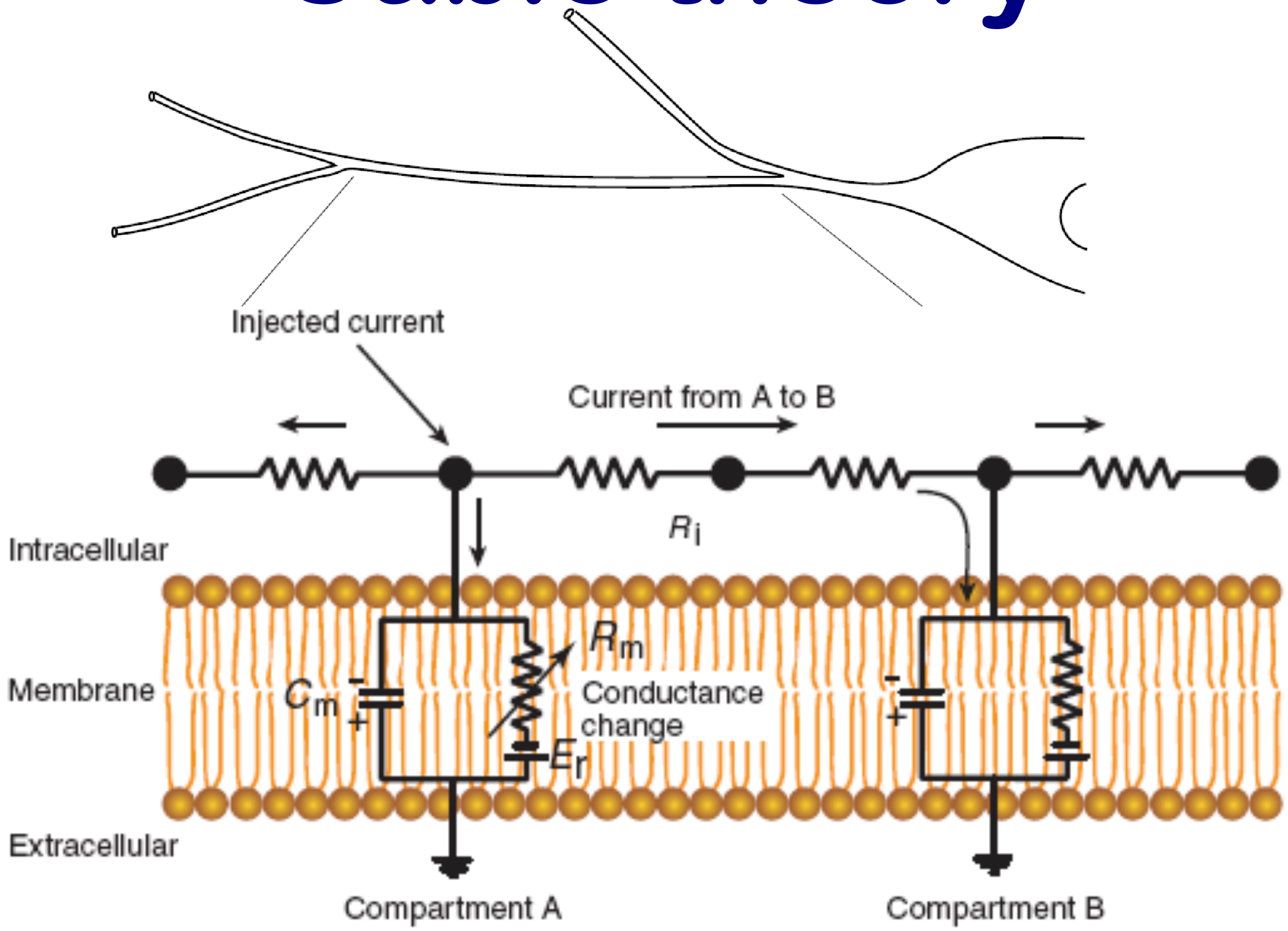
Modelling framework



Quasi-active membrane



Cable theory



Wilfrid Rall

$$\tau \frac{\partial V}{\partial t} = \lambda^2 \frac{\partial^2 V}{\partial x^2} - \sum_i g_i (V - V_i) + I_{\text{app}}$$

space constant

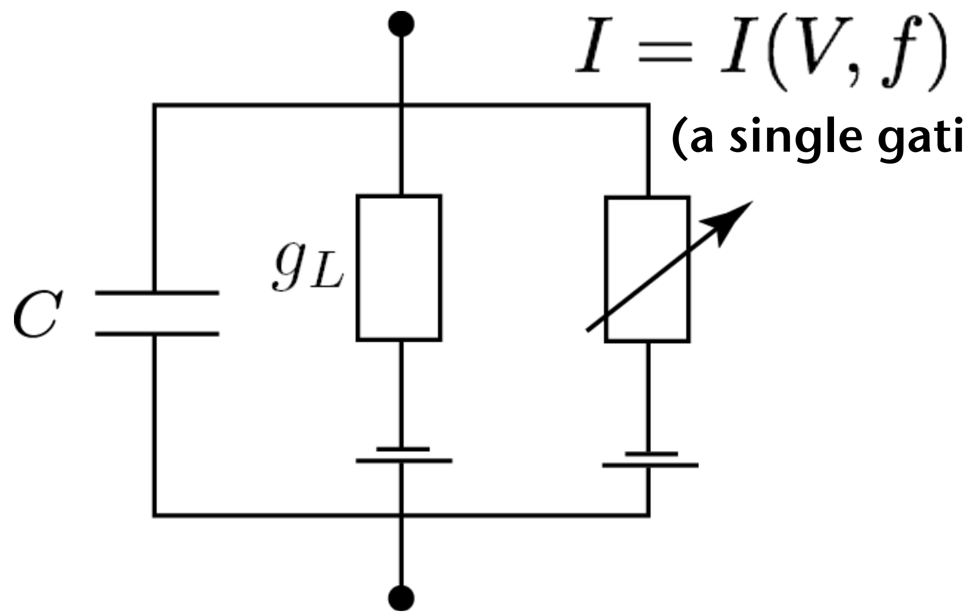
$$\lambda = \sqrt{r_m / r_a}$$

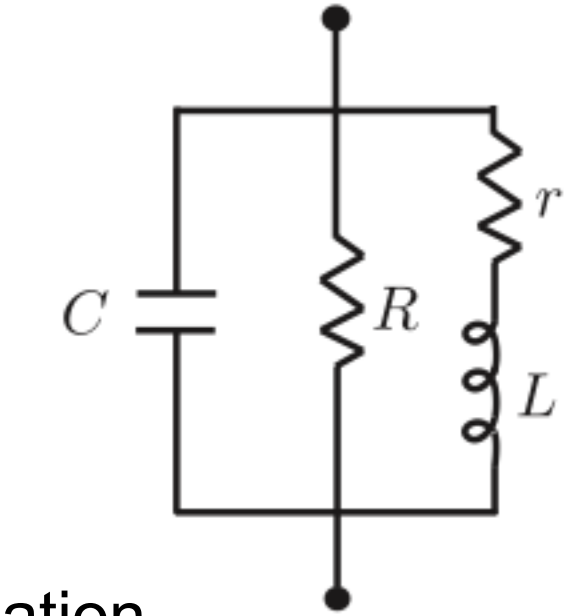
membrane time constant

$$\tau = r_m c_m$$

The Theoretical Foundations of Dendritic Function (The collected papers of Wilfrid Rall)
edit. by I Segev, J Rinzel & G M Shepherd, 1994

Quasi-active (resonant) dendrites





After linearisation

$$\frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} - \frac{V}{\tau} - I(V) + I_{syn}$$

$$\boxed{\begin{aligned} \frac{\partial V}{\partial t} &= D\frac{\partial^2 V}{\partial x^2} - \frac{V}{\tau} - I + I_{\mathrm{syn}} \\ L\frac{\mathrm{d}I}{\mathrm{d}t} &= V - rI \end{aligned}}$$

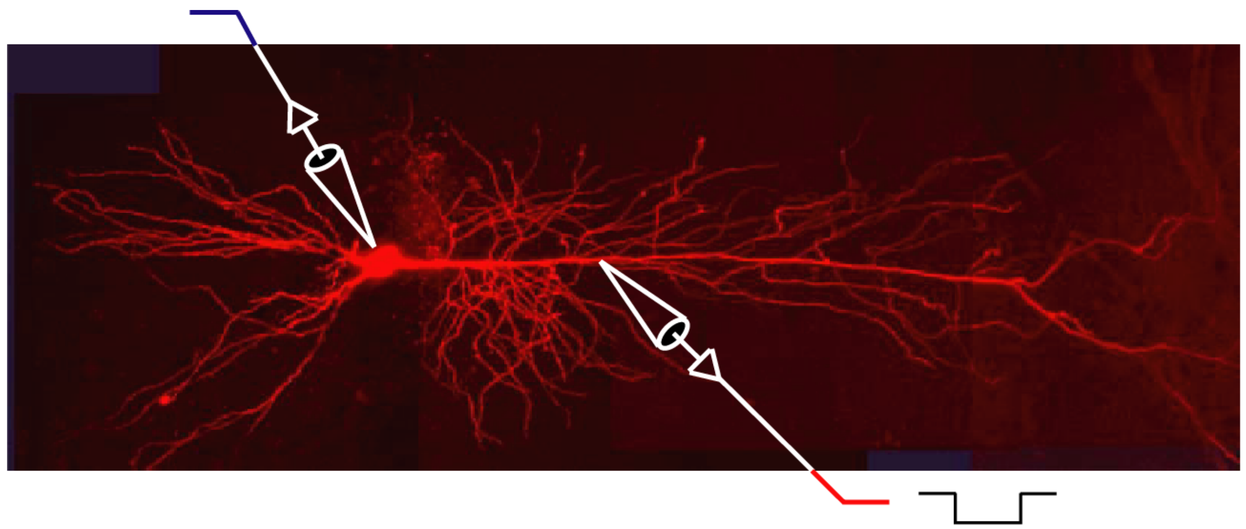
Taking Laplace transform we obtain

$$G_\infty(x,s) = \frac{\mathrm{e}^{-\gamma(s)|x|}}{2D\gamma(s)}$$

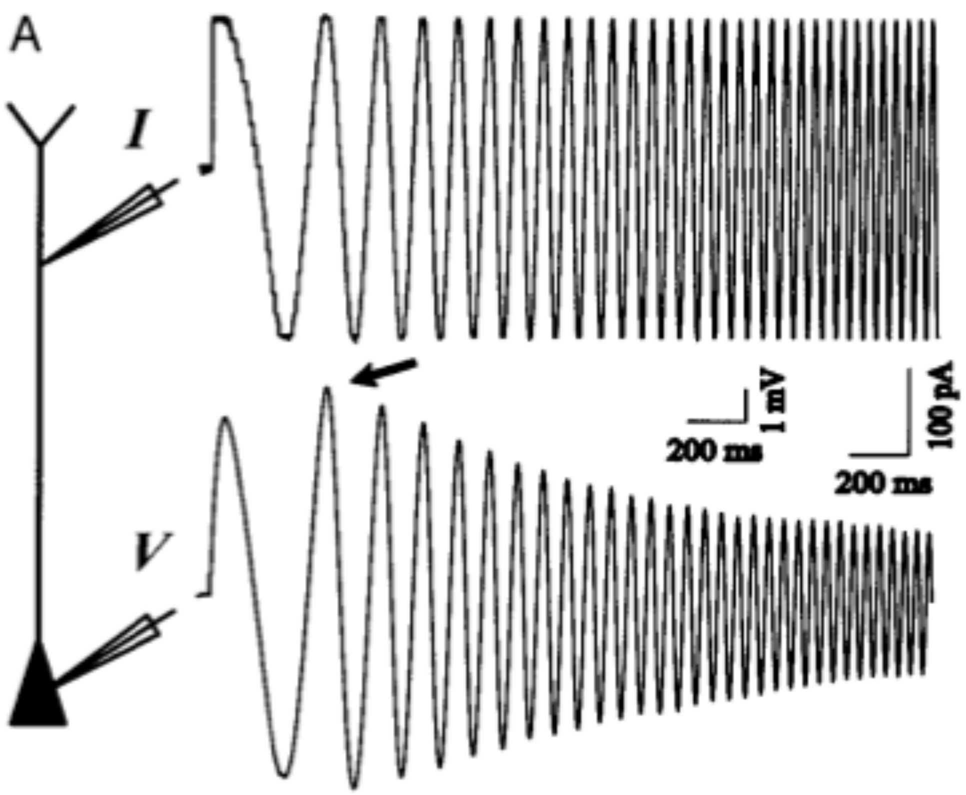
for a single infinite branch

$$\gamma(s)^2 = (s + 1/\tau + 1/(r + sL))/D$$

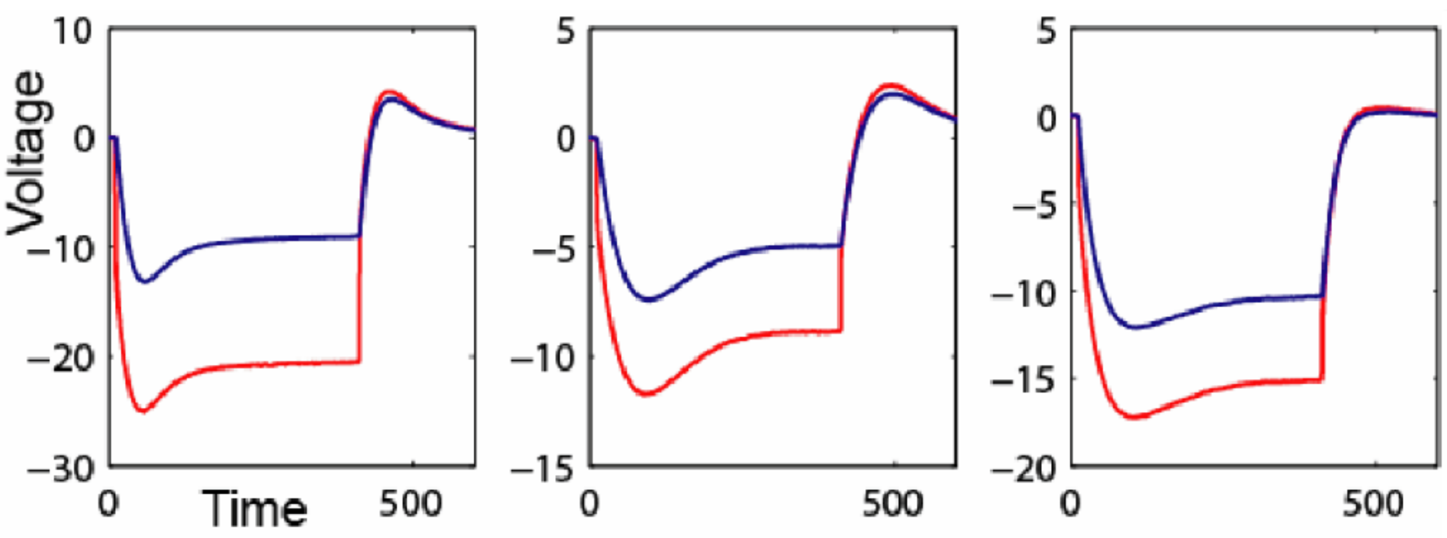
Dendrites with Ih (hyperpolarisation-activated) channels



A rat CA1 hippocampal pyramidal cell (C Colbert's data)



D Ulrich, J Neurophysiol, 2002

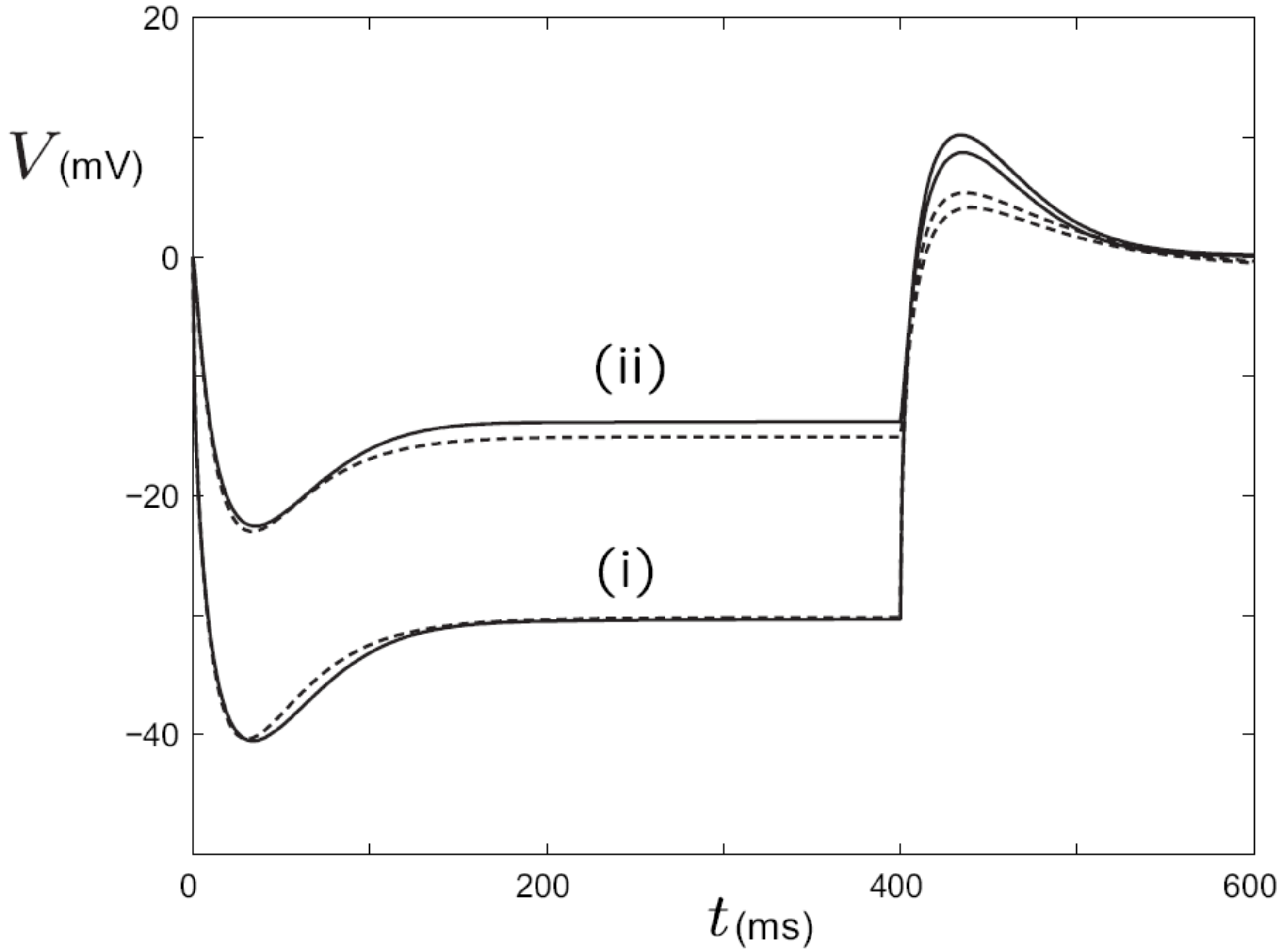


Nonlinear vs linear model of Ih current

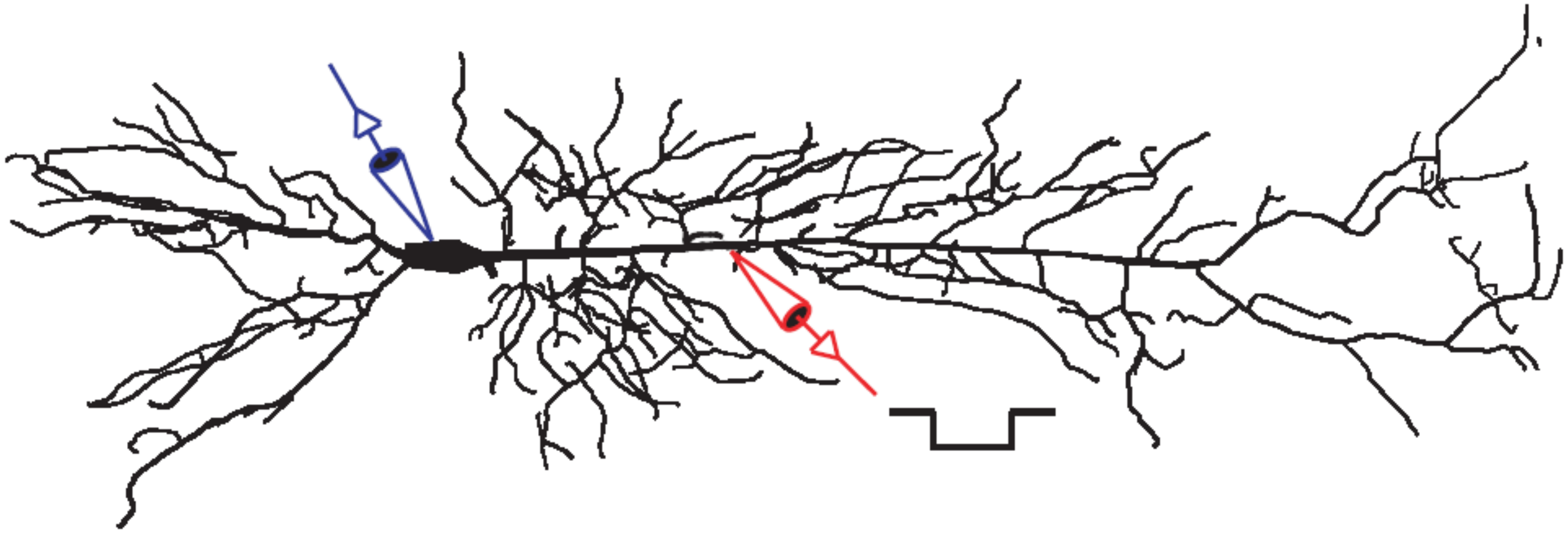
Model of nonlinear I_h current (Magee (1998) Journal of Neuroscience 18)

$$I_h = g_h(V - V_h)f$$

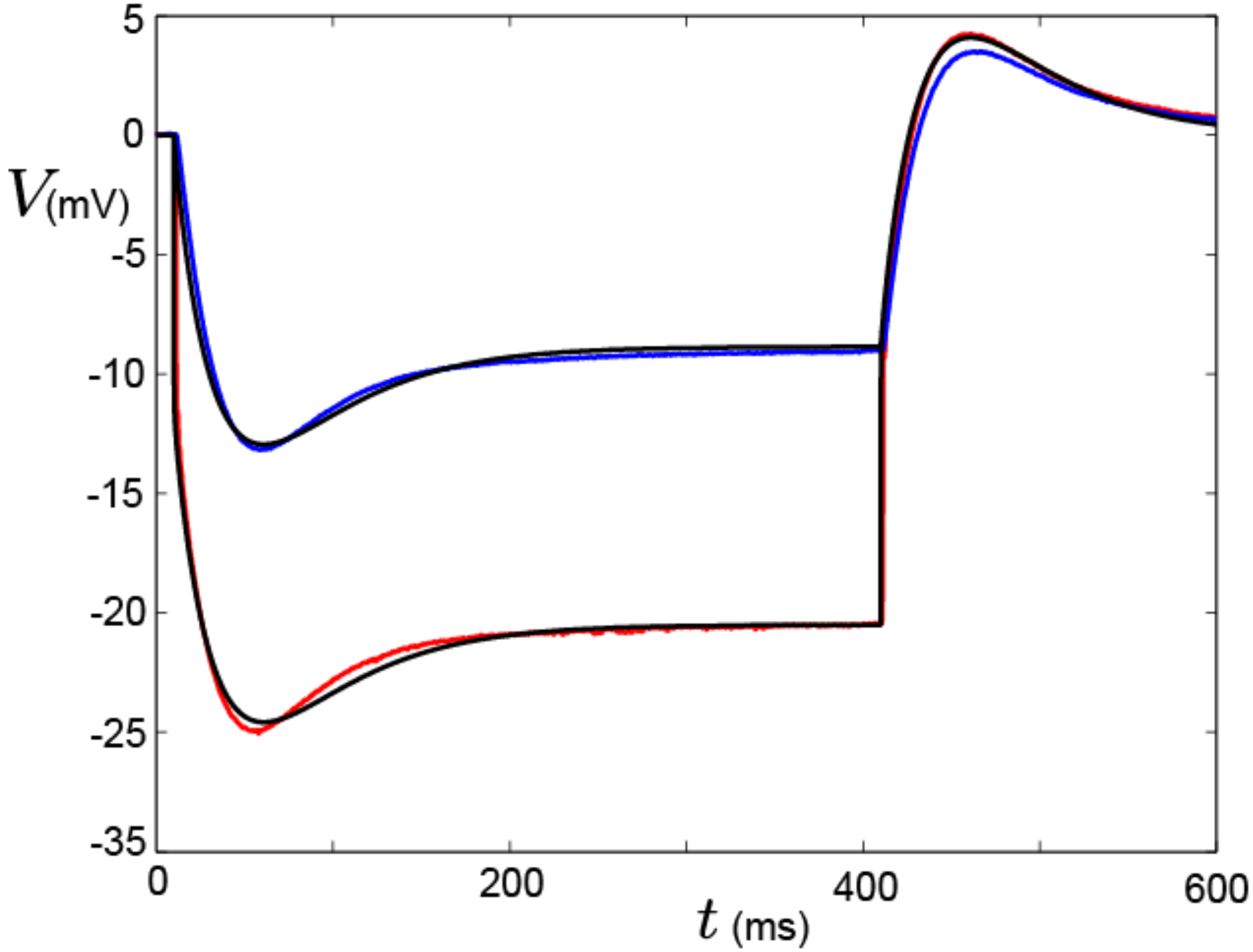
$f(V)$ **- a single gating variable (satisfies a nonlinear ODE)**



Dashed line: Magee’s current
Solid line: ‘LRC’ circuit



A reconstructed rat CA1 hippocampal pyramidal cell

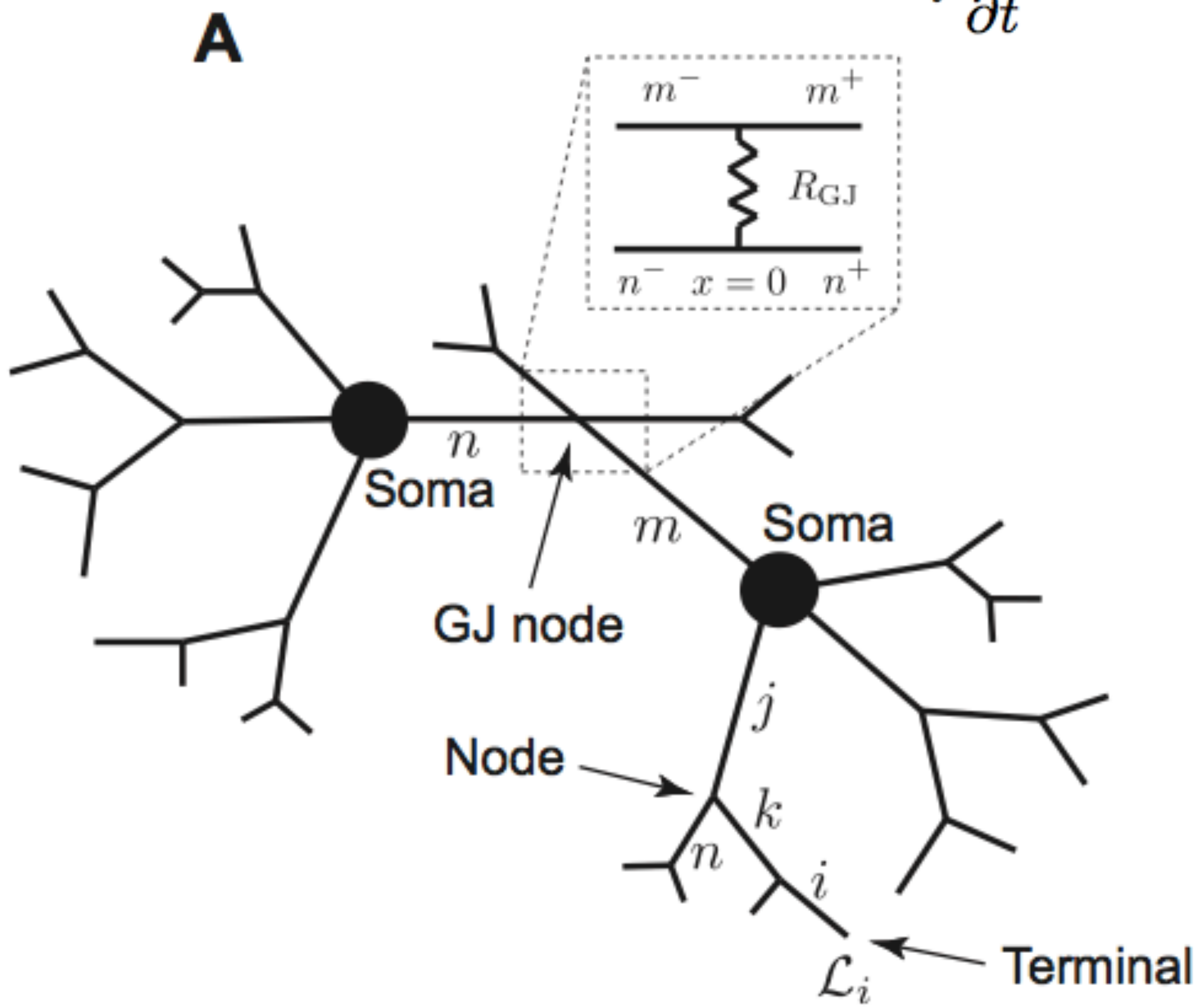


Biol. Cybern. 97, 2007

Modelling framework

$$\frac{\partial V_i}{\partial t} = D_i \frac{\partial^2 V_i}{\partial x^2} - \frac{V_i}{\tau_i} - \frac{1}{C_i}\left[I_i - I_{\mathrm{inj},i}\right],$$

$$L_i \frac{\partial I_i}{\partial t} = -r_i I_i + V_i, \qquad 0 \le x \le \mathcal{L}_i, \qquad t \ge 0$$

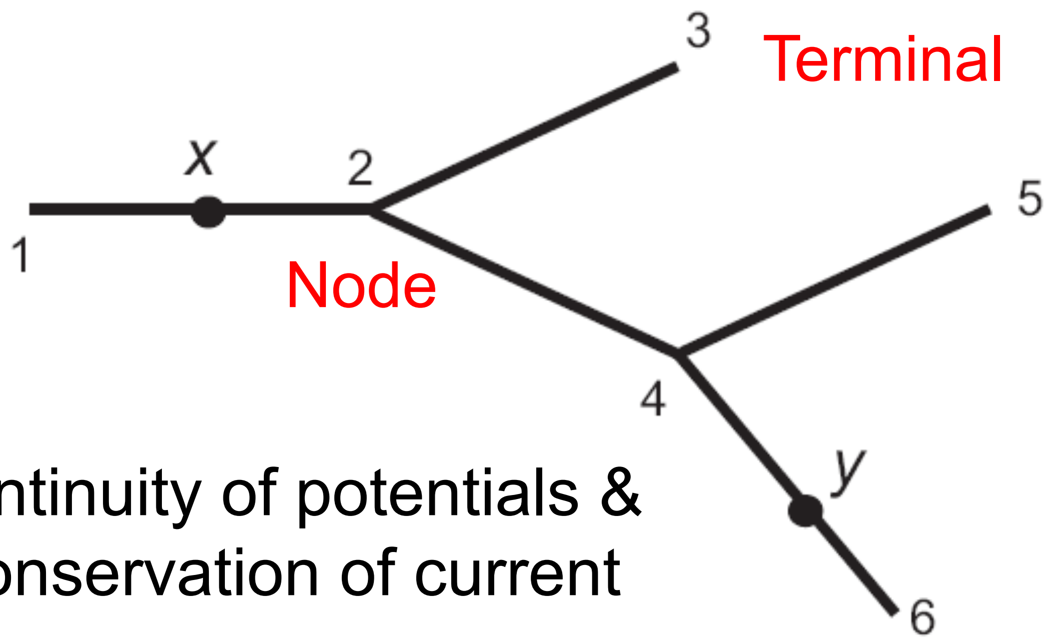


Boundary conditions at

- nodes
- terminals
- somas
- GJ

J Math Neurosci, 2013

Sum-over-trips approach for single cell



continuity of potentials &
conservation of current

$$G_{ij}(x, y, t)$$

Abbott et al. Biol. Cybern. 66, 1991

$$\boxed{G_{ij}(x, y, t) = \sum A_{\text{trip}} G_{\infty}(L_{\text{trip}}, t)}$$

Trips

$x \longrightarrow 2 \longrightarrow 4 \longrightarrow y$

$x \longrightarrow 1 \longrightarrow 2 \longrightarrow 4 \longrightarrow y$

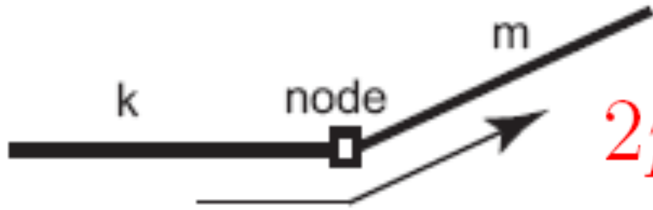
$x \longrightarrow 2 \longrightarrow 4 \longrightarrow 6 \longrightarrow y$

$x \longrightarrow 1 \longrightarrow 2 \longrightarrow 4 \longrightarrow 6 \longrightarrow y$

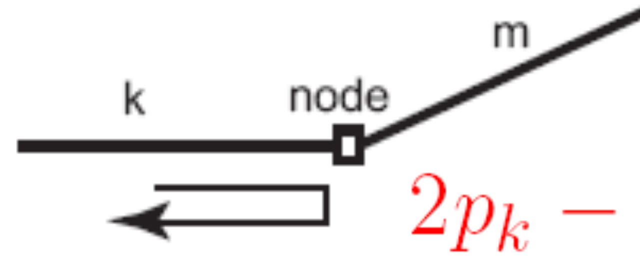
$$G_{\infty}(x, t) = \frac{1}{\sqrt{4\pi D t}} \mathrm{e}^{-t/\tau} \mathrm{e}^{-x^2/(4Dt)}$$

Coefficients A_{trip}

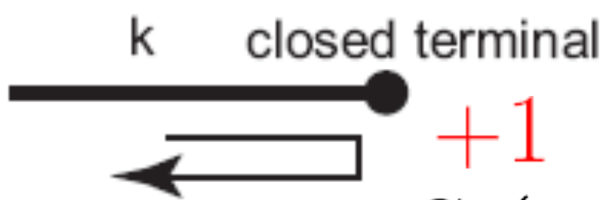
Factor of segment $$p_m = \frac{a_m^{3/2}}{\sum_{k\ on\ node} a_k^{3/2}}$$



$2p_m$

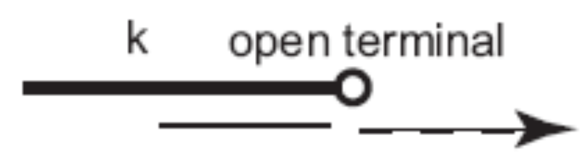


$2p_k - 1$



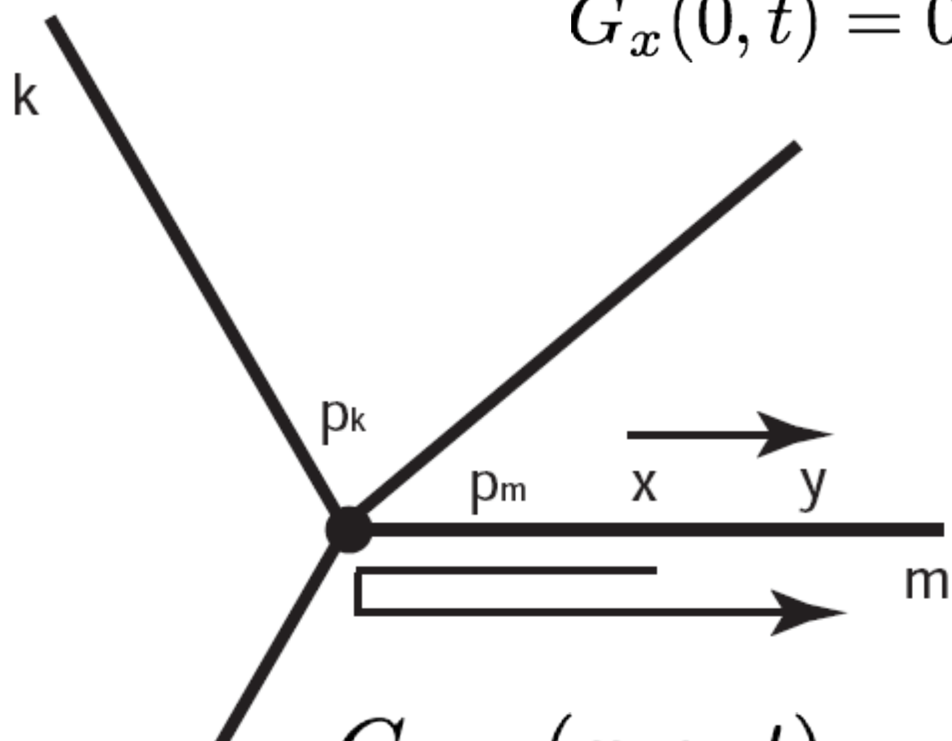
$+1$

$G_x(0,t) = 0$



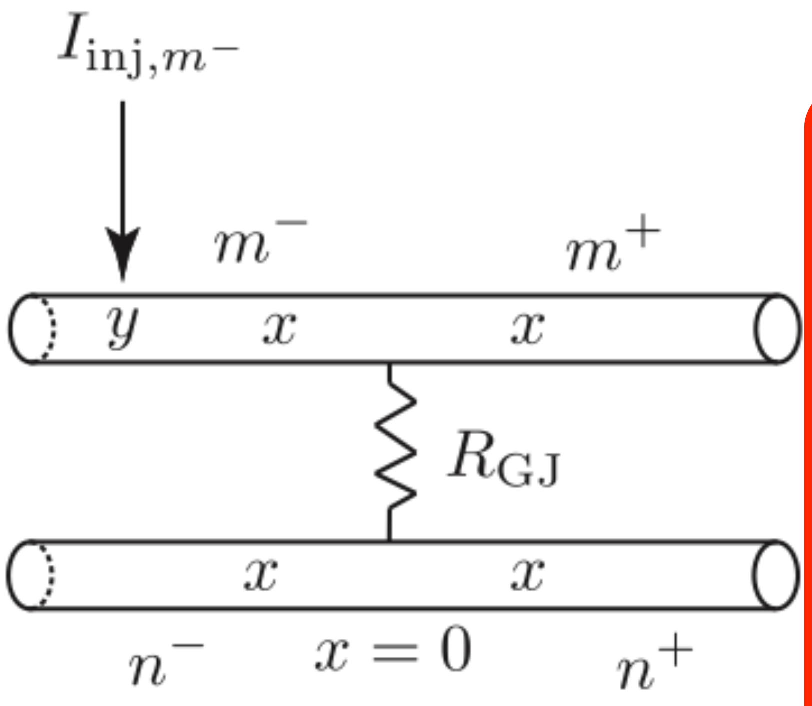
-1

$G(0,t) = 0$



$$G_{mm}(x,y,t) = G_\infty(x-y,t) + (2p_m - 1)G_\infty(x+y,t)$$

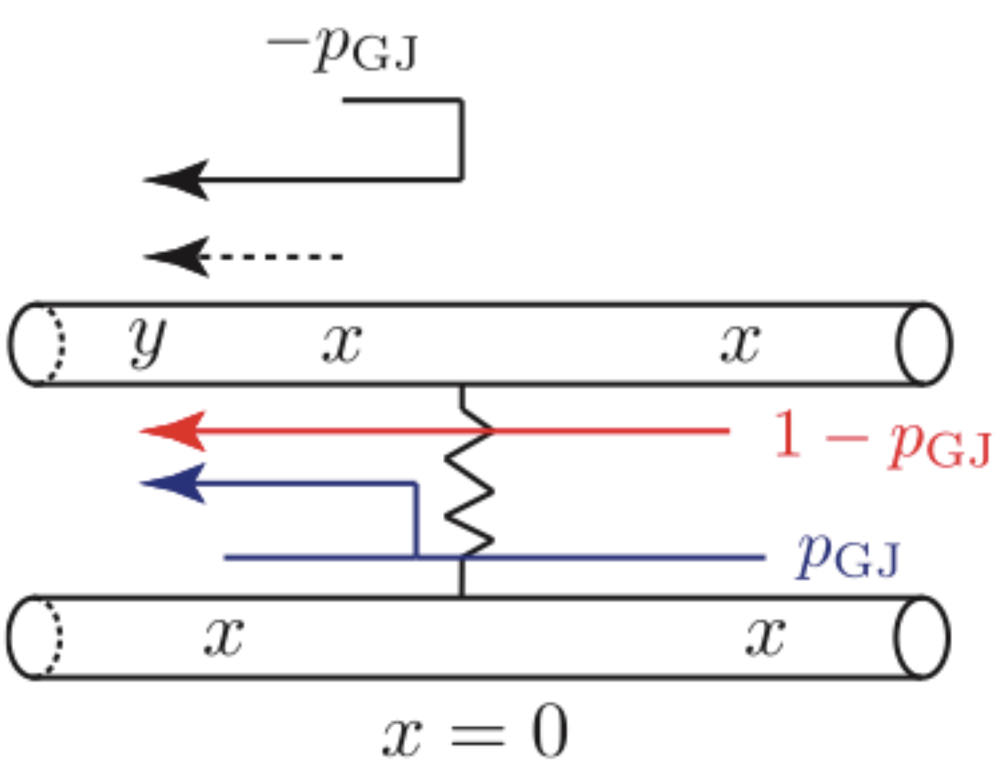
Two simplified identical cells



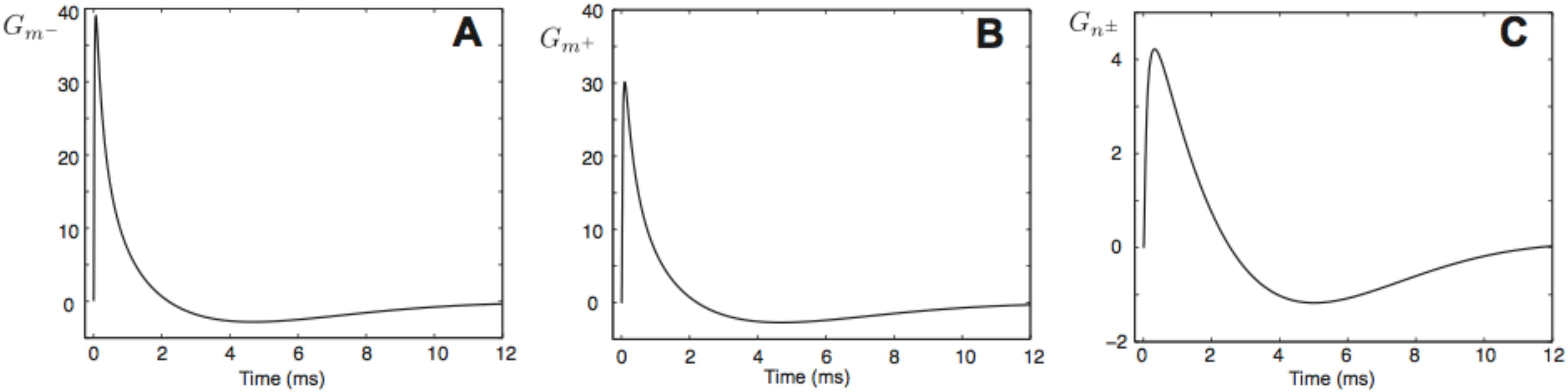
$$
\begin{aligned}
\widehat{G}_{m^-}(x,y,\omega) &= \frac{1}{C}\left[\frac{\mathrm{e}^{-\gamma(\omega)|x-y|}}{2D\gamma(\omega)} - p_{\mathrm{GJ}}(\omega)\frac{\mathrm{e}^{-\gamma(\omega)|x+y|}}{2D\gamma(\omega)}\right], \\
\widehat{G}_{m^+}(x,y,\omega) &= \frac{1}{C}\left[(1-p_{\mathrm{GJ}}(\omega))\frac{\mathrm{e}^{-\gamma(\omega)|x+y|}}{2D\gamma(\omega)}\right], \\
\widehat{G}_{n^-}(x,y,\omega) &= \widehat{G}_{n^+}(x,y,\omega) = \frac{1}{C}\left[p_{\mathrm{GJ}}(\omega)\frac{\mathrm{e}^{-\gamma(\omega)|x+y|}}{2D\gamma(\omega)}\right]
\end{aligned}
$$

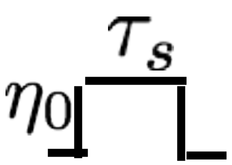
$$\gamma^2(\omega) = \frac{1}{D}\left[\frac{1}{\tau} + \omega + \frac{1}{C(r+\omega L)}\right]$$

$$p_{\mathrm{GJ}}(\omega) = \frac{1}{2(z(\omega)R_{\mathrm{GJ}}+1)}, \quad z(\omega) = \gamma(\omega)/r_a$$

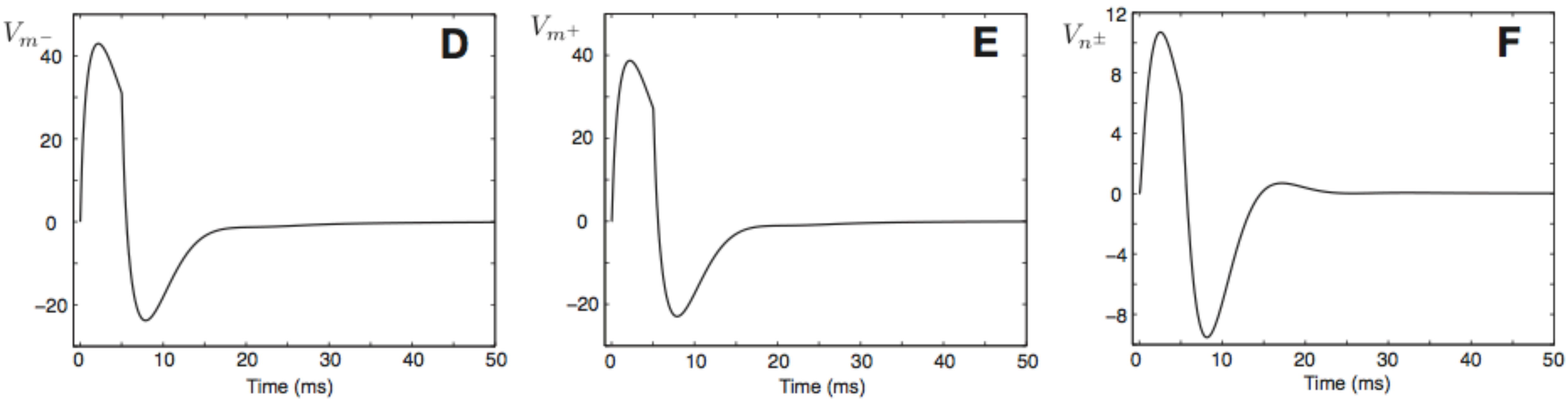


Response function





$$V_k(x,t) = \mathfrak{L}^{-1}\left[\widehat{G}_k(x,y,\omega)\widehat{I}(\omega)\right], \qquad k \in \{m^-, m^+, n^-, n^+\}$$



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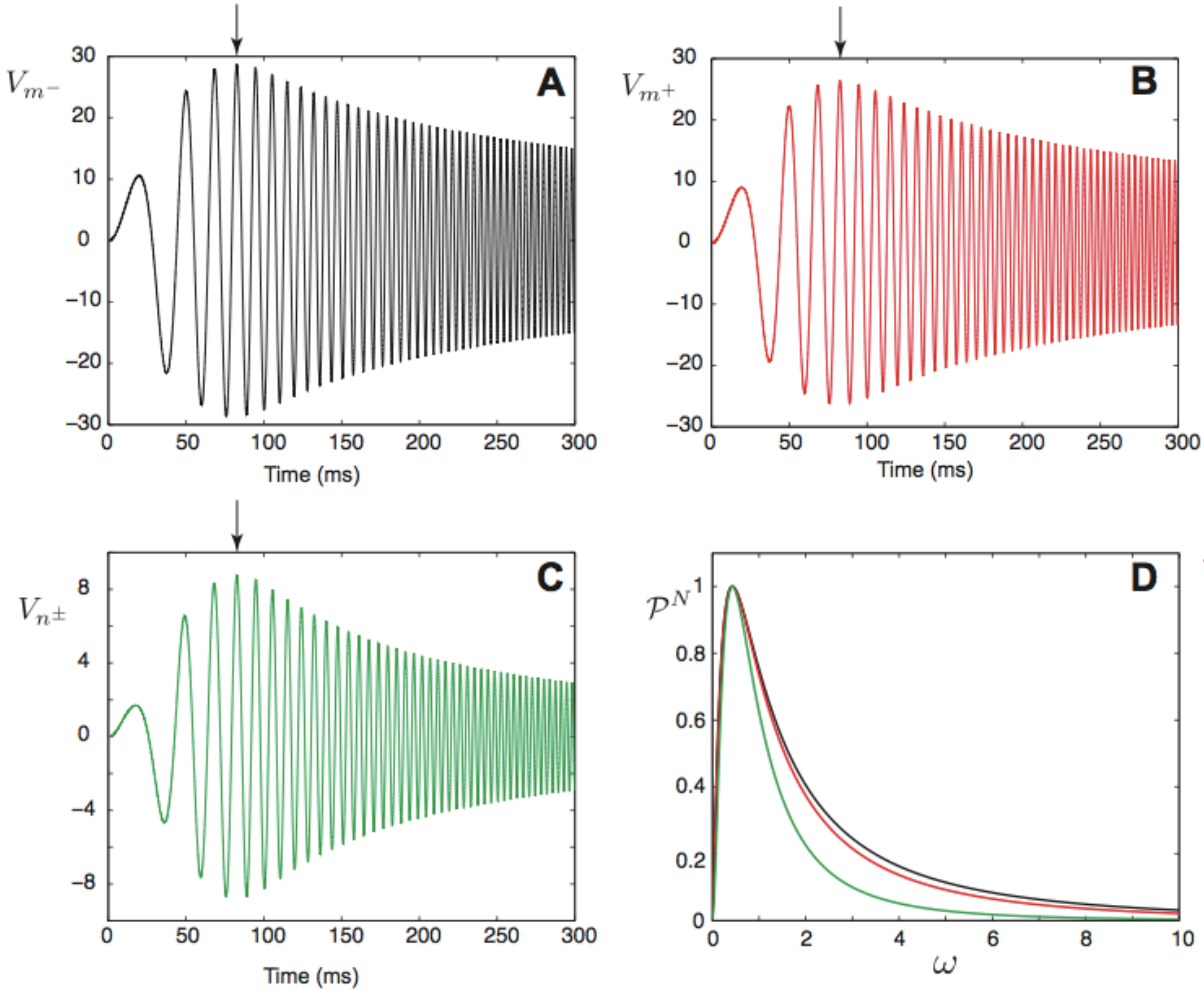
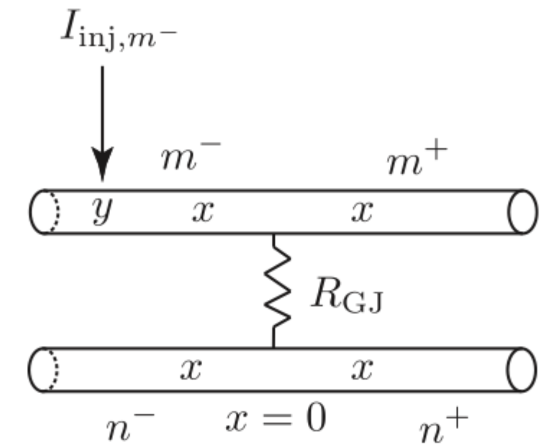
$$I_{\text{chirp}}(t) = A_{\text{chirp}}\sin(\omega_{\text{chirp}}\ t^2)$$

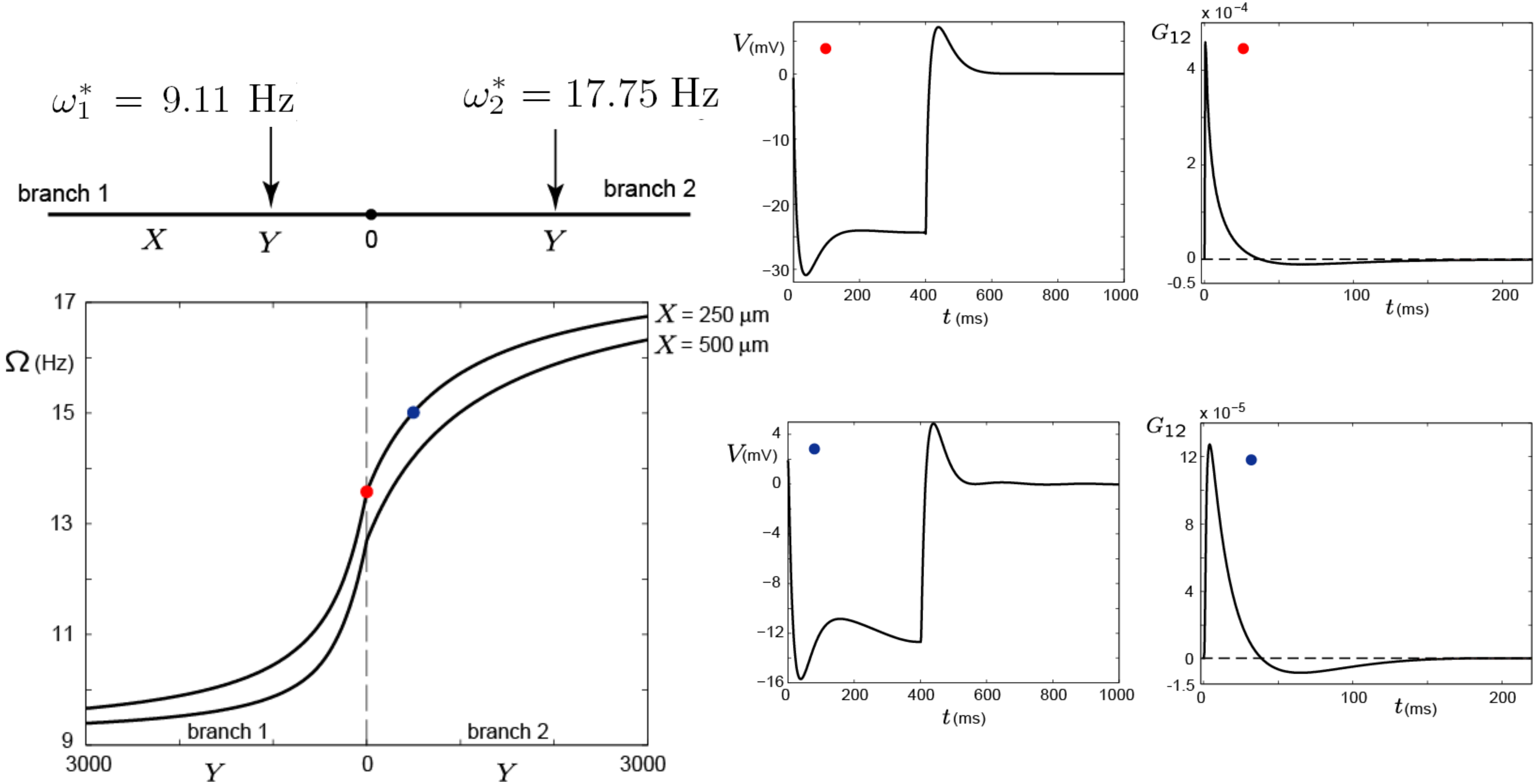




power function

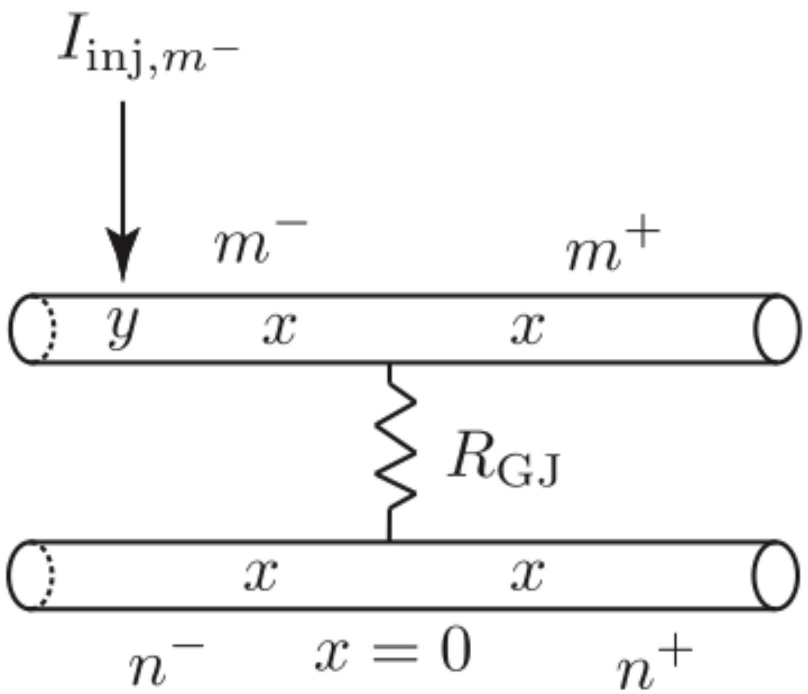
$$\mathcal{P}_k(x,y,\omega) = \left|\widehat{G}_k(x,y,\omega)\right|^2$$

Preferred frequency as a function of location



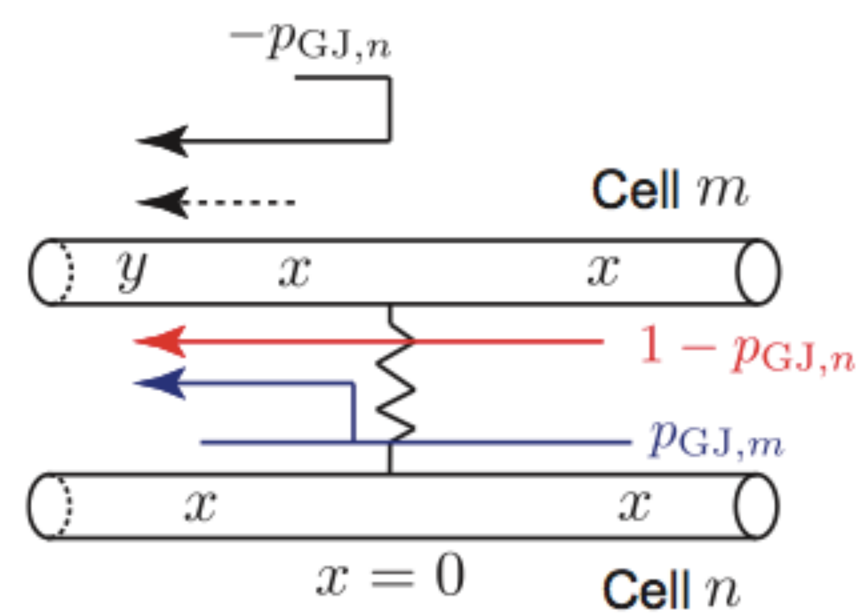
Biol. Cybern. 97, 2007

Two simplified nonidentical cells



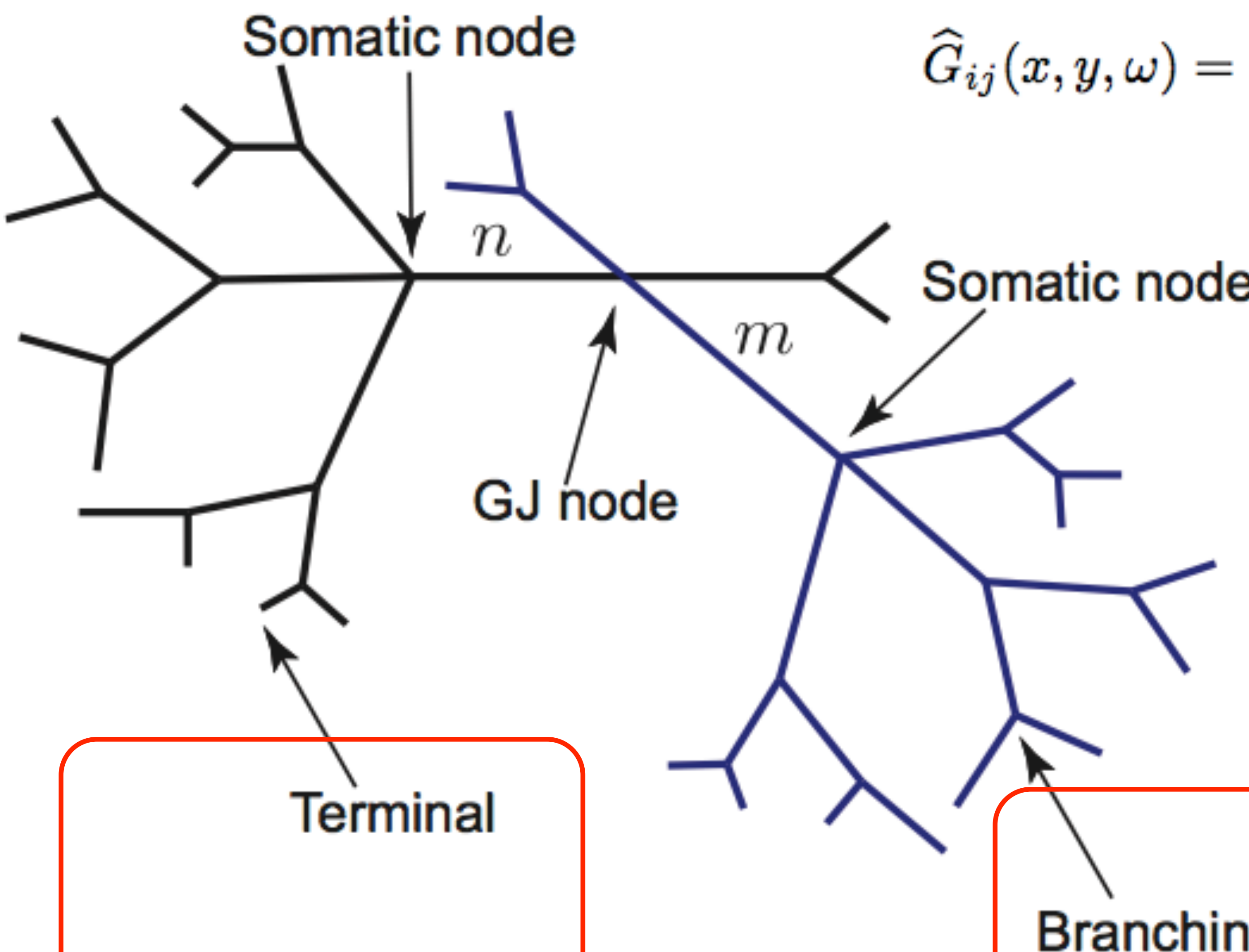
$$
\begin{aligned}
\widehat{G}_{m^-}(x,y,\omega) &= \frac{1}{C_m}\left[\frac{\mathrm{e}^{-\gamma_m(\omega)|x-y|}}{2D_m\gamma_m(\omega)} - p_{\mathrm{GJ},n}(\omega)\frac{\mathrm{e}^{-\gamma_m(\omega)|x+y|}}{2D_m\gamma_m(\omega)}\right], \\
\widehat{G}_{m^+}(x,y,\omega) &= \frac{1}{C_m}\left[(1-p_{\mathrm{GJ},n}(\omega))\frac{\mathrm{e}^{-\gamma_m(\omega)|x+y|}}{2D_m\gamma_m(\omega)}\right], \\
\widehat{G}_{n^-}(x,y,\omega) &= \widehat{G}_{n^+}(x,y,\omega) = \frac{1}{C_m}\left[p_{\mathrm{GJ},m}(\omega)\frac{\mathrm{e}^{-|\gamma_n(\omega)x+\gamma_m(\omega)y|}}{2D_m\gamma_m(\omega)}\right]
\end{aligned}
$$

$$
\begin{aligned}
\gamma_m^2(\omega) &= \frac{1}{D_m}\left[\frac{1}{\tau_m} + \omega + \frac{1}{C_m(r_m + \omega L_m)}\right] \\
\gamma_n^2(\omega) &= \frac{1}{D_n}\left[\frac{1}{\tau_n} + \omega + \frac{1}{C_n(r_n + \omega L_n)}\right]
\end{aligned}
$$



$$
\begin{aligned}
p_{\mathrm{GJ},m}(\omega) &= \frac{z_m(\omega)}{z_m(\omega) + z_n(\omega) + 2R_{\mathrm{GJ}}z_m(\omega)z_n(\omega)}, \qquad z_m(\omega) = \gamma_m(\omega)/r_{a,m}, \\
p_{\mathrm{GJ},n}(\omega) &= \frac{z_n(\omega)}{z_m(\omega) + z_n(\omega) + 2R_{\mathrm{GJ}}z_m(\omega)z_n(\omega)}, \qquad z_n(\omega) = \gamma_n(\omega)/r_{a,n}.
\end{aligned}
$$

Arbitrary network geometry



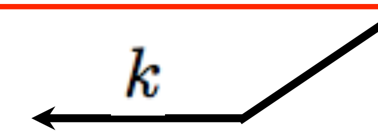
$$\widehat{G}_{ij}(x,y,\omega)=\frac{1}{D_j\gamma_j(\omega)}\sum_{\text{trips}}A_{\text{trip}}(\omega)\widehat{H}_\infty\left(\mathcal{L}_{\text{trip}}(i,j,x,y,\omega)\right)$$

$$\widehat{H}_\infty(x)=\mathrm{e}^{-|x|}/2$$

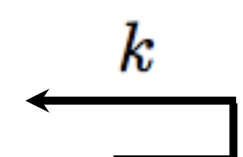
Rules for the trip coefficients

Initiate $A_{\text{trip}}(\omega)=1$

+1 (-1)



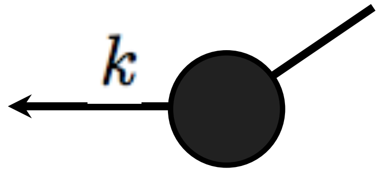
$2p_k(\omega)$



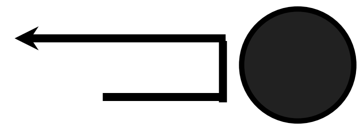
$2p_k(\omega)-1$

$$p_k(\omega)=\frac{z_k(\omega)}{\sum_n z_n(\omega)},\qquad z_k(\omega)=\frac{\gamma_k(\omega)}{r_{a,k}}$$

Rules for the trip coefficients



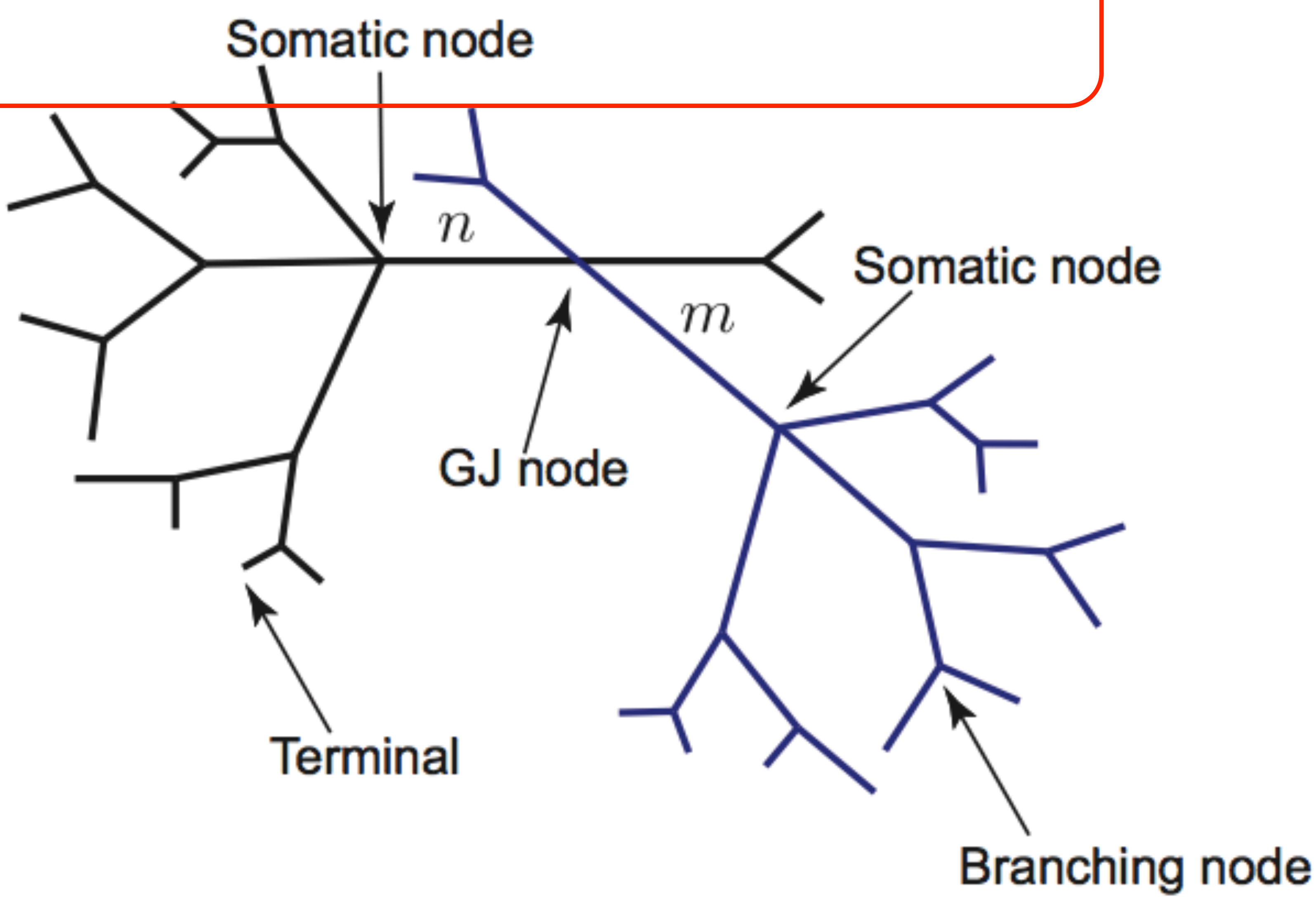
$2p_{\mathrm{s},k}(\omega)$



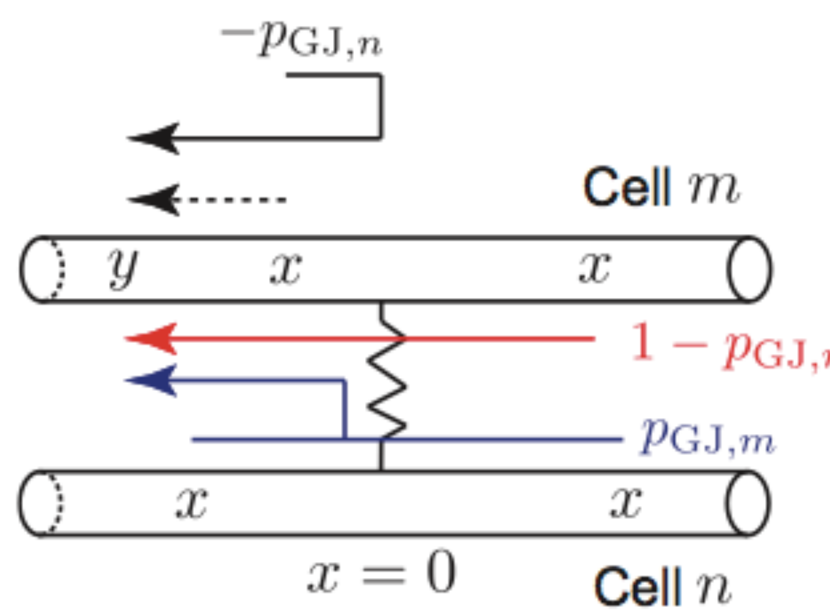
$2p_{\mathrm{s},k}(\omega) - 1.$

k

$$p_{\mathrm{s},k}(\omega) = \frac{z_k(\omega)}{\sum_n z_n(\omega) + \gamma_{\mathrm{s}}(\omega)}, \qquad \gamma_{\mathrm{s}}(\omega) = C_{\mathrm{s}}\omega + \frac{1}{R_{\mathrm{s}}} + \frac{1}{r_{\mathrm{s}} + L_{\mathrm{s}}\omega}$$

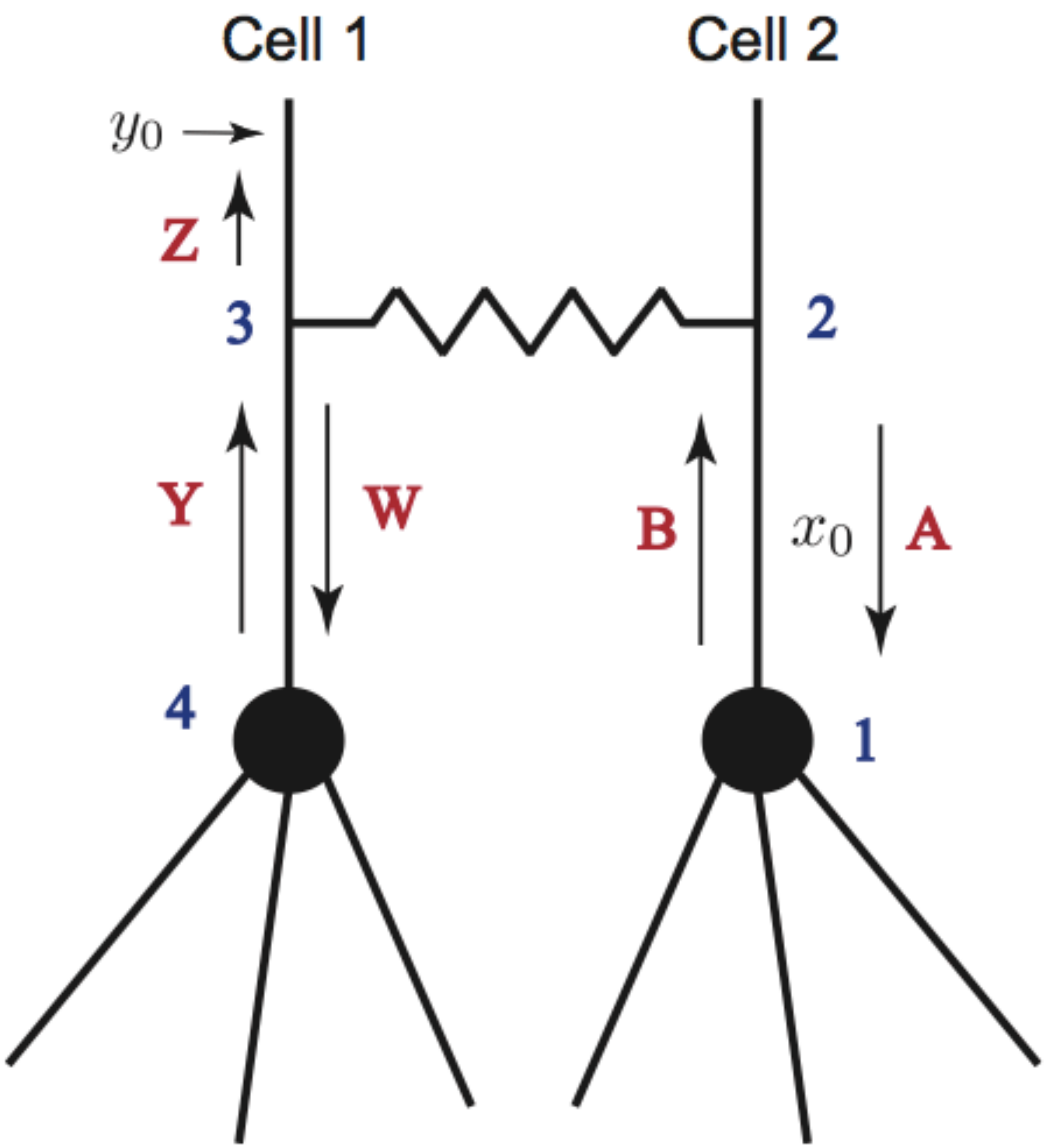


GJ node



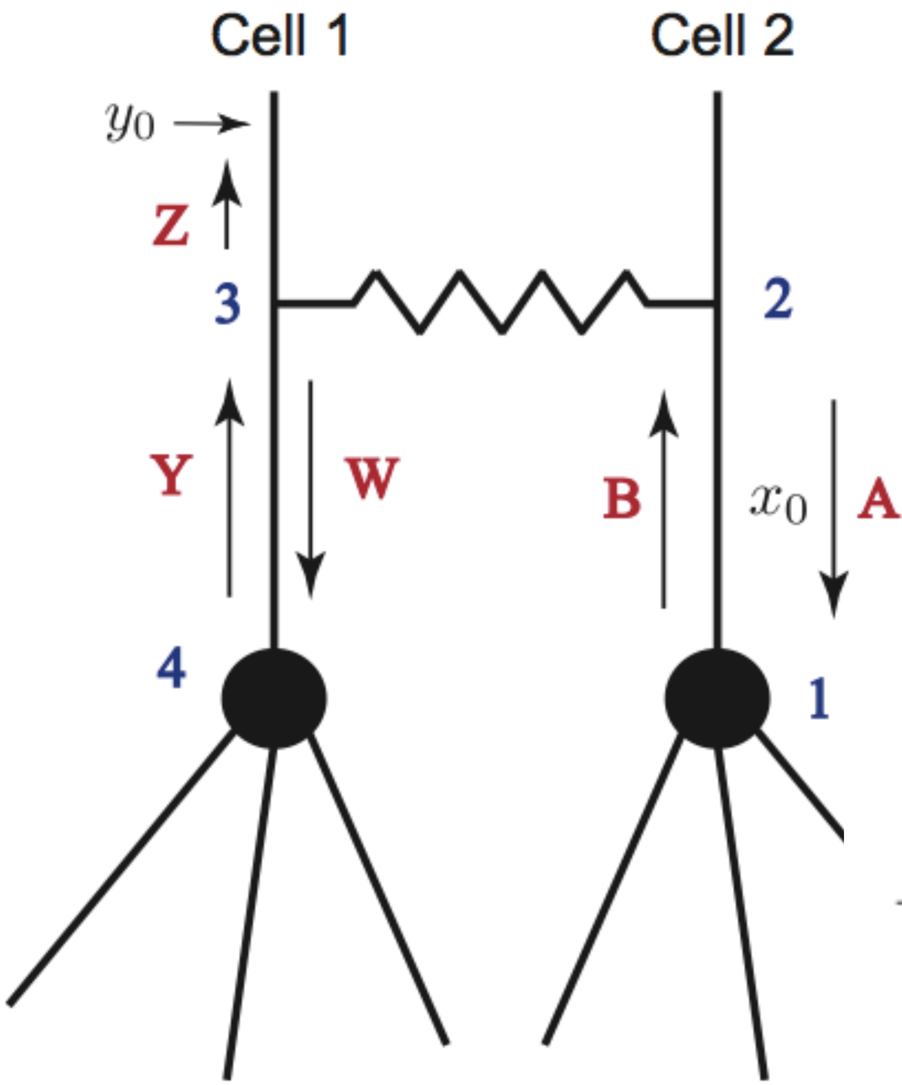
Two-cell network

Davide Michieletto



Method of words

- From $x_0 \to 1$ or from $2 \to 1$: letter $\mathbf{A}$.
- From $x_0 \to 2$ or from $1 \to 2$: letter $\mathbf{B}$.
- From $3 \to 4$: letter $\mathbf{W}$.
- From $4 \to 3$: letter $\mathbf{Y}$.
- From $3 \to y_0$: letter $\mathbf{Z}$.



class 1 $x_0 \to 2 \to 3 \to y_0$ the (ordered) word **BZ**

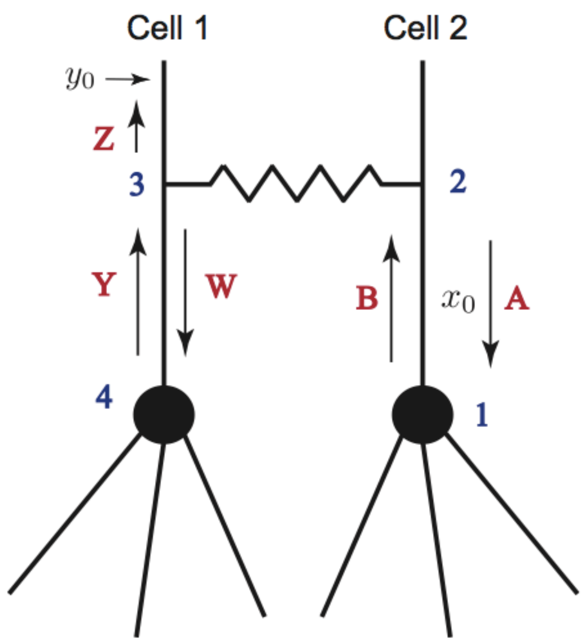
class 2 $x_0 \to 1 \to 2 \to 3 \to y_0$ the word **ABZ**

	A	**B**	**W**	**Y**	**Z**
A	0	$2p_s(\omega) - 1$	0	0	0
B	$-p_{GJ}(\omega)$	0	$p_{GJ}(\omega)$	0	$p_{GJ}(\omega)$
W	0	0	0	$2p_s(\omega) - 1$	0
Y	$p_{GJ}(\omega)$	0	$-p_{GJ}(\omega)$	0	$1 - p_{GJ}(\omega)$
Z	0	0	0	0	0

class 3 $x_0 \to 2 \to 3 \to 4 \to 3 \to y_0$ **BWYZ**.

class 4 $x_0 \to 1 \to 2 \to 3 \to 4 \to 3 \to y_0$ **ABWYZ**.

$$\mathbf{BZ}+\mathbf{ABZ}+\mathbf{BWYZ}+\mathbf{ABWYZ}=\underbrace{(1+\mathbf{A})\mathbf{BZ}}_{\text{class 1 and class 2}}+\underbrace{(1+\mathbf{A})\mathbf{BWYZ}}_{\text{class 3 and class 4}}$$



$$\underbrace{(1+\mathbf{A})\mathbf{B}\left[\dots\quad\dots\right]'\mathbf{Z}}_{\text{class 1 and class 2}}+\underbrace{(1+\mathbf{A})\mathbf{B}\left[\dots\quad\dots\right]\mathbf{WYZ}}_{\text{class 3 and class 4}}$$

$$\left[\dots\quad\dots\right]'=\left[1+\left[\dots\quad\dots\right]\mathbf{AB}\right]$$

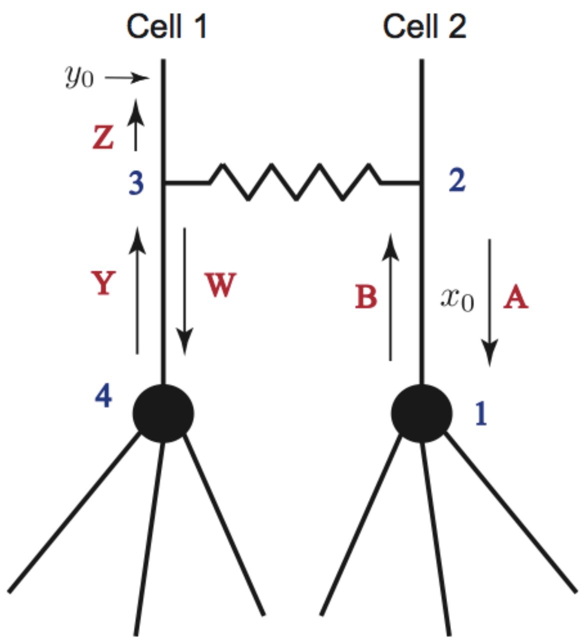
$$\begin{aligned}\left[\dots\quad\dots\right] &= \sum_{k=0}^{n}\binom{n}{k}(\mathbf{AB})^k(\mathbf{WY})^{n-k}\\ &= \binom{n}{0}(\mathbf{WY})^n+\sum_{k=1}^{n-1}\binom{n}{k}(\mathbf{AB})^k(\mathbf{WY})^{n-k}+\binom{n}{n}(\mathbf{AB})^n\end{aligned}$$

$$= \binom{n}{0}(2p_{\mathrm{s}}(\omega)-1)^n(-p_{\mathrm{GJ}}(\omega))^{n-1}-\sum_{k=1}^{n-1}\binom{n}{k}(2p_{\mathrm{s}}(\omega)-1)^n(-p_{\mathrm{GJ}}(\omega))^{n-1}$$

$$+ \binom{n}{n}(2p_{\mathrm{s}}(\omega)-1)^n(-p_{\mathrm{GJ}}(\omega))^{n-1}.$$

Compact solutions

$$\widehat{G}_2(x_0,y_0,\omega)=p_{\mathrm{GJ}}(\omega)\left[\widehat{G}_\infty(y_0-x_0,\omega)+(2p_{\mathrm{s}}(\omega)-1)\widehat{G}_\infty(y_0+x_0,\omega)\right]$$
$$+\sum_{n=0}^{\infty}2^n(-p_{\mathrm{GJ}}(\omega)(2p_{\mathrm{s}}(\omega)-1))^{n+1}(2p_{\mathrm{GJ}}(\omega)-1)$$
$$\times\left[\widehat{G}_\infty(y_0-x_0+2(n+1)\mathcal{L}_{\mathrm{GJ}},\omega)+(2p_{\mathrm{s}}(\omega)-1)\widehat{G}_\infty(y_0+x_0+2(n+1)\mathcal{L}_{\mathrm{GJ}},\omega)\right]$$



$$\widehat{G}_1(x_0,y_0,\omega)=(1-p_{\mathrm{GJ}}(\omega))\left[\widehat{G}_\infty(y_0-x_0,\omega)+(2p_{\mathrm{s}}(\omega)-1)\widehat{G}_\infty(y_0+x_0,\omega)\right]$$
$$+\sum_{n=0}^{\infty}2^n(-p_{\mathrm{GJ}}(\omega)(2p_{\mathrm{s}}(\omega)-1))^{n+1}(1-2p_{\mathrm{GJ}}(\omega))$$
$$\times\left[\widehat{G}_\infty(y_0-x_0+2(n+1)\mathcal{L}_{\mathrm{GJ}},\omega)+(2p_{\mathrm{s}}(\omega)-1)\widehat{G}_\infty(y_0+x_0+2(n+1)\mathcal{L}_{\mathrm{GJ}},\omega)\right]$$

Studying the role of a GJ

Responses at the somas

$$\begin{aligned}\widehat{G}_1(0,y_0,\omega) &= 2p_{\mathrm{s}}(\omega)(1-p_{\mathrm{GJ}}(\omega))\widehat{G}_{\infty}(y_0,\omega)+\sum_{n=0}^{\infty}2^n(-p_{\mathrm{GJ}}(\omega)(2p_{\mathrm{s}}(\omega)-1))^{n+1}(1-2p_{\mathrm{GJ}}(\omega))\\ &\times \; 2p_{\mathrm{s}}(\omega)\widehat{G}_{\infty}(y_0+2(n+1)\mathcal{L}_{\mathrm{GJ}},\omega),\end{aligned}$$

$$\begin{aligned}\widehat{G}_2(0,y_0,\omega) &= 2p_{\mathrm{s}}(\omega)p_{\mathrm{GJ}}(\omega)\widehat{G}_{\infty}(y_0,\omega)+\sum_{n=0}^{\infty}2^n(-p_{\mathrm{GJ}}(\omega)(2p_{\mathrm{s}}(\omega)-1))^{n+1}(2p_{\mathrm{GJ}}(\omega)-1)\\ &\times \; 2p_{\mathrm{s}}(\omega)\widehat{G}_{\infty}(y_0+2(n+1)\mathcal{L}_{\mathrm{GJ}},\omega).\end{aligned}$$

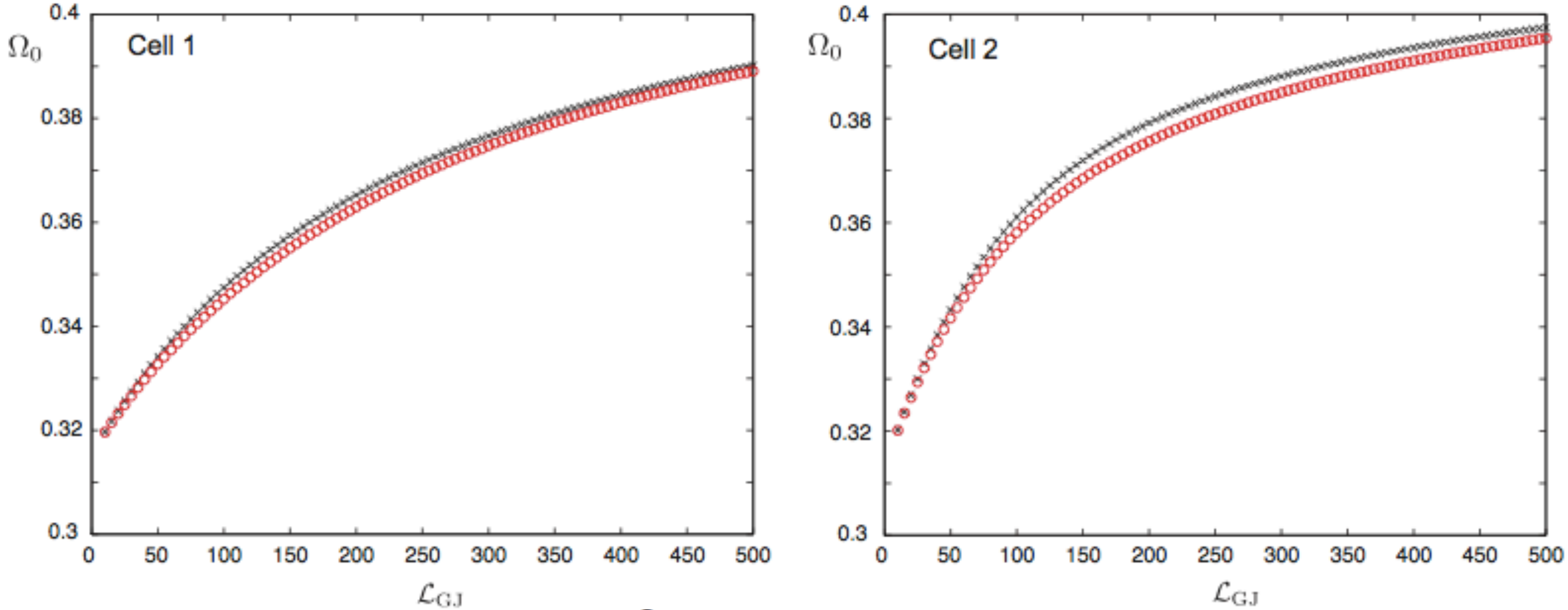
$$\mathcal{P}_1(\omega)=|\widehat{G}_1(0,y_0,\omega)|^2$$

$$\Omega_0: \quad \partial\mathcal{P}_1(\omega)/\partial\omega=0$$

$$\mathcal{P}_2(\omega)=|\widehat{G}_2(0,y_0,\omega)|^2$$

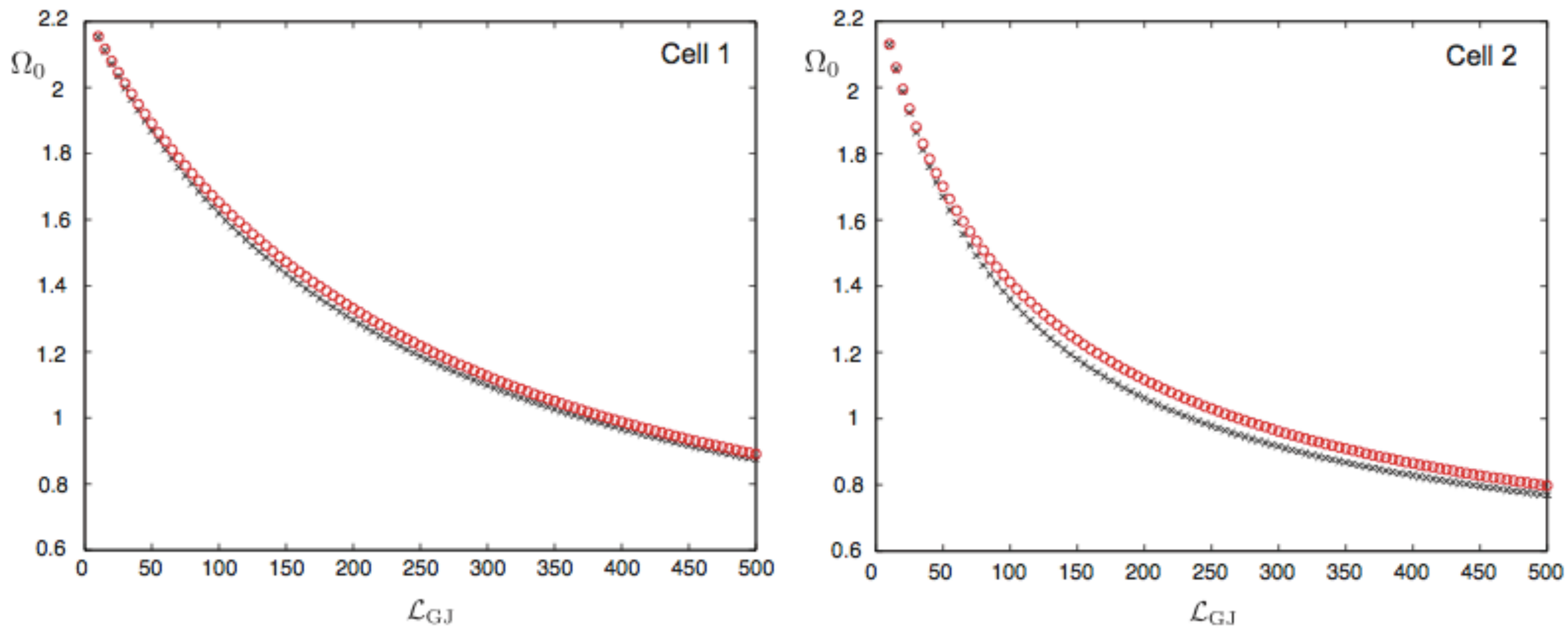
$$\Omega_0: \quad \partial\mathcal{P}_2(\omega)/\partial\omega=0$$

Passive somas, resonant dendrites

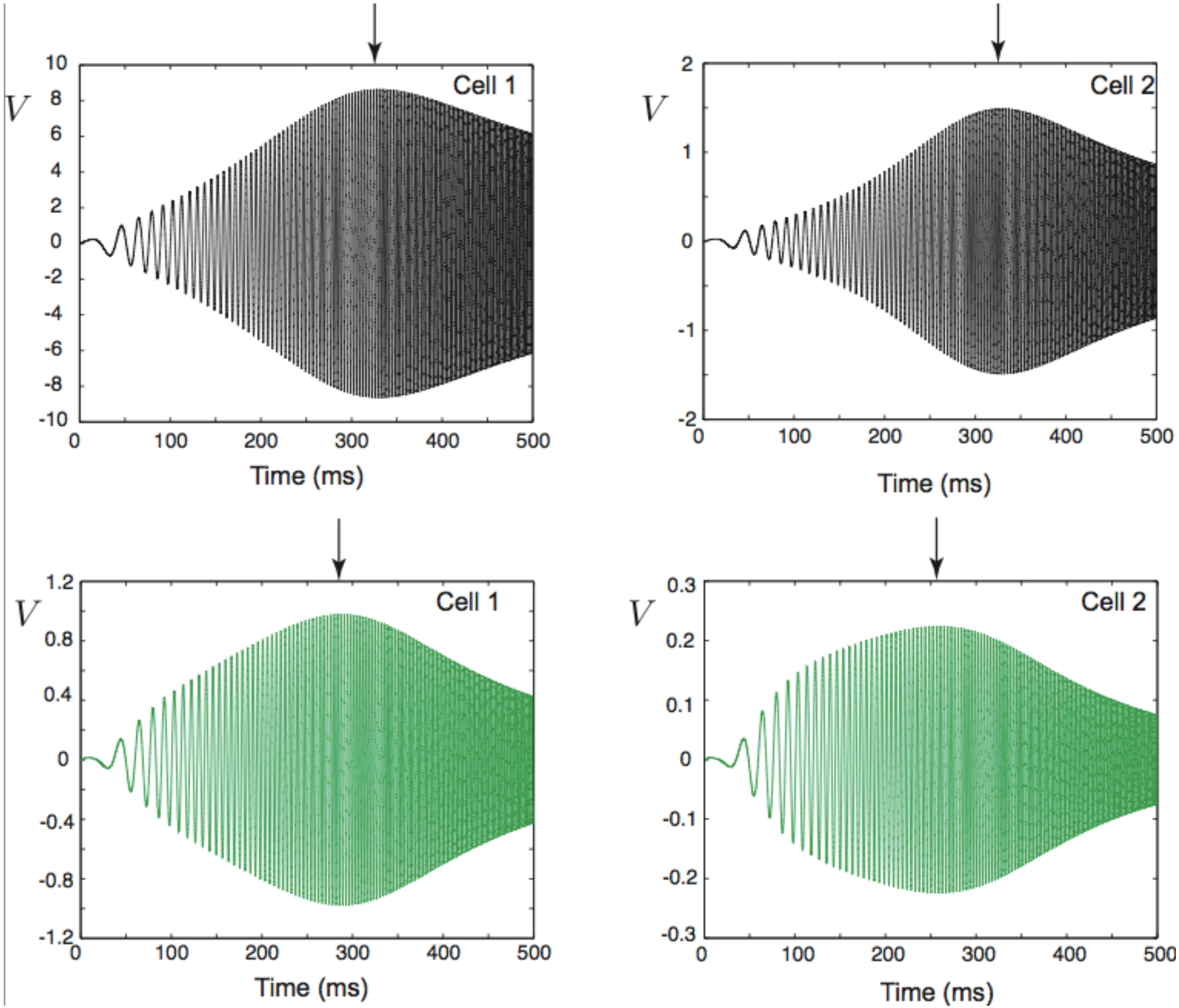


$R_{\mathrm{GJ}} = 100\ \mathrm{M\Omega}$ (red circles), $R_{\mathrm{GJ}} = 1000\ \mathrm{M\Omega}$ (black crosses)

Resonant somas, resonant dendrites



Resonant somas, resonant dendrites

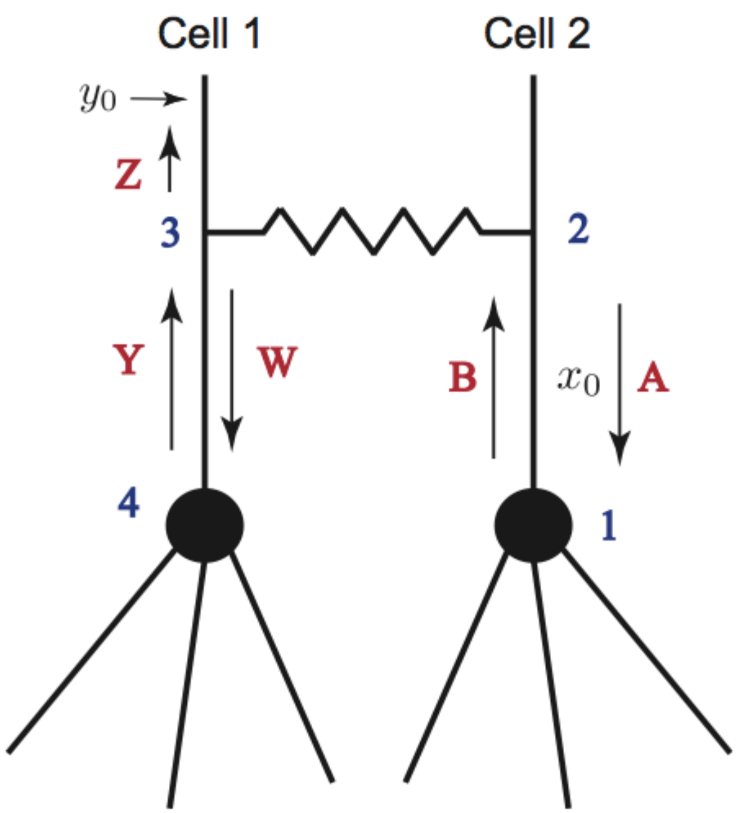


$\mathcal{L}_{\mathrm{GJ}} = 50\ \mu\mathrm{m},$

$\mathcal{L}_{\mathrm{GJ}} = 500\ \mu\mathrm{m}$

An alternative method

Yihe Lu



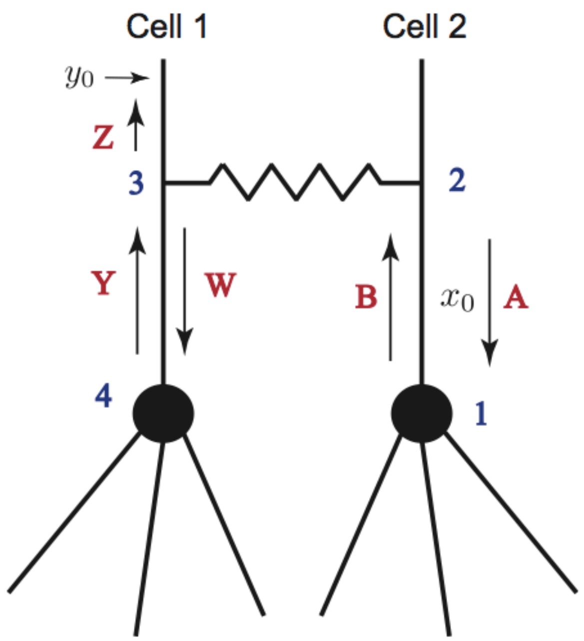
$$J_Y = J_W f(L_{GJ})(2p_s - 1)$$

$$J_B = J_A f(L_{GJ})(2p_s - 1) + J_{x_0} f(x_0)(2p_s - 1)$$

$$J_W = J_Y f(L_{GJ})(-p_{GJ}) + J_B f(L_{GJ}) p_{GJ} + J_{x_0} f(L_{GJ} - x_0) p_{GJ}$$

$$J_A = J_Y f(L_{GJ}) p_{GJ} + J_B f(L_{GJ})(-p_{GJ}) + J_{x_0} f(L_{GJ} - x_0)(-p_{GJ})$$

$$J_{x_0} = 1$$



Closed form solutions

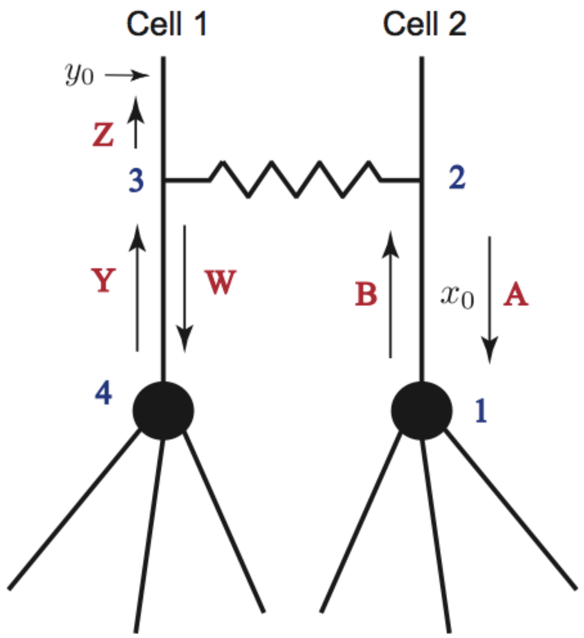
$$G_{\overline{DC}}(x_0, y_0, \omega) = \frac{1}{2D\gamma}\frac{p_{GJ} + p_{GJ}(2p_s - 1)f(2L_{GJ})}{1 + 2p_{GJ}(2p_s - 1)f(2L_{GJ})}\widetilde{F}(x_0, y_0)$$

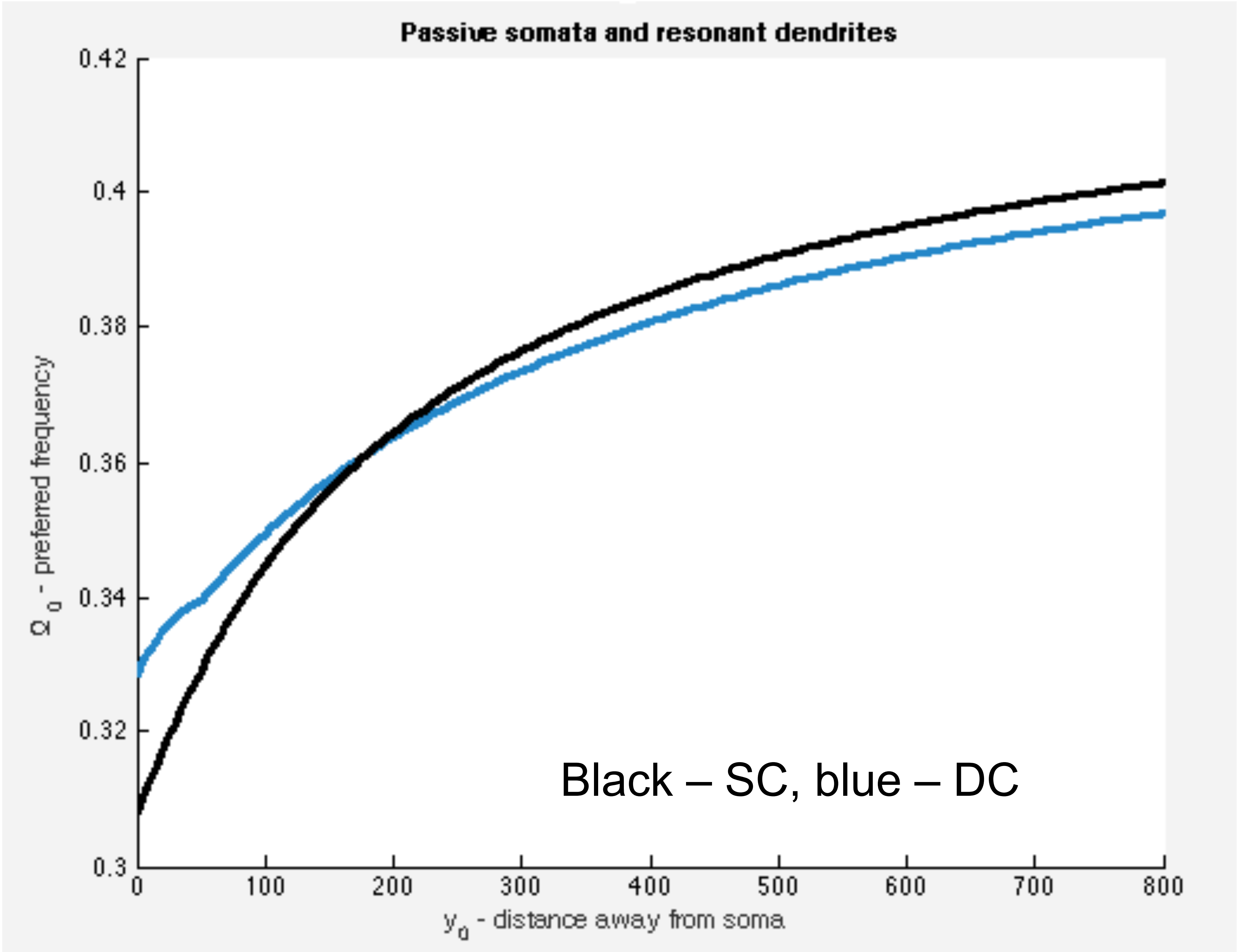
$$G_{\overline{SC}}(x_0, y_0, \omega) = \frac{1}{2D\gamma}\frac{1 - p_{GJ} + p_{GJ}(2p_s - 1)f(2L_{GJ})}{1 + 2p_{GJ}(2p_s - 1)f(2L_{GJ})}\widetilde{F}(x_0, y_0)$$

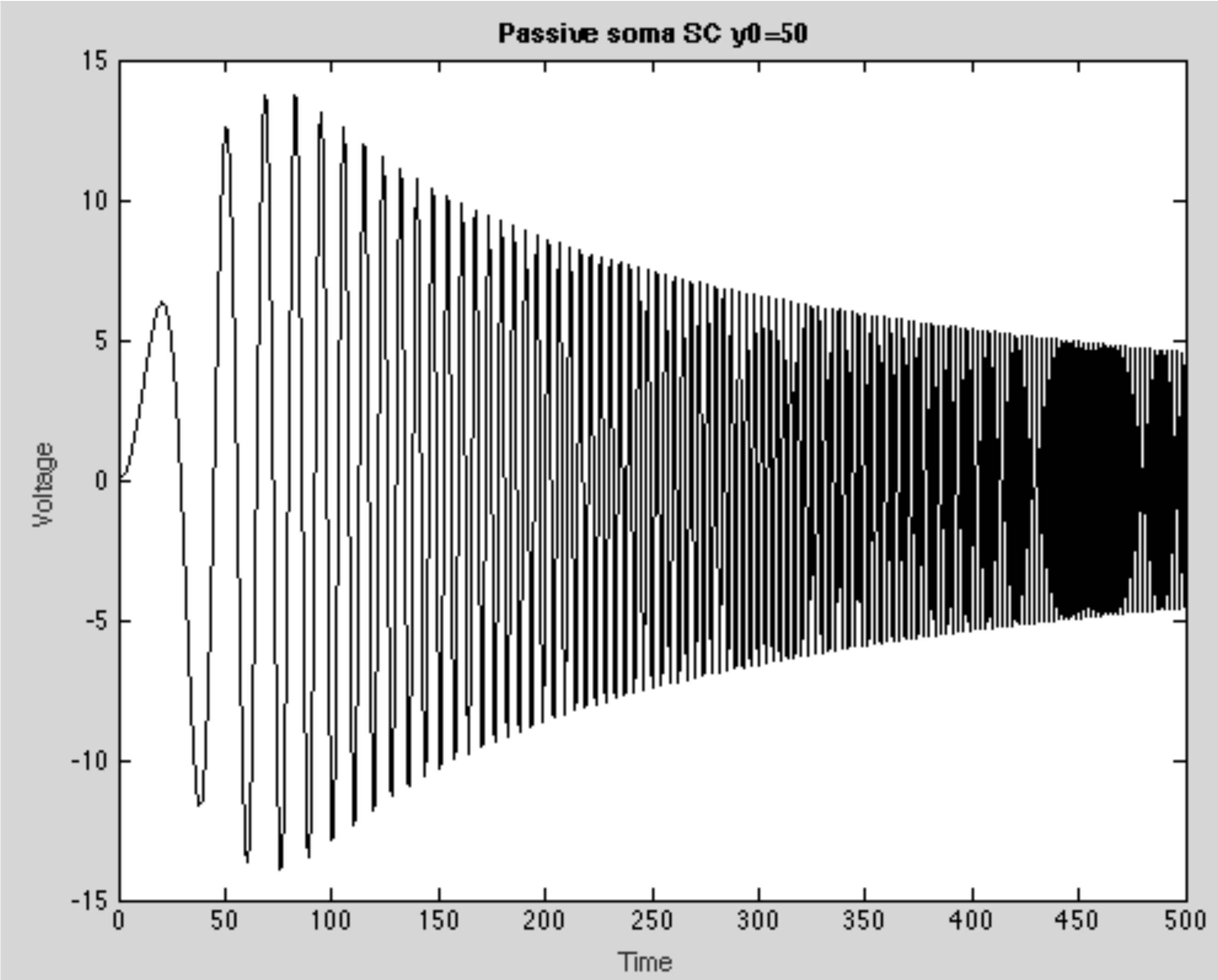
$$G_{\underline{DC}}(x_0, y_0, \omega) = \frac{1}{2D\gamma}\frac{p_{GJ} f(2L_{GJ})}{1 + 2p_{GJ}(2p_s - 1)f(2L_{GJ})}\widetilde{F}(x_0, 0)\widetilde{F}(y_0, 0)$$

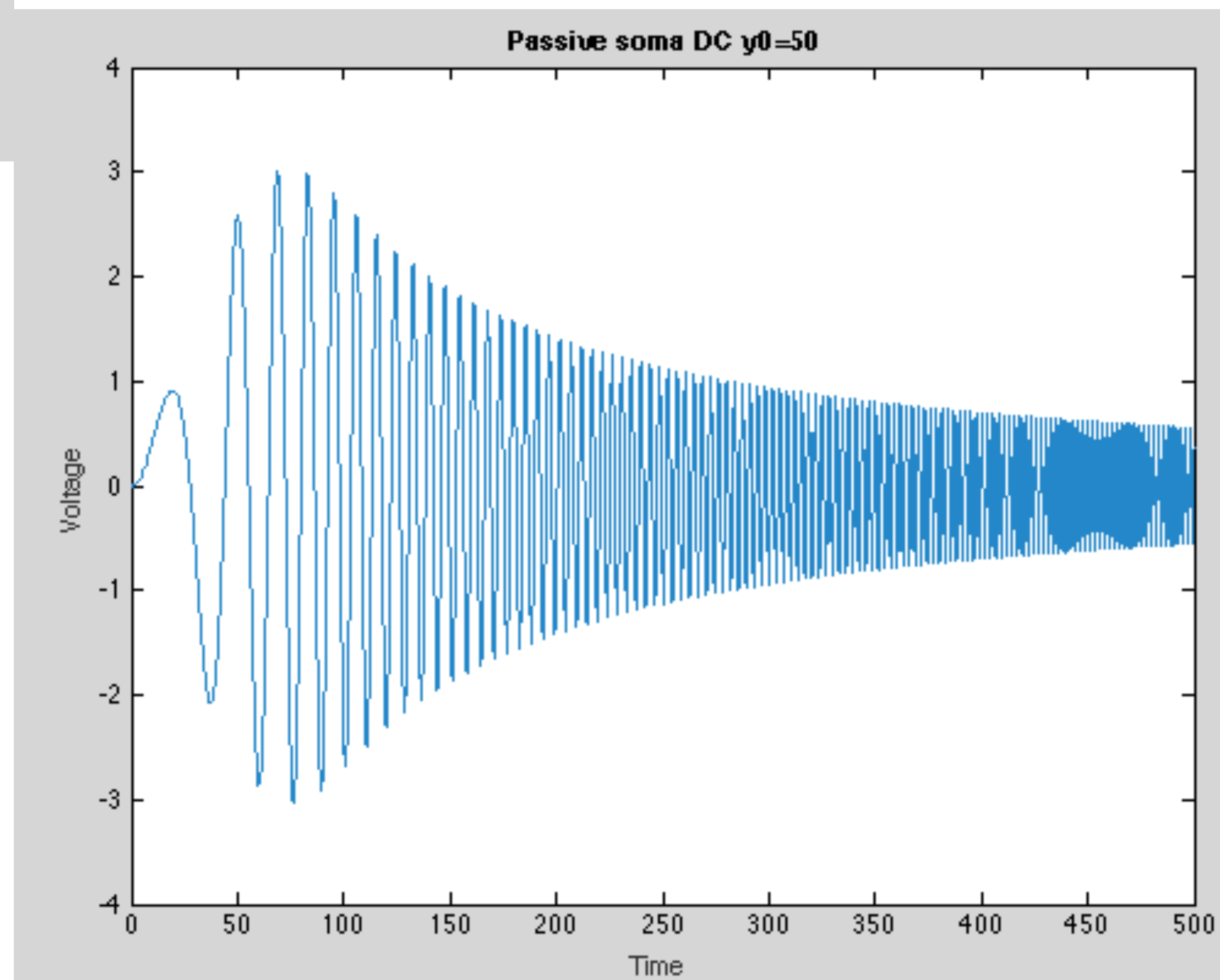
$$G_{\underline{SC}}(x_0, y_0, \omega) = \frac{1}{2D\gamma}\Bigg[f(x_0 + y_0)(2p_s - 1) + f(|x_0 - y_0|) - \frac{p_{GJ} f(2L_{GJ})}{1 + 2p_{GJ}(2p_s - 1)f(2L_{GJ})}\widetilde{F}(x_0, 0)\widetilde{F}(y_0, 0)\Bigg]$$

Passive somas, resonant dendrites



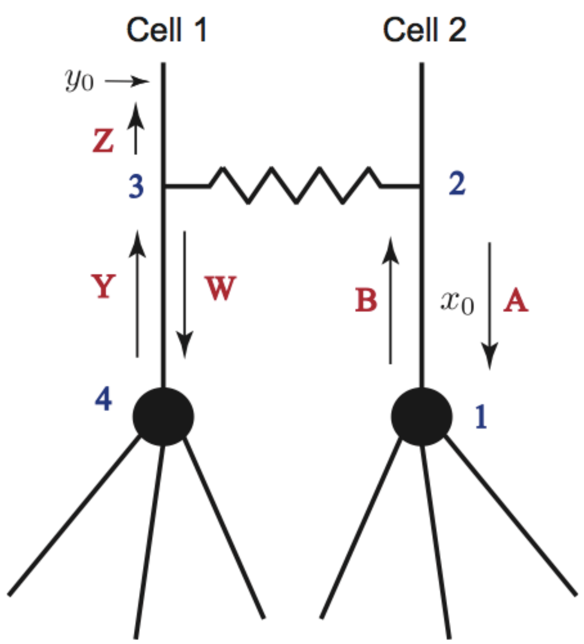


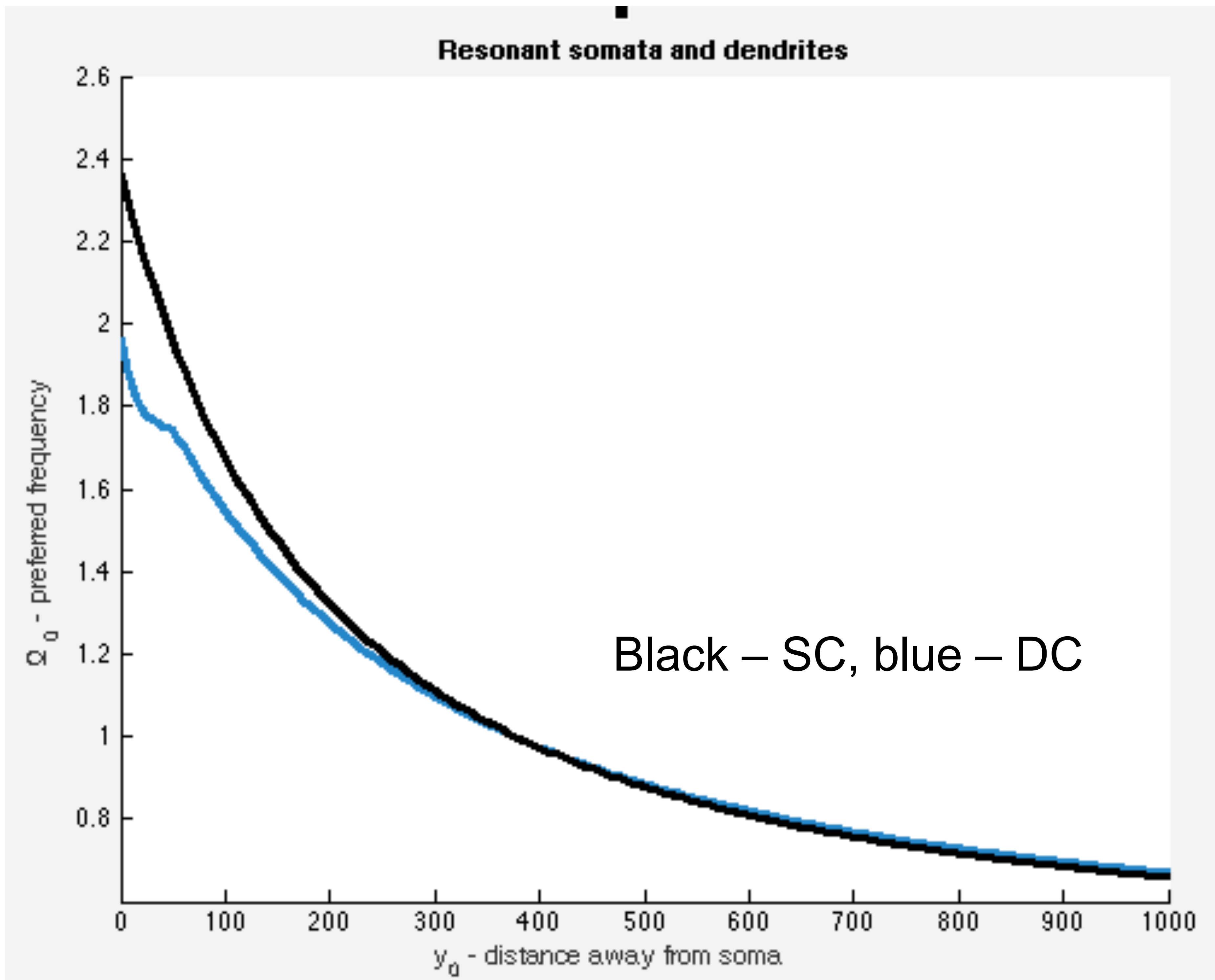


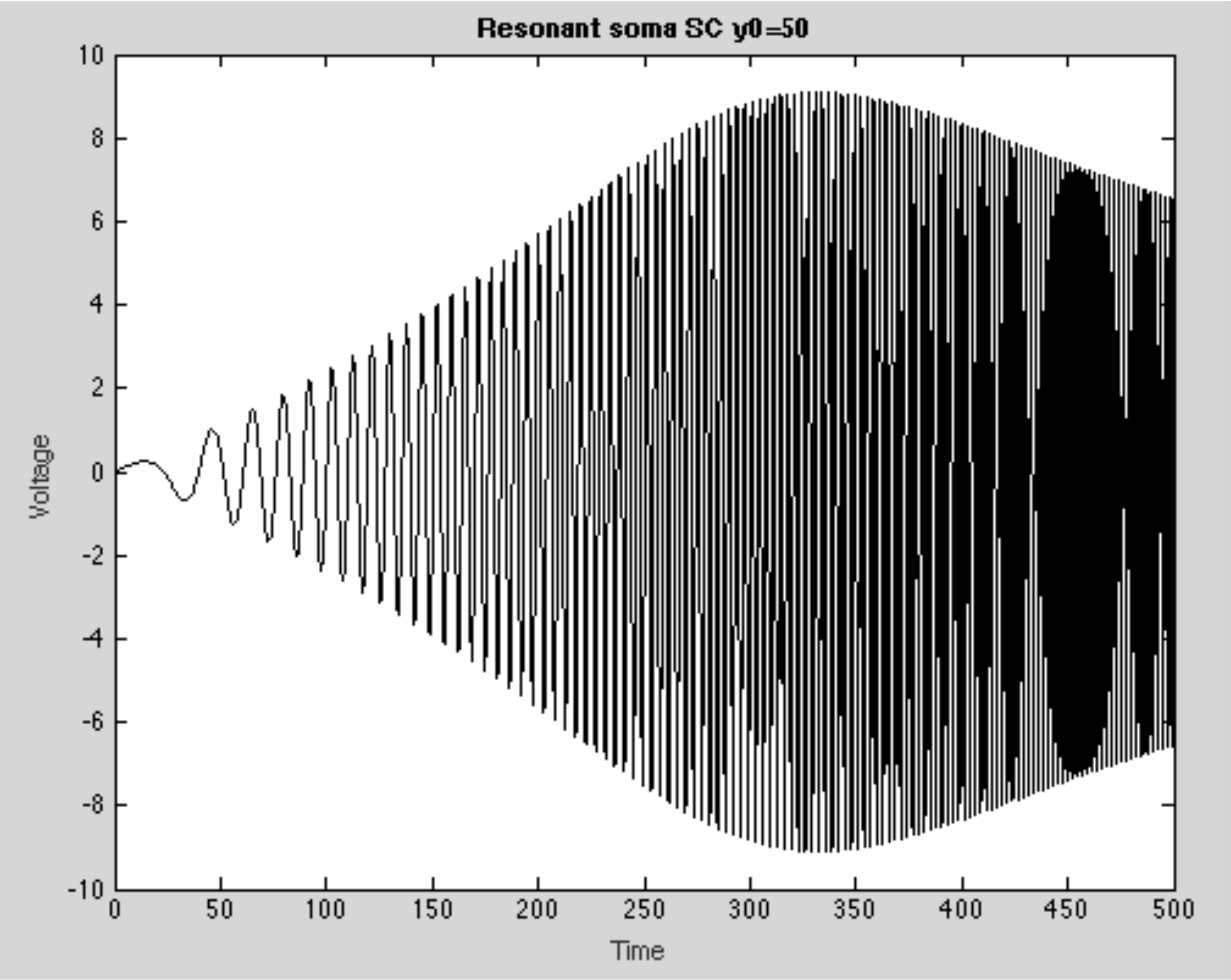


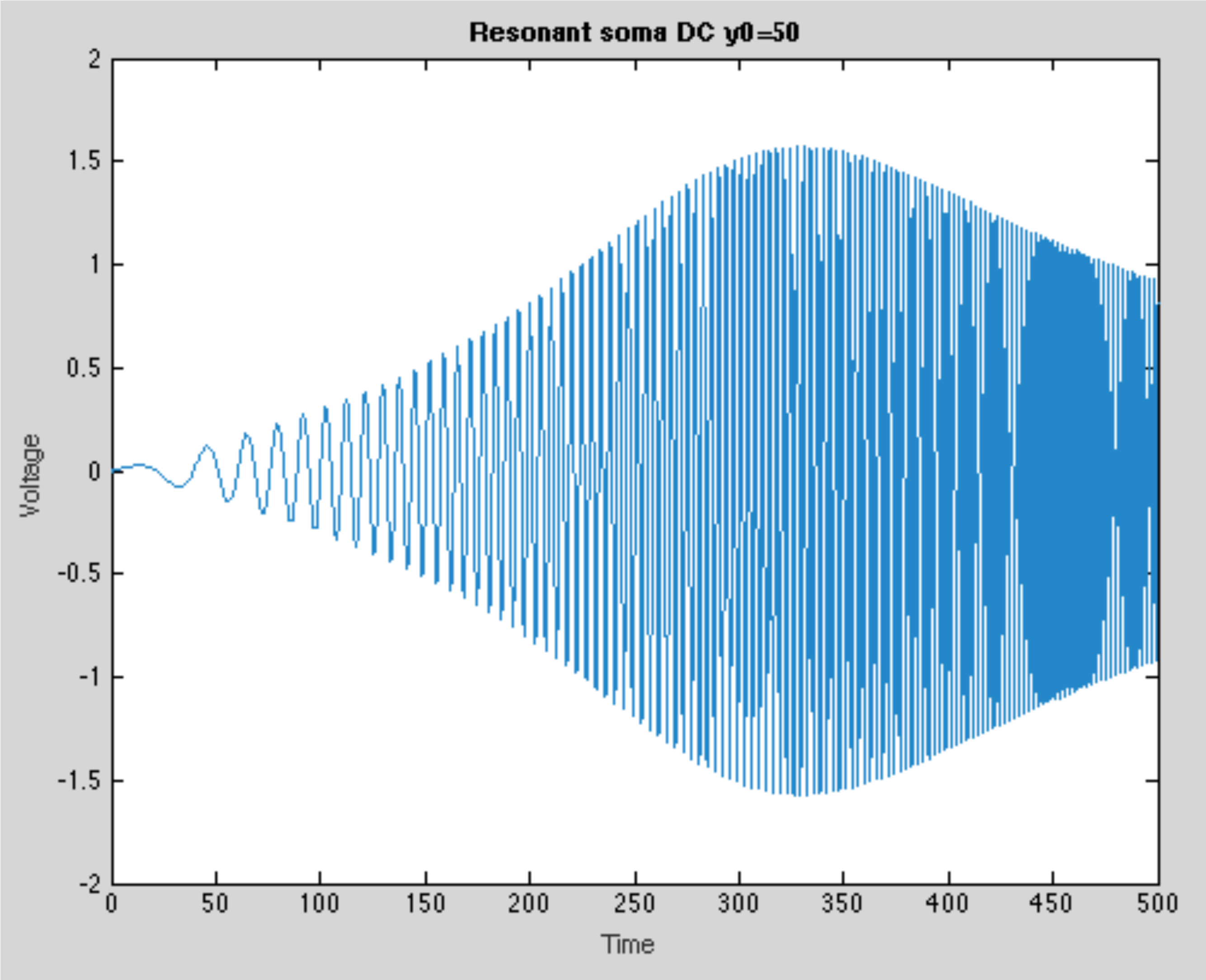
Black – SC, blue – DC

Resonant somas, resonant dendrites





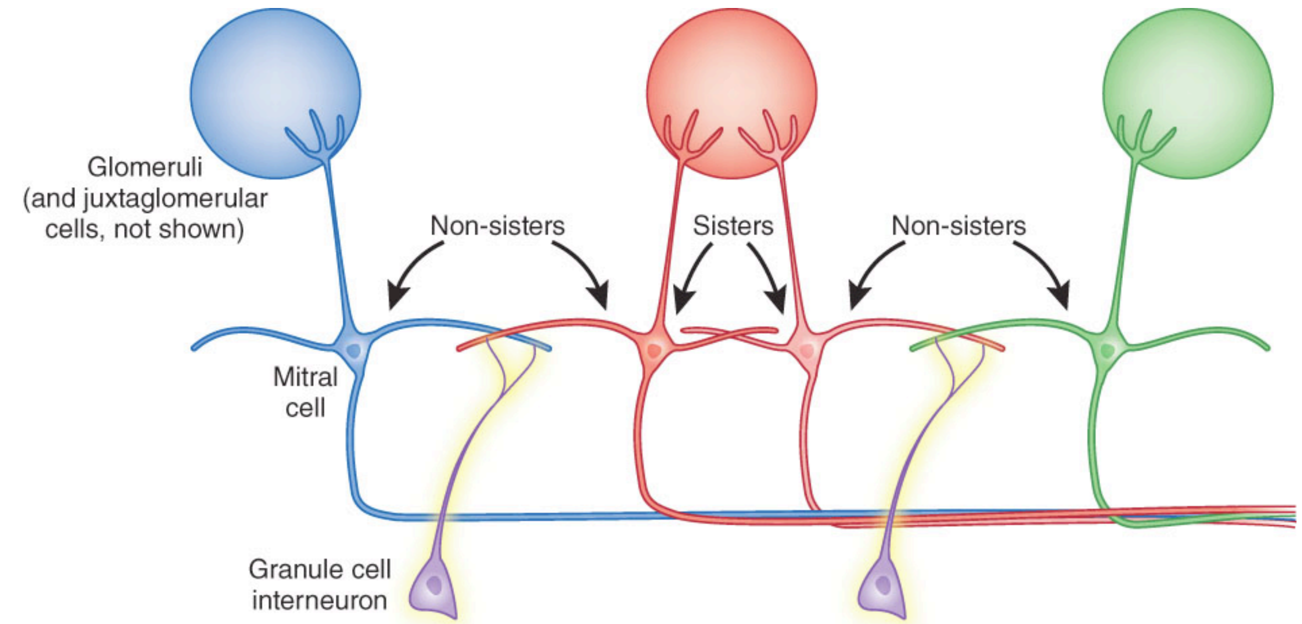




Black – SC, blue – DC

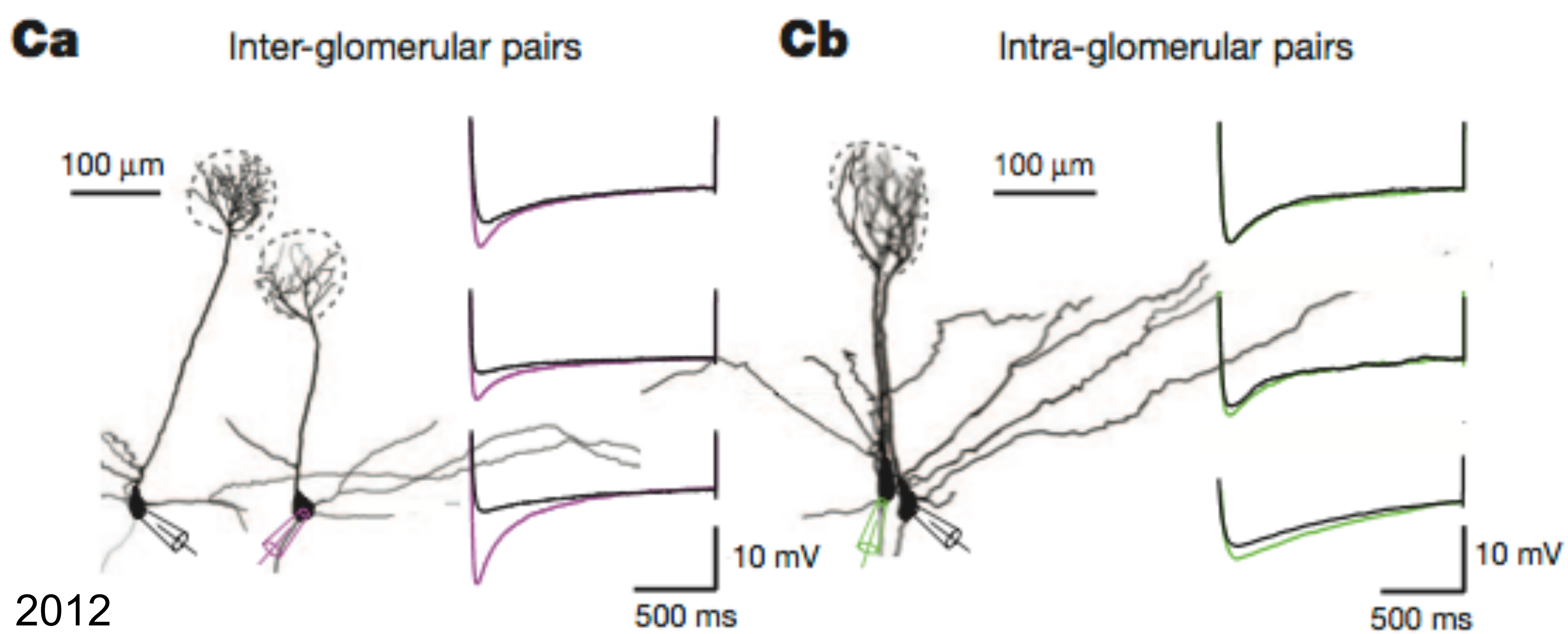
Application: the olfactory bulb

a layered structure



Cx36 presence:

- Exclusively in the glomerulus
- Known to synchronise electrical activity of sister mitral cells
- Generates glomerular-specific synchronous assemblies



Angelo et. Al. Nature 488, 2012

Main conclusions

- Sum-over-trips framework can be generalised for a network of cells coupled by gap junctions.
- Method of words for constructing compact solutions with infinite series.
- An alternative method for finding closed form solutions.
- Location and strength of a GJ tune somatic responses.
- Next steps: Application to mitral cells