Model Details

The reconstructed CA1 pyramidal neuron model was adapted from that in our previous studies [1,2]. The morphology of the neuron model was obtained from Duke-Southampton Archive of neuronal morphology [3], which included 200 compartments. The passive cable properties and the density and distribution of active conductances in the model neuron were based on published experimental data obtained from hippocampal and cortical pyramidal neurons. Below are the details of the neuron model.

Active Property

For active conductances, the model neuron included voltage-gated sodium conductance g_{Na}, the delayed rectifier potassium conductance g_{K_d}, two variants of A-type potassium conductance $g^p_{K_A}$ and $g^d_{K_A}$ that were applied to the proximal and distal dendrites respectively, and the hyperpolarization-activated conductance g_h. It also contained AMPA, NMDA, GABA_A, and GABA_B receptors, with kinetic properties described previously [4–6]. The receptors of AMPA, NMDA, and GABA_A followed a first-order kinetics of transmitter binding to the postsynaptic receptors

$$\frac{dR}{dt} = \alpha \cdot [T] \cdot (1 - R) - \beta \cdot R,$$

where R is the fraction of open receptors, α and β are forward and backward rate constants for transmitter binding, and $[T]$ is the transmitter concentration. The postsynaptic current is given by

$$I_{syn} = g \cdot (V - E_{rev}),$$

where V is the postsynaptic potential, E_{rev} the reversal potential, and g the synaptic conductance. For AMPA and GABA_A receptors,

$$g = g_{max} \cdot R,$$

where g_{max} is the maximum synaptic conductance. And for NMDA receptor,

$$g = \frac{g_{max} \cdot R}{1 + 0.33 \cdot [Mg^{2+}] \cdot e^{-0.06 \cdot V}},$$

where $[Mg^{2+}]$ is the extracellular magnesium concentration. For GABA_B receptor, the kinetic equations are

$$\frac{dR}{dt} = K_1 \cdot [T] \cdot (1 - R) - K_2 \cdot R,$$
$$\frac{dG}{dt} = K_3 \cdot R - K_4 \cdot G,$$

where K_1 and K_2, similar to α and β, are forward and backward transmitter binding rate, K_3 and K_4 the rate constants of G protein production and decay. G is the fraction of activated G proteins;

$$g = \frac{g_{max} \cdot G^n}{G^n + K_D},$$

where K_D is the dissociation constant of potassium channel.

The parameters used in the four types of receptors are largely the same as previous reports [4–8], with minor adjustments to match the results from our previous iontophoretic experiment [1]. Sodium channels were distributed with a largely constant density along the somatodendritic axis [9]. The A-type

potassium channels differed in their kinetics between the proximal and distal populations, and their density increased progressively by more than 6-fold from the soma to a distance of 350 μm along the apical trunk [10, 11]. The density of hyperpolarization-activated cationic current I_h increased by more than 6 folds from the soma to the distal dendrites [12]. The distribution of AMPA receptors was set with a gradient along the dendrite to achieve a distance-dependent scaling property [13–16].

Based upon the above experimental results, the parameters used in the model were set as follows: the peak sodium conductance $g_{Na} = 30$ mS/cm^2 in the soma and dendrites, $g_{Na} = 60$ mS/cm^2 in the axon; $g_{Kd} = 5$ mS/cm^2 (uniform distribution); $g^p_{K_A}(x) = g^{p_0}_{K_A} \cdot (1 + x/70)$, if the distance from the soma $x \leq 100$ μm; $g^d_{K_A}(x) = g^{d_0}_{K_A} \cdot (1 + x/70)$, if 100 μm $< x \leq 350$ μm; and $g^d_{K_A}(x) = 6.5 \cdot g^{d_0}_{K_A}$ if $x > 350$ μm, where $g^{p_0}_{K_A} = g^{d_0}_{K_A} = 5$ mS/cm^2; $g_h(x) = g_{h_0} + 9 \cdot g_{h_0}/[1.0 + e^{(300-x)/50}]$, where $g_{h_0} = 20$ μS/cm^2; the ratio of maximal NMDA conductance to AMPA conductance was of the form $r_{N/A} = 0.6/(1 + x/300)$ for the dendrite located in the stratum radiatum and the ratio of GABA$_B$ to GABA$_A$ was set as 0.6.

Passive Property

The resting membrane resistance R_m was set to be nonuniform along the dendritic tree [17]. The passive biophysical properties include: $R_m = R_{m_0} + (R_{m_1} - R_{m_0})/[1.0 + e^{-(x-300)/50}]$, where $R_{m_0} = 60$ kΩcm^2 and $R_{m_1} = 20$ kΩcm^2; the axial resistance $R_i = 80$ Ωcm; the capacitance $C_m = 1$ μF/cm^2. The temperature was 34 ^{o}C and the resting membrane potential was -70 mV. Reversal potentials were set as: $E_{Na} = +55$ mV, $E_K = -90$ mV, $E_h = -30$ mV, $\mathrm{E_{AMPA}} = \mathrm{E_{NMDA}} = 0$ mV, $\mathrm{E_{GABA_A}} = -80$ mV, $\mathrm{E_{GABA_B}} = -90$ mV.

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