

Supplementary Material: Modulating STDP balance impacts the dendritic mosaic

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1 SUPPLEMENTARY DATA: LAYER 2/3 PYRAMIDAL CELL MODEL DETAILS

We present the set of ionic currents used in our layer 2/3 pyramidal cell model. The descriptions of the ionic currents used in the simulations were the same or similar to those used in previous modeling studies (Iannella et al., 2010; Iannella and Tanaka, 2006; Iannella et al., 2004; Mainen et al., 1995; Rhodes and Gray, 1994; Rhodes and Llinás, 2001; Traub et al., 2003) and are given below. Note that the values of maximal conductances for each respective ion channel are listed below.

The values of maximal conductances for each respective ion channel are listed in Table 1. at the end of this document.

Leak current I_{leak}

$$I_{\text{leak}} = g_{\text{l}}(E_{\text{leak}} - V)$$

Sodium current $I_{\rm Na}$

$$\begin{split} I_{\rm Na} &= \overline{g}_{\rm Na} m^3 h(E_{\rm Na} - V) \\ \frac{\partial m}{\partial t} &= \alpha_{\rm m}(V)(1-m) - \beta_{\rm m}(V)m \\ \alpha_{\rm m}(V) &= 0.182(V+35)/(1-\exp(-(V+35)/9)) \\ \beta_{\rm m}(V) &= -0.124(V+35)/(1-\exp((V+35)/9)) \\ \frac{\partial h}{\partial t} &= \frac{h_{\infty}(V) - h}{\tau_{\rm h}(V)} \\ \alpha_{\rm h}(V) &= 0.024(V+50)/(1-\exp(-(V+50)/5)) \\ \beta_{\rm h}(V) &= -0.0091(V+75)/(1-\exp((V+75)/5)) \\ h_{\infty}(V) &= 1/(1+\exp((V+65)/6.2)) \\ \tau_{\rm h}(V) &= 1/(\alpha_{\rm h}(V) + \beta_{\rm h}(V)) \end{split}$$

Potassium current $I_{\rm K}$

$$I_{\rm K} = \overline{g}_{\rm K} n (E_{\rm Kdr} - V)$$

$$\frac{\partial n}{\partial t} = \alpha_{\rm n}(V)(1 - n) - \beta_{\rm n}(V)n$$

$$\alpha_{\rm n}(V) = 0.02(V - 20)/(1 - \exp(-(V - 20)/9))$$

$$\beta_{\rm n}(V) = -0.002(V - 20)/(1 - \exp((V - 20)/9))$$

Transient potassium A-current $I_{\rm K(A)}$

Potassium H-current $I_{\rm K(H)}$

$$\begin{split} I_{\rm K(H)} &= \overline{g}_{\rm K(H)} m(E_{\rm K(H)} - V) \\ \frac{\partial m}{\partial t} &= \frac{m_{\infty}(V) - m}{\tau_{m_{\rm K(H)}}(V)} \\ m_{\infty}(V) &= 1/(1 + \exp((V + 75)/5.5)) \\ \tau_{m_{\rm K(H)}}(V) &= 1/[\exp(-0.086V - 14.6) + \exp(-1.87 + 0.07V)], \end{split}$$

High-Voltage-Activated (HVA) L-type calcium current $I_{\rm Ca(HVA)}$

$$I_{Ca(HVA)} = \overline{g}_{Ca(HVA)} m^2 h ([Ca]_i) (E_{Ca(HVA)} - V)$$

$$E_{Ca(HVA)} = \frac{RT}{2F} ln \left(\frac{[Ca]_o}{[Ca]_i} \right)$$

$$\frac{\partial m}{\partial t} = \alpha_m(V)(1-m) - \beta_m(V)m$$

$$\frac{\partial h}{\partial t} = \frac{h_{\infty}(V, [Ca]_i) - h}{\tau_{h_{Ca}(HVA)}}$$

$$\alpha_m(V) = 1.6/(1 - \exp(-0.072(V-5)))$$

$$\beta_m(V) = -0.02(V + 8.9)/(1 - \exp((V + 8.9)/5))$$

$$\begin{aligned} h_{\infty}(V, [\text{Ca}]_i) &= \left(\frac{2 \ \mu M}{2 \ \mu M + [\text{Ca}]_i}\right) \frac{1}{(1 + \exp((V + 42)/8))} \\ \tau_{h_{\text{Ca}(\text{HVA})}} &= 0.02 \end{aligned}$$

Low-Voltage-Activated T-type calcium current $I_{Ca(T)}$

$$\begin{split} I_{\text{Ca}(\text{T})} &= \overline{g}_{\text{Ca}(\text{T})} m^2 h \text{ GHK}(V, [\text{Ca}]_i, [\text{Ca}]_o) \\ \text{GHK}(V, [\text{Ca}]_i, [\text{Ca}]_o) &= 0.0853 \frac{\mathcal{T}}{2} \left(\frac{\exp(2V\mathcal{F}/R\mathcal{T})[\text{Ca}]_i/[\text{Ca}]_o - 1}{(\exp(2V\mathcal{F}/R\mathcal{T}) - 1)} \right) \\ \frac{\partial m}{\partial t} &= \alpha_{\text{m}}(V)(1 - m) - \beta_{\text{m}}(V)m \\ \frac{\partial h}{\partial t} &= \frac{h_{\infty}(V) - h}{\tau_{h_{\text{Ca}(\text{T})}}} \\ \alpha_{\text{m}}(V) &= -0.2(V - 19.26)/(\exp(-(V - 19.26)/10) - 1) \\ \beta_{\text{m}}(V) &= 0.009 \exp(-V/22.03) \\ \alpha_{\text{h}}(V) &= 10^{-6} \exp(-V/16.26) \\ \beta_{\text{h}}(V) &= 1/(\exp(-(V - 29.79)/10) + 1) \\ m_{\infty}(V) &= \alpha_{\text{m}}(V)/(\alpha_{\text{m}}(V) + \beta_{\text{m}}(V)) \\ h_{\infty}(V) &= \alpha_{\text{h}}(V)/(\alpha_{\text{h}}(V) + \beta_{\text{h}}(V)) \\ \tau_{m_{\text{Ca}(\text{T})}} &= 1/(\alpha_{\text{m}}(V) + \beta_{\text{m}}(V)) \\ \tau_{h_{\text{Ca}(\text{T})}} &= 1/(\alpha_{\text{h}}(V) + \beta_{\text{h}}(V)) \end{split}$$

Calcium gated potassium current $I_{\rm K(Ca)}$

Muscarinic potassium current $I_{\rm M}$

$$I_{\rm M} = \overline{g}_{{\rm K}_{\rm M}} n(E_{{\rm K}_{\rm M}} - V)$$

$$\frac{\partial n}{\partial t} = \frac{n_{\infty}(V) - n}{\tau_n(V)}$$

$$\alpha_{\rm n}(V) = 0.001(V - 30)/(1 - \exp(-(V - 30)/9))$$

$$\beta_{\rm n}(V) = -0.001(V - 30)/(1 - \exp((V - 30)/9))$$

$$n_{\infty}(V) = \alpha_{\rm n}(v)/(\alpha_{\rm n}(V) + \beta_{\rm n}(V))$$

$$\tau_{\mathbf{n}_{\mathbf{M}}}(V) = 1/(\alpha_{\mathbf{n}}(V) + \beta_{\mathbf{n}}(V))$$

Medium afterhyperpolarization current I_{mAHP}

$$I_{mAHP} = \overline{g}_{mAHP} m(E_{mAHP} - V)$$

$$\frac{\partial m}{\partial t} = \frac{m_{\infty}(V) - m}{\tau_{m_{mAHP}}}$$

$$\alpha_{m}(V) = 0.48/(1 + 0.18/[Ca]_{i} \exp(-1.68V\mathcal{F}/RT))$$

$$\beta_{m}(V) = 0.28/\left(1 + \frac{[Ca]_{i}}{0.011 \exp(-2V\mathcal{F}/RT)}\right)$$

$$m_{\infty}(V) = \alpha_{m}(V)/(\alpha_{m}(V) + \beta_{m}(V))$$

$$\tau_{mAHP}(V) = 1/(\alpha_{m}(V) + \beta_{m}(V))$$

Slow afterhyperpolarization current $I_{\rm sAHP}$

$$I_{\text{sAHP}} = \overline{g}_{\text{sAHP}} m^{3}(E_{\text{sAHP}} - V)$$

$$\frac{dm}{dt} = \frac{m_{\infty}([\text{Ca}]_{i}) - m}{\tau_{\text{sAHP}}([\text{Ca}]_{i})}$$

$$m_{\infty}([\text{Ca}]_{i}) = \frac{[\text{Ca}]_{i}^{2}}{(0.025^{2} + [\text{Ca}]_{i}^{2})}$$

$$\tau_{\text{sAHP}}([\text{Ca}]_{i}) = \max(\frac{1}{(0.003(1 + ([\text{Ca}]_{i}/0.025)^{2}))3^{(T-251.16)/10}}, 0.5))$$

where $E_{\text{leak}} = -80 \text{ mV}$, $E_{\text{Na}} = 50 \text{ mV}$, $E_{\text{Kdr}} = E_{\text{K(A)}} = E_{\text{K(Ca)}} = E_{\text{mAHP}} = E_{\text{sAHP}} = -90 \text{ mV}$, and $E_{\text{K(H)}} = -35 \text{ mV}$, $\mathcal{F} = 96485 \text{ C mol}^{-1}$ is Faraday's constant, $R = 8.1345 \text{ J} {}^{o}\text{K}^{-1} \text{ mol}^{-1}$ is the gas constant, and \mathcal{T} denotes absolute temperature in ${}^{o}\text{K}$ (degrees kelvin). *Intracellular calcium dynamics* Calcium accumulation, extrusion, diffusion and buffering was simulated according to the following simple model which accounts for these processes by a simple exponential decay,

$$\frac{d[\mathrm{Ca}]_i}{dt} = \frac{[\mathrm{Ca}]_{\infty} - [\mathrm{Ca}]_i}{\tau_{\mathrm{Ca}}} + \frac{1}{2\mathcal{F}d} \left(I_{\mathrm{Ca(HVA)}} + I_{\mathrm{Ca(T)}} + I_{\mathrm{Ca(NMDA)}} \right)$$

where $[Ca]_{\infty} = 20 \mu M$ is the equilibrium concentration of intracellular calcium, $[Ca]_i$ denotes the concentration of intracellular free calcium, $\tau_{Ca} = 20$ msec is the diffusion rate constant, d is the depth of a shell just beneath the membrane, $I_{Ca(HVA)}$ and $I_{Ca(T)}$ respectively denotes the calcium current through L-type and T-type calcium channels, and $I_{Ca(NMDA)} = 0.1I_{NMDA}$ is a fractional calcium current through postsynaptic NMDA receptors where 10% of the NMDA-mediated current is carried by calcium (Garaschuk et al., 1996; Burnashev et al., 1995).

The synaptic currents that are generated due to the incoming spike activity transmitted by impinging afferent fibers onto various locations across the dendrite result in depolaration and neuronal firing. The description of the four different synaptic currents generated by their respective underlying receptor types: AMPA, GABA_A, GABA_B, and NMDA, were modeled as follows,

AMPA conductance and current:

$$g_j^{\text{AMPA}}(t) = \overline{g}^{\text{AMPA}} w_j(t) F\left(e^{-(t-t_i)/\tau_d^{AMPA}} - e^{-(t-t_i)/\tau_o^{AMPA}}\right) H(t-t_i),$$

$$I_j^{\text{AMPA}}(t) = g_j^{\text{AMPA}}(t) \left(V - E_{\text{rev}}^{\text{AMPA}}\right)$$

Note that only the synaptic efficacies or weights of AMPA currents generated at dendritic location j are denoted by $w_j(t)$ and altered via STDP. All other weights (maximal conductances) associated with the other synaptic currents (NMDA, GABA_A, and GABA_B) are fixed.

GABA_A conductance and current:

$$g_{j}^{\text{GABA}_{\text{A}}}(t) = \overline{g}^{\text{GABA}_{\text{A}}} F\left(e^{-(t-t_{i})/\tau_{d}^{\text{GABA}_{\text{A}}}} - e^{-(t-t_{i})/\tau_{o}^{\text{GABA}_{\text{A}}}}\right) H(t-t_{i}),$$

$$I_{j}^{\text{GABA}_{\text{A}}}(t) = g_{j}^{\text{GABA}_{\text{A}}}(t) \left(V - E_{\text{rev}}^{\text{GABA}_{\text{A}}}\right)$$

where $E_{\rm rev}^{\rm AMPA} = 0 \text{ mV}$, $E_{\rm rev}^{\rm GABA_A} = -80 \text{ mV}$, H(t) is the Heaviside step function, w_j denotes the efficacy of the AMPA conductance in synapse j, and F is a normalization factor such that an event with $\overline{g} = 1$ generates a peak conductance of 1 μ S. The maximal AMPA $\overline{g}^{\rm AMPA}$ and GABA_A $\overline{g}^{\rm GABA_A}$ conductance were 5 and 2 nS, respectively. Onset and decay time constants were $\tau_o^{\rm AMPA} = 0.2$ msec and $\tau_d^{\rm AMPA} = 1.5$ msec for AMPA and $\tau_o^{\rm GABA_A} = 1.2$ msec and $\tau_d^{\rm GABA_A} = 9$ msec GABA_A conductances, respectively. Excitatory AMPA weights were initialized to $w_j(t) = 0.5$, but later changed by STDP.

NMDA conductance and current:

The postsynaptic NMDA conductance was modeled using a simple two state kinetic scheme represented by the following two state diagram

$$C + T \stackrel{\alpha}{\rightleftharpoons} O$$

where α and β represent forward and backward voltage independent reaction rates. Defining ζ as the fraction of receptors in the open state of synapse j, then the above two state reaction is described by the following first order kinetic equation:

$$\frac{d\zeta_j}{dt} = \alpha \left[T\right] \left(1 - \zeta_j\right) - \beta \zeta_j$$

where $\alpha = 10 \text{ (msec)}^{-1}$ and $\beta = 0.0125 \text{ (msec)}^{-1}$ denotes the forward binding and backward unbinding rates, respectively. The concentration [T] denotes a pulse of neurotransmitter of duration 1.1 msec in the synaptic cleft. The NMDA conductance is given by,

$$g_{j}^{\text{NMDA}}(t) = \overline{g}^{\text{NMDA}}\zeta_{j}(t)$$

while the NMDA current is,

$$I_{j}^{\text{NMDA}}(t) = g_{j}^{\text{NMDA}}(t)B(V)(V - E_{\text{rev}}^{\text{NMDA}})$$

where the reversal potential is $E_{rev}^{\text{NMDA}} = 0$, and B(V) represents magnesium block described by the following voltage dependent process,

$$B(V) = \frac{1}{1 + \exp(-0.062V) \left[Mg^{2+}\right]_{o}/3.57},$$

where the extracellular magnesium concentration was set to a value of $[Mg^{2+}]_o = 1$ mM.

GABA_B conductance and current:

Post synaptic GABA_B receptor responses are activated by an intracellular second messenger system, mediated by fast G-protein binding to K^+ channels, whose state diagram is represented by the following kinetic scheme

$$R_{o} + T \rightleftharpoons R \rightleftharpoons D$$

$$R + G_{o} \rightleftharpoons RG \rightarrow R + G$$

$$G \rightarrow G_{o}$$

$$C_{1} + nG \rightleftharpoons O$$

The activated and desensitized forms of the receptor G and D respectively arise after neurotransmitter T binds to the receptor R_o . Concurrently, the active form of the G-protein G is produced after the inactive form G_o has been catalyzed by R, and consequently binds to open K^+ channels, with n = 4 binding sites. The above kinetic scheme can be simplified, by assuming Michaelis-Menton kinetics, fast binding to K^+ channels, quasi stationarity of the intermediate enzymatic reactions, no receptor desensitization, and an excess of inactive G-proteins G_o , to the following system,

$$\frac{d [\mathbf{R}_{j}]}{dt} = K_{1} [\mathbf{T}] (1 - [\mathbf{R}_{j}]) - K_{2} [\mathbf{R}_{j}]$$
$$\frac{d [\mathbf{G}_{j}]}{dt} = K_{3} [\mathbf{T}] [\mathbf{R}_{j}] - K_{4} [\mathbf{G}_{j}]$$
$$g_{j}^{\mathrm{GABA}_{\mathrm{B}}}(t) = \overline{g}_{j}^{\mathrm{GABA}_{\mathrm{B}}} \frac{[G(t)]^{n}}{[G(t)]^{n} + K_{d}}$$
$$I_{j}^{\mathrm{GABA}_{\mathrm{B}}} = g_{j}^{\mathrm{GABA}_{\mathrm{B}}}(t) \left(V - E_{\mathrm{rev}}^{\mathrm{GABA}_{\mathrm{B}}}\right)$$

where $\overline{g}_{j}^{\text{GABA}_{\text{B}}}$ is the maximal conductance of GABA_{B} receptors, $g_{j}^{\text{GABA}_{\text{B}}}(t)$ denotes the GABA_{B} conductance, K_{d} is the dissociation constant of G-protein binding to K^{+} channels, and $E_{\text{rev}}^{\text{GABA}_{\text{B}}} = -95$ mV is the reversal potential.

Table 1: Ion Channel densities used in the Layer 2/3 pyramidal cell model			
Symbol	Conductance density name	Density (pS/ μ m ²)	Reference(s)
$g_{ m L}$	Leak	0.25; (With spines 0.3827)	(Mainen et al. , 1995)
$g_{ m Na}$	Sodium	45	(Hamill et al., 1991; Huguenard et al., 1988)
$g_{ m K}$	Potassium	68	(Hamill et al., 1991)
$g_{\rm K(A)}$	A-type potassium	50	(Zhou and Hablitz, 1996)
$g_{\rm K(H)}$	Potassium H-current	Monotonically increasing	(Traub et al. , 2003)
$g_{ m Ca(HVA)}$	HVA L-type calcium	Monotonically increasing	(Hamill et al., 1991)
$g_{ m Ca(T)}$	LVA T-type calcium	4	(Hamill et al., 1991)
$g_{ m Ca(N)}$	N-type calcium	Monotonically increasing	(Lazarewicz et al., 2002)
$g_{ m K(Ca)}$	Ca ²⁺ -gated potassium	40	(Kang et al. , 1996)
$g_{\rm K_M}$	M-type potassium	3.5	(Rhodes and Gray, 1994; Rudolph and Destexhe, 2003)
$g_{ m mAHP}$	Medium hyperpolarization	15	(Rhodes and Gray, 1994; Poirazi et al., 2003)
$g_{ m sAHP}$	Slow hyperpolarization	1.5	(Traub et al., 2003; Poirazi et al., 2003)

TABLE

Stimulation was provided by a group of 250 inhibitory afferent fibers and two equally sized groups of 500 correlated excitatory afferents. Inhibitory and excitatory afferents are not correlated with each other. Furthermore, any afferent from one excitatory group was not correlated with any afferent from the other excitatory group. Put simply, the groups of correlated excitatory afferents were not correlated with each other (the correlation between any two different groups is zero). These groups of excitatory fibers will be referred to as groups A and B (when two groups are considered) and A,B,C, and D (when four groups are used). Each fiber, either excitatory or inhibitory, forms five random synaptic contacts in the model, as suggested by current anatomical data (**Markram et al.**, 1997; **Feldmeyer et al.**, 2002; **Thomson et al.**, 1994, 2002).

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