**Name**: Oriens Lacunosum-Moleculare (OLM) (Ali and Thomson, 1998) – Hippocampal CA3 Interneuron

**Biological Data**

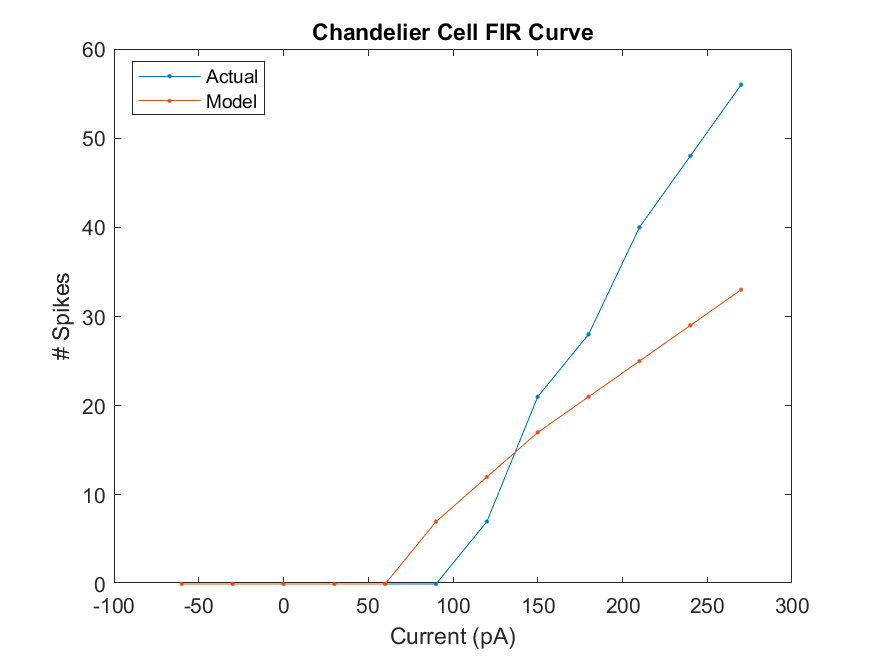
**Passive properties**: Vrest = -65 mV to -85 mV Tau = 12·8 ± 1·5 ms Rin = 70 ± 13·72 MΩ (Ali and Thomson, 1998)

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**Passive properties of model OLM Interneuron:**

|  |
| --- |
| **1. V\_rest = -68.5 mV**  **2. Calculation of time constant:**  Start inject: 300ms / -68.5mV Final Value: ~ -74.94mV Difference: -6.44 | 63.2% = -4.07 | -68.5 - 4.07 = - 70.4352 Time at - 72.57: 113.7ms τ = 310.55-300  τ = 10.55 ms  **τ = .01055 s**  **3. Input Resistance**  ΔV/ΔI = ( -68.5 – (-74.94) )/( 0 – (-100) )  = 6.44mV / 60pA  **R\_in =64.417 MΩ** |

**Comparison of F-I curves**:



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

|  |  |  |
| --- | --- | --- |
| **-60** |  |  |
| **pA** | **Real** | **Cell Model** |

|  |  |  |
| --- | --- | --- |
| **120** |  |  |
| **pA** | **Real** | **Cell Model** |

**ADD ALL CURRENT INJECTIONS IN BIOLOGY PLUS MATCH IN MODEL**

**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* |  |  |  |  |
| *IKM* | *p=2* |  |  |  |  |
| *ICa* | *p=2* | ― | ― |  |  |
| *q=1* | ― | ― |  | 420 |
| *INap* | *p=1* | ― | ― |  |  |
| *IsAHP* | *p=1* |  |  |  | 48 |

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

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Chandelier interneuron | | Basket interneuron | | Type A Principal neuron | | | Type C Principal neuron | | |
|  | soma | dendrites | soma | dendrites | soma | dendrites | axon | soma | dendrites | axon |
| Cm (µF/cm2) | 0.8 | 0.8 | 1.4 | 1.4 | 1.5 | 1.5 | 0.4 | 1.5 | 1.5 | 0.4 |
| Ra (Ωcm) | 100 | 100 | 100 | 100 | 150 | 150 | 150 | 150 | 150 | 150 |
| Conductance  (mho/cm2)  gNabar  gKdrbar  gLeak  gNapbar  gHdbar  gCabar  gMbar  gsAHPbar  gKapbar | 0.096  0.0045  0.0001  --  --  --  --  --  -- | 0.024  0.0011  0.0001  --  --  --  --  --  -- | 0.156  0.0103  1.5e-4  --  --  --  --  --  -- | 7.82e-3  2.77e-3  1.5e-4  --  --  --  --  --  -- | 0.015  0.002  4.8e-5  5.59e-4  1.5e-5  5.5e-4  2.2e-3  0.05  0.002 | 0.015  0.002  4.8e-5  5.59e-4  1.5e-5  5.5e-4  2.2e-3  0.05  0.002 | \*\*  0.002  0.001  --  --  --  --  --  -- | 0.015  0.002  4.8e-5  5.59e-4  1.5e-5  5.5e-4  2.2e-3  0.0002  0.002 | 0.015  0.002  4.8e-5  5.59e-4  1.5e-5  5.5e-4  2.2e-3  0.0002  0.002 | \*\*  0.002  0.001  --  --  --  --  --  -- |

\*\* Sodium channel densities were exponentially distributed along the axon as in Hu et al. (*59*)

**Table 2-2. SYNAPTIC PARAMETERS**

|  |  |  |  |
| --- | --- | --- | --- |
| **Pre-Post** | **AMPA/NMDA** reversal potential (mV) and rise/decay time constant (ms) and conductance (uS) | **GABA** reversal potential (mV) and rise/decay time constants (ms) and conductance (uS) | **Synaptic Current (pA)** |
| **Chn – PN** | -- | -50 mV; Rise: 0.83 ms;  Decay: 6.27 ms; 3.0e-3 uS  (Veres et al. 2014) | 41 ± 35  (Galaretta and Hestrin 1997) |
| **PV – PN** | -- | -70 mV; Rise: 0.3 ms;  Decay: 7.5/33.2 ms; 8e-3 uS  (Galaretta and Hestrin 1997) | 39 ± 9  (Galaretta and Hestrin 1997) |
| **PN- PN** | -- | -- | -- |
| **PN- Chn** | 0 mV; Rise: 0.88 ms;  Decay: 2.3 ms; 2.35e-3 uS  (Sah Lab – personal communication) | -- | 144.4 ± 107.7  (Sah Lab – personal communication) |
| **PV- Chn\*** | -- | -70 mV; Rise: 1.1 ms;  Decay: 6.8/30.74 ms; 8e-3 uS | 39 ± 9 |
| **Chn – Chn\*** | -- | -70 mV; Rise: 1.1 ms;  Decay: 6.8 ms; 4e-3 uS  **Gap junction coupling coeff.**  0.2 (unitless) | 39 ± 9 |
| **PV – PV** | *--* | -70 mV; Rise: 1.1 ms;  Decay: 6.8 ms; 4e-3 uS  **Gap junction** **coupling coeff.**  0.2 (unitless)  (Woodruff and Sah 2007) | 39 ± 9  (Woodruff et al. 2006) |
| **Chn – PV\*** | -- | -70 mV; Rise: 1.1 ms;  Decay: 6.8 ms; 4e-3 uS | 39 ± 9 |
| **PN- PV** | 0 mV; Rise: 0.69 ms;  Decay: 1.83 ms; 2.0e-3  (Sah Lab – personal communication) | *--* | 139.9 ± 75.95  (Sah Lab – personal communication) |

\* - Unknown. Assumed similar to PV-PV.

Finally, a writeup for inclusion in manuscripts:

**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**

Ali AB, Thomson AM. 1998. Facilitating pyramid to horizontal oriens-alveus interneurone inputs: Dual intracellular recordings in slices of rat hippocampus. J Physiol 507:185–199.