**Name**: Granule Cell (Staley et al. 1992) –Dentate Gyrus granule cell

**Biological Data**

**Passive properties**: Vrest = Tau = Rin = (Staley et al. 1992)

Current injection responses: injection, spiking frequency

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Model data**

**Model cell morphology**: Included in table S2

**Model cell conductances**: Included in table S2

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**Calculation of model granule neuron passive properties:**

|  |
| --- |
| **1. V\_rest = -84 mV**  **2. Calculation of time constant:**  Start inject: 300ms / -84 mV Final Value: ~ -112.941mV Difference: -28.941 | 63.2% = 18.2907 | -84 – 18.2907 = -102.2907  Time at -102.2907: 327.7ms τ = 327.7-300  τ = 27.7 ms  **τ = .0277 s**  **3. Input Resistance**  ΔV/ΔI = ( -84 – (-112.941) )/( 0 – (-100) )  = 28.941/ 100pA   = .028941 V/.0000000001 A = 289410000 Ω **R\_in = 289.41 MΩ** |

**Match with reported current injection responses (provide all):**

|  |  |  |
| --- | --- | --- |
| **-200** |  |  |
| **pA** | **Real** | **Cell Model** |

**Note:** this model does not exhibit adaptation behavior as reported in (Staley et al. 1992). This is a known weakness in this model and requires further improvement.

**Table 2-1. GATING PARAMETERS OF ION CHANNELS**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Current Type** | **Gating Variable** | **α** | **β** |  | **τx (ms)** |
| *INa* | *p=3* |  |  |  |  |
| *q=1* |  |  |  |  |
| *IKdr* | *p=1* |  |  |  |  |
| *IH* | *q=1* |  |  |  |  |

**Table S2. Parameters of single cell models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Dentate Gyrus Granule Cell | | |
|  | Soma | Dendrite 0 | Dendrite 1 |
| Cm (µF/cm2) | 0.8 | 0.8 | 0.8 |
| Ra (Ωcm) | 35.4 | 35.4 | 35.4 |
| diam (µm) | 15 | 3 | 5 |
| L (µm) | 20 | 270 | 555 |
| nseg | 1 | 8 | 7 |
| Conductance  (mho/cm2)  gNabar  gKdrbar  gLeak  gHdbar | 0.07  0.003 | 0.07  0.003 | 0.009  0.003 |

**Model implementation**

Models of single neurons and of the network were developed using experimental cellular and microcircuit parameters from our Lab and the literature, including for network connectivity and synaptic strengths. The network model was run on the parallel NEURON 7.4 simulator (*53*), with a fixed time step of 25 µs.

*Mathematical equations for voltage-dependent ionic currents:* The dynamics for each compartment (soma or dendrite) followed the Hodgkin-Huxley formulation as previously described (*54*) in eqn. 1,

(1)

where are the somatic/dendritic membrane potential (mV), and are the intrinsic and synaptic currents in the soma, is the electrode current applied to the soma, is the membrane capacitance, is the conductance of the leak channel, and is the coupling conductance between the soma and the dendrite (similar term added for other dendrites connected to the soma). The intrinsic current *,* was modeled as, where is its maximal conductance, *m* its activation variable (with exponent *p*), *h* its inactivation variable (with exponent *q*), and its reversal potential (a similar equation is used for the synaptic current but without *m* and *h*). The kinetic equation for each of the gating variables *x* (*m* or *h*) takes the form but without *m* and *h*). The kinetic equation for each of the gating variables *x* (*m* or *h*) takes the form

(2)

where is the steady state gating voltage- and/or Ca2+- dependent gating variable and is the voltage**-** and/or Ca2+**-** dependent time constant. The equation for the dendrite follows the same format with ‘*s*’ and ‘*d*’ switching positions in eqn. 1.   
*Principal neuron (PN) models*: PN had five compartments: soma (diameter 24.75 µm, length 25 µm), an apical dendrite (a-dend; diameter 3µm; length 270 µm), another dendrite (p-dend; diameter 5 µm; length 555µm) to match passive properties, an axon initial segment (AIS; diameter 0.5 µm; length 50 µm), and an axon (diameter 0.5 µm; length 100 µm). Values of specific membrane resistance, membrane capacity and cytoplasmic (axial) resistivity were, respectively, Rm = 40 ± 5 kΩ-cm2, Cm = 1.5 µF/cm2, and Ra = 150 Ω-cm. Leakage reversal potential (*E*L) was set to -75 ± 4 mV. The resulting Vrest was -66 ± 4 mV, input resistance (*R*IN) was 140 ± 20 MΩ, and time constant (τm) was ~30 ms, all of which were within the ranges reported in previous physiological studies (*55*). Soma and dendrite compartments had the following currents: leak (*I*L), voltage-gated persistent muscarinic (*I*M), high-voltage activated Ca2+ (*I*Ca), spike-generating sodium (*I*Na), potassium delayed rectifier (*I*DR), A-type potassium (*I*A) (*56, 57*) and hyperpolarization-activated nonspecific cation (*I*h) current. In addition, the soma had a slow apamin-insensitive, voltage-independent afterhyperpolarization current (*I*sAHP) (*57, 58*). The axonal compartments had the following currents: leak (*I*L*),* high-threshold sodium *(I*Na1.2*),* low-threshold sodium *(I*Na1.6*)*, and potassium delayed rectifier (*I*DR) (*59*). See Tables S1 and S2 for equations of current kinetics and maximal densities. Based on firing patterns observed in slices, PNs in the model had Type-A (adapting) and Type C (continuous) generated by adjusting magnitude of Ca2+-dependent K+ current, either 50 or 0.2 mS/cm2, respectively (*54*). PN models contained properties for low- and high- threshold oscillation to mimic physiological parameters as closely as possible (*54, 56, 60, 61*).   
*Interneuron (IN) models:* Since most INs sampled in experiments showed fast-spiking Int (FSI) characteristics they were modelled as FSI. The IN model contained five compartments; a soma (diameter 10 µm; length 20 µm) and four dendrites (diameter 3 µm; length 100 µm). Each compartment contained a fast Na+ (*I*Na) and a delayed rectifier K+ (*I*DR) current. Network contains two types of INs: (a) Basket INs that target PN at the soma, and (b) Chandelier IN (Chn) that target PN at the AIS. Both models reproduced APs with short half-width (<1 ms). Passive membrane properties of Basket INs and Chns were Rm = 10 ± 1 and 15 ± 1 kΩ-cm2, Cm = 1.4 and 0.8 µF/cm2, Ra = 100 and 100 Ω-cm, respectively.   
*Network size and cell type proportions:* To model a 400 µm (1.4 x 1.4 x 0.4 mm) basal amygala slice, we generated 20,572 neurons with cellular composition of 40% PNA (n=8,229), 40% PNC (n=8,229), 18% Basket INs (n=3,708), and 2% Chandelier INs (n=406).

*Mathematical equations for synaptic currents:* All excitatory transmission was mediated by AMPA/NMDA receptors, and inhibitory transmission by GABAA receptors. The corresponding synaptic currents were modelled by dual exponential functions (*62, 63*), as shown in eqns. 3-5,

(3)

(4)

(5)

where *V* is the membrane potential (mV) of the compartment (dendrite or soma) where the synapse is located, *I* is the current injected into the compartment (nA), *G* is the synaptic conductance (µS), is the synaptic weight (unitless), and *E* is the reversal potential of the synapse (mV). *gx,max* is the maximal conductance (µS), *F* implements short-term plasticity as defined in the next section, and *rx* determines the synaptic current rise and decay time constants based on the terms *αTmax*and β (*62*). The voltage-dependent variable *s*(*V*) which implements the Mg2+ block was defined as: *s*(*V*) = [1 + 0.33 exp(-0.06 *V*)]-1 (*64*). The terms *ONNMDA* and *ONAMPA* are set to 1 if the corresponding receptor is open, else to 0. Synaptic parameter values are listed in Table S3 as mean ± std. For all connections, synaptic weight *w* was distributed log-normally with a cut off of three times the mean to prevent non-physiological values.

*Short-term presynaptic plasticity:* The term Int represents both Chns and Basket INs. All model AMPA and GABA synapses also exhibited short term pre-synaptic plasticity (*54*). Short-term depression was modelled at Int->PN and PN->Int connections based on experimental findings in this study and previous reports (*49*). Short term plasticity was implemented as follows (*65*): For facilitation, the factor F was calculated using the equation: and was constrained to be ≥ 1.After each stimulus, F was multiplied by a constant, f (≥ 1) representing the amount of facilitation per pre-synaptic action potential and updated as F→F\*f. Between stimuli, F recovered exponentially back toward 1. A similar scheme was used to calculate the factor D for depression: τ\_D\*dD/dt=1-D and D constrained to be ≤ 1.After each stimulus, D was multiplied by a constant d (≤ 1) representing the amount of depression per pre-synaptic action potential and updated as D→D\*d. Between stimuli, D recovered exponentially back toward 1.We modelled depression using two factors d1 and d2 with d1 being fast and d2 being slow subtypes, and d=d\_1\*d\_2 and was constrained to be ≥ 1. After each stimulus, F was multiplied by a constant, f (≥ 1) representing the amount of facilitation per pre-synaptic action potential and updated as F→F\*. Parameters for modelling short-term plasticity are listed in Table S4. Our model did not have long-term synaptic plasticity.

*Intrinsic connections:* Except for Int->Int connectivity that had both chemical and electrical components, all other connections were via chemical synapses; hereafter, unless qualified by ‘electrical’, the connections are assumed to be via chemical synapses. PN->PN connections were not detected in BLA (our unpublished data) and so were not included. For all the other connection types, we used published data (*49*), limiting connectivity from/to INs to within ~300 µm. Using such data, probabilities in the model for unidirectional Int->PN and PN->Int synaptic connections, and for Int->Int electrical connections were, respectively, 34%, 12%, and 8%. Also, reciprocal connections between PNs and INs was set to 16%. These connectivity numbers in our model resulted in an overall synaptic Basket->Basket and Basket->Chn connectivity of 26% of which 20% was unidirectional and 3% bi-directional. Chns contacted only PNs so there were no Chn->Chn or Chn->Basket IN connections. These probabilities resulted in the intrinsic connectivity shown in Table S4. Axonal conduction delay was distance-dependent using a conduction velocity of 500 μm/ms.

**References**

Staley, K., Otis, T., & Mody, I., (1992) Membrane Properties of Dentate Gyrus Granule Cells: Comparison of Sharp Microelectrode and Whole-Cell Recordings*. Journal of Neuroscience*, 67(5) 1346–1358.