## Supplementary file 1A: Parameters of the mathematical model – intracellular dynamics

| Description | Name | Values | Units | Reference |
|---|---|---|---|---|
| $I_{NMDAR}$ to Ca flow conversion | $\xi_{NMDAR}$ | 98 | µM/pCol | set to match Ca2+ amplitudes in [1] |
| $I_{VSCC}$ to Ca flow conversion | $\xi_{VSCC}$ | 140 | µM/pCol | set to match Ca2+ amplitudes in [2] |
| $I_{TRPV1}$ to Ca flow conversion | $\xi_{TRPV1}$ | 290 | µM/pCol | set to match Ca2+ amplitudes in [1] |
| Total endogenous Ca buffer | $B_T$ | 4.5 | µM | Estimated from our experimental data |
| Basal cytoplasmic [Ca] | $Ca_b$ | 0.1 | µM | [1,3] |
| Time scale for Ca exit | $\tau_{Ca_b}$ | 0.007 | s | Idem |
| Endogenous Ca buffer affinity | $K_{dB}$ | 0.5 | µM | [3,4] |
| ER-to-cytosol volume ratio | $\rho_{ER}$ | 0.3 | - | Adapted from [4] |
| IP3R binding rate (inactivation) | $a_2$ | 0.5 | µM/s | Idem |
| Maximal SERCA pump rate | $v_{ER}$ | 8 | µM/s | Idem |
| IP3R affinity for IP3 | $d_3$ | 0.9434 | µM | [5] |
| Maximal IP3R rate | $r_C$ | 4 | 1/s | Adapted from [5] |
| Basal [Ca] in the ER | $Ca_{ER,b}$ | 65 | µM | [6] |
| Ca leak from the ER | $r_l$ | 0.1 | 1/s | [5] |
| IP3R affinity for Ca | $d_5$ | 0.12 | µM | Adapted from [5] |
| IP3R dissociation constant | $d_2$ | 3.049 | µM | Idem |
| SERCA pump affinity for Ca | $K_{ER}$ | 0.05 | µM | [5] |
| IP3R affinity for IP3 | $d_1$ | 0.13 | µM | Idem |
| PLCδ product inhibition | $\kappa_d$ | 1.5 | µM | Idem |
| PLCδ Ca-activation | $K_\delta$ | 0.1 | µM | Idem |
| 5P-IP maximal rate | $r_{5P}$ | 0.2 | 1/s | Adapted from [5] |
| PI3K maximal rate | $v_{3K}$ | 0.001 | µM/s | Idem |
| PI3K Ca-activation constant | $K_D$ | 1.5 | µM | Idem |
| PLCδ maximal rate | $v_\delta$ | 0.02 | µM/s | [5] |
| PI3K affinity for IP3 | $K_3$ | 1 | µM | Idem |
| Glutamate affinity to mGluR | $K_R$ | 1.3 | µM | Idem |
| regulation by PLCβ termination | $K_P$ | 10 | µM | Idem |
| PLCβ maximal rate | $v_\beta$ | 0.8 | µM/s | Adapted from [5] |
| PKC Ca-activation constant | $K_\pi$ | 0.6 | µM | [5] |
| Total CaMKIIα concentration | $CaMK_{tot}$ | 16.6 | µM | [7] |
| Total Calmodulin concentration | $CaM_{tot}$ | 0.07085 | µM | Adapted from [7] |
| PKA Hill number | $n_{PKA}$ | 3 | - | Idem |

Referenced articles: [1] Sabatini, B.L., Oertner, T.O. and Svoboda, K. (2002) *Neuron* 33(3):439-452 [2] Carter, A.G. and Sabatini, B.L. (2004) *Neuron* 44(3):483-493 [3] Jackson, M.B. and Redman, S.J. (2003) *J Neurosci* 23:1612–1621 [4] Nägerl, U.V. *et al.* (2000) *Biophys J* 79: 3009–3018 [5] De Pittà M. *et al.* (2009) *J Biol Phys* 35:383-411 [6] Solovyova, N. *et al.* (2002) *EMBO J* 21:622-630 [7] Graupner, M. and Brunel, N. (2007) *PLoS Comput Biol* 3:e221.

## Supplementary file 1B: Parameters of the mathematical model – electrophysiology

| Description | Name | Values | Units | Reference |
|---|---|---|---|---|
| TRPV1R max. conductance | $g_{TRPV1}$ | 0.0003 | nS | Estimated from our experimental data |
| Permeability of L-type VSCC | $p_{VSCC}$ | 0.00000102 | µM/s | Value of [1], scaled to ~5,000 spines, radius 1 µm |
| AMPAR maximal conductance | $g_{AMPAR}$ | 5.1 | nS | Estimated from our experimental data |
| AMPAR closing rate constant | $\beta_{AMPAR}$ | 190 | 1/s | Adapted from [2] |
| AMPAR opening rate constant | $\alpha_{AMPAR}$ | 1.02 | 1/(µM.s) | Idem |
| NMDAR maximal conductance | $g_{NMDAR}$ | 1.53 | nS | Estimated from our experimental data |
| Magnesium concentration | Mg | 1 | mM | Directly measured in our experiments |
| NMDAR opening rate constant | $\alpha_{NMDAR}$ | 0.072 | 1/(µM.s) | Set to emulate the experimental kinetics of NMDAR-transported Ca in [3] |
| NMDAR closing rate constant | $\beta_{NMDAR}$ | 100 | 1/s | Idem |
| Resting membrane potential | $V_L$ | -70 | mV | Directly measured in our experiments |
| Leak conductance | $g_L$ | 10 | nS | Idem |
| Membrane capacitance | $C_m$ | 0.1 | nF | Idem |
| Extracellular Ca2+ concentration | $Ca_{out}$ | 5000 | µM | [1] |
| Duration of depolarization step | $DC_{dur}$ | 0.03 | s | From the experimental stimulation protocol |
| Amplitude of depolarization step | $DC_{\max}$ | 495 | pA | Idem |
| Amplitude of action current | $AP_{\max}$ | 7020 | pA | [4] |
| Time constant of action current | $\tau_{bAP}$ | 0.001 | s | Idem |
| Glutamate peak concentration in the cleft | $G_{\max}$ | 2000 | µM | Estimated from our experimental data |
| Glutamate decay time constant in the cleft | $\tau_G$ | 0.005 | s | Estimated from our experimental data |
| Delay to bAP outset | $\delta$ | 0.015 | s | From the experimental stimulation protocol |
| Stimulation frequency | Frequency | 1 | Hz | From the experimental stimulation protocol |

Referenced articles: [1] Wolf, J.A. *et al.* (2005) *J Neurosci* 25(40):9080-9095 [2] Destexhe, A., Mainen, Z., and Sejnowski, T. (1994) *J Comput Neurosci* 1:195-230 [3] Sabatini, B.L., Oertner, T.O. and Svoboda, K. (2002) *Neuron* 33(3):439-452 [4] Fino, E., *et al*. (2010) *J Physiol* 588:3045-3062.

## Supplementary file 1C: Parameters of the mathematical model – endocannabinoid dynamics

| Description | Name | Values | Units | Reference |
|---|---|---|---|---|
| Scaling factor for endocannabinoid contribution to plasticity | $k_{CB1R}$ | 3000 | 1/µM | Estimated from our experimental data |
| AEA efficiency for CB1R activation (compared to 2-AG) | $\alpha$ | 0.1 | - | Idem |
| presynaptic plasticity time scale | $P_1$ | 1e-9 | s | Set to yield rapid / slow changes of Wpre for high / low 2-AG values, respectively |
| presynaptic plasticity time scale | $P_2$ | 1e-5 | - | Idem |
| presynaptic plasticity time scale | $P_3$ | 7 | - | Idem |
| presynaptic plasticity time scale | $P_4$ | 2 | s | Idem |
| The lower limit of LTD induction | $\theta_{LTD}^{start}$ | 0.027 | - | Estimated from our experimental data |
| The upper limit of LTD induction | $\theta_{LTD}^{stop}$ | 0.047 | - | Idem |
| The constant determining the rate of LTD induction | $A_{LTD}$ | 0.65 | - | Idem |
| The lower limit of LTP induction | $\theta_{LTP}^{start}$ | 0.087 | - | Idem |
| The constant determining the rate of LTP induction | $A_{LTP}$ | 10.8 | - | Idem |
| CB1R opening rate constant | $\alpha_{CB1R}$ | 0.2402 | 1/(µM.s) | Idem |
| CB1R closing rate constant | $\beta_{CB1R}$ | 11.072 | 1/s | Idem |
| CB1R desensitization rate constant | $\gamma_{CB1R}$ | 416.38 | 1/s | Idem |
| CB1R closing rate constant | $\varepsilon_{CB1R}$ | 0.047796 | 1/s | Idem |
| DAGL α affinity for DAG | $K_{DAGL}$ | 30 | µM | [1] |
| Maximal rate of MAG lipase | $r_{MAGL}$ | 0.5 | µM/s | Set for rapid turnover dynamics. |
| Maximal DAGL α rate | $r_{DGL}$ | 20000 | µM/s | Idem |
| Maximal DAG kinase activity | $r_{DAGK}$ | 2 | µM/s | Idem |
| Hill number for DAGL activation by Ca | $n_c$ | 6 | - | Estimated from our experimental data |
| DAGL dephosphorylation rate | $r_P$ | 380 | $s^{-1}$ | Idem |
| DAGL phosphorylation rate | $r_K$ | 50 | $\mu M^{-1}.s^{-1}$ | Idem |
| Total DAGL concentration | $DAGL$ | 1 | µM | Idem |
| N-acetyltransferase activity | $v_{AT}$ | 0.2 | 1/s | Idem |
| FAAH Michaelis-Menten constant | $K_{FAAH}$ | 1 | µM | [1] |
| FAAH enzyme activity | $r_{FAAH}$ | 4 | µM/s | Estimated from our experimental data |

Referenced articles: [1] Okamoto, Y. et *al.* (2004) *J Biol Chem* 279:5298-5305.