**Tables**

**Table 1 Population sizes for neuron types utilized in the network models**

|  |  |  |
| --- | --- | --- |
| Neuron Type | Super Type | Population Size |
| CA3 Pyramidal | Glutamatergic PC:Pyramidal:CA3 | 74,366 |
| CA3 Axo-axonic | Perisomatic-targeting:Axo-axonic:CA3 | 1,909 |
| CA3 Basket | Perisomatic-targeting:Basket:CA3 | 515 |
| CA3 Basket CCK+ | Perisomatic-targeting:Basket CCK+:CA3 | 665 |
| CA3 Bistratified | Collateral-related:RO-targeting:CA3 | 4,631 |
| CA3 Ivy | Ivy/Neurogliaform Family:Ivy/Neurogliaform:CA3 | 2,334 |
| CA3 MFA ORDEN | Mossy Fiber-related:L-targeting:CA3 | 1,526 |
| CA3 QuadD-LM | O-LM Family:O-LM-Like:CA3 | 3,280 |
| Total |  | 89,226 |

Abbreviations: CCK+, Cholecystokinin positive; O-LM, Oriens-Lacunosum Moleculare

**Table 2 Izhikevich parameters by neuron type**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Neuron Type | k | a | b | d | C | Vr | Vt | Vmin | Vpeak |
| CA3 Pyramidal | 0.792 | 0.008 | -42.552 | 588 | 366 | -63.204 | -33.604 | -38.868 | 35.861 |
| CA3 Axo-Axonic | 3.961 | 0.005 | 8.684 | 15 | 165 | -57.100 | -51.719 | -73.969 | 27.799 |
| CA3 Basket | 0.995 | 0.004 | 9.264 | -6 | 45 | -57.506 | -23.379 | -47.556 | 18.455 |
| CA3 BC CCK+ | 0.583 | 0.006 | -1.245 | 54 | 135 | -58.997 | -39.398 | -42.771 | 18.275 |
| CA3 Bistratified | 3.935 | 0.002 | 16.580 | 19 | 107 | -64.673 | -58.744 | -59.703 | -9.929 |
| CA3 Ivy | 1.916 | 0.009 | 1.908 | 45 | 364 | -70.435 | -40.859 | -53.400 | -6.920 |
| CA3 MFA ORDEN | 1.380 | 0.008 | 12.933 | 0 | 209 | -57.076 | -39.102 | -40.681 | 16.313 |
| CA3 QuadD-LM | 1.776 | 0.006 | -3.449 | 52 | 186 | -73.482 | -54.937 | -64.404 | 7.066 |

**Table 3 Connection probability for each connection type in the network model**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Pre-Post | CA3 Pyramidal | CA3 Axo-Axonic | CA3 Basket | CA3 BC CCK+ | CA3 Bistratified | CA3 Ivy | CA3 MFA ORDEN | CA3 QuadD-LM |
| CA3 Pyramidal | 0.025 | 0.015 | 0.020 | 0.017 | 0.016 | 0.025 | 0.021 | 0.013 |
| CA3 Axo-Axonic | 0.150 |  |  |  |  |  |  |  |
| CA3 Basket | 0.150 | 0.025 | 0.005 | 0.005 | 0.025 |  | 0.005 | 0.005 |
| CA3 BC CCK+ | 0.150 | 0.025 | 0.005 | 0.005 | 0.025 |  | 0.005 | 0.025 |
| CA3 Bistratified | 0.028 | 0.007 | 0.009 | 0.004 | 0.033 | 0.004 | 0.009 | 0.008 |
| CA3 Ivy | 0.072 | 0.004 | 0.016 | 0.011 | 0.017 | 0.004 | 0.017 | 0.002 |
| CA3 MFA ORDEN | 0.042 | 0.004 | 0.007 | 0.005 | 0.005 | 0.003 | 0.002 | 0.004 |
| CA3 QuadD-LM | 0.119 | 0.005 | 0.067 | 0.050 |  |  |  |  |

Presynaptic cell types are listed in the first column, while postsynaptic cell types are listed in the first row

**Table 4 STP parameters and synaptic delays for each connection type in the model**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Presynaptic** | **Postsynaptic** | **g** | **τd** | **τr** | **τf** | **U** | **Synaptic Delay** |
| CA3 Pyramidal | CA3 Pyramidal | 0.66 | 10.22 | 318.51 | 21.45 | 0.28 | 1 |
| CA3 Pyramidal | CA3 Axo-Axonic | 0.65 | 4.92 | 630.73 | 26.26 | 0.26 | 1 |
| CA3 Pyramidal | CA3 Basket | 1.70 | 3.97 | 691.42 | 21.16 | 0.12 | 1 |
| CA3 Pyramidal | CA3 Basket CCK+ | 0.85 | 4.29 | 530.40 | 22.45 | 0.20 | 1 |
| CA3 Pyramidal | CA3 Bistratified | 0.62 | 5.37 | 569.15 | 23.85 | 0.26 | 1 |
| CA3 Pyramidal | CA3 Ivy | 1.77 | 5.67 | 552.27 | 26.73 | 0.12 | 1 |
| CA3 Pyramidal | CA3 Mossy Fiber-Associated ORDEN | 0.88 | 5.95 | 444.99 | 29.01 | 0.15 | 1 |
| CA3 Pyramidal | CA3 QuadD-LM | 0.87 | 5.82 | 453.29 | 27.16 | 0.15 | 1 |
| CA3 Axo-Axonic | CA3 Pyramidal | 1.22 | 7.62 | 361.03 | 12.93 | 0.13 | 1 |
| CA3 Basket | CA3 Pyramidal | 1.02 | 7.64 | 384.34 | 16.74 | 0.13 | 1 |
| CA3 Basket | CA3 Axo-Axonic | 2.63 | 3.80 | 725.03 | 23.21 | 0.19 | 1 |
| CA3 Basket | CA3 Basket | 1.80 | 3.01 | 689.51 | 11.19 | 0.39 | 1 |
| CA3 Basket | CA3 Basket CCK+ | 1.69 | 4.21 | 636.76 | 16.72 | 0.24 | 1 |
| CA3 Basket | CA3 Bistratified | 2.30 | 4.72 | 680.33 | 16.72 | 0.18 | 1 |
| CA3 Basket | CA3 Mossy Fiber-Associated ORDEN | 1.36 | 5.23 | 581.94 | 19.60 | 0.30 | 1 |
| CA3 Basket | CA3 QuadD-LM | 1.31 | 5.16 | 589.20 | 19.31 | 0.31 | 1 |
| CA3 Basket CCK+ | CA3 Pyramidal | 0.85 | 9.10 | 376.87 | 13.76 | 0.08 | 1 |
| CA3 Basket CCK+ | CA3 Axo-Axonic | 1.94 | 5.44 | 477.43 | 18.50 | 0.12 | 1 |
| CA3 Basket CCK+ | CA3 Basket | 0.96 | 4.69 | 505.12 | 14.86 | 0.28 | 1 |
| CA3 Basket CCK+ | CA3 Basket CCK+ | 0.97 | 4.89 | 283.28 | 23.38 | 0.12 | 1 |
| CA3 Basket CCK+ | CA3 Bistratified | 1.78 | 5.97 | 478.31 | 15.25 | 0.13 | 1 |
| CA3 Basket CCK+ | CA3 Mossy Fiber-Associated ORDEN | 1.02 | 6.54 | 421.42 | 17.84 | 0.21 | 1 |
| CA3 Basket CCK+ | CA3 QuadD-LM | 1.00 | 6.48 | 398.15 | 17.34 | 0.22 | 1 |
| CA3 Bistratified | CA3 Pyramidal | 0.93 | 7.49 | 481.85 | 16.61 | 0.12 | 1 |
| CA3 Bistratified | CA3 Axo-Axonic | 2.15 | 4.57 | 686.28 | 19.16 | 0.17 | 1 |
| CA3 Bistratified | CA3 Basket | 1.10 | 3.86 | 695.21 | 14.60 | 0.37 | 1 |
| CA3 Bistratified | CA3 Basket CCK+ | 1.44 | 4.58 | 592.19 | 17.69 | 0.22 | 1 |
| CA3 Bistratified | CA3 Bistratified | 2.01 | 4.58 | 775.04 | 13.60 | 0.17 | 1 |
| CA3 Bistratified | CA3 Ivy | 1.34 | 5.33 | 649.83 | 18.17 | 0.30 | 1 |
| CA3 Bistratified | CA3 Mossy Fiber-Associated ORDEN | 1.57 | 5.54 | 605.25 | 18.30 | 0.29 | 1 |
| CA3 Bistratified | CA3 QuadD-LM | 1.12 | 5.53 | 594.33 | 17.89 | 0.30 | 1 |
| CA3 Ivy | CA3 Pyramidal | 1.00 | 9.01 | 439.50 | 23.01 | 0.12 | 1 |
| CA3 Ivy | CA3 Axo-Axonic | 2.29 | 5.67 | 651.64 | 25.51 | 0.17 | 1 |
| CA3 Ivy | CA3 Basket | 1.16 | 4.75 | 665.16 | 19.12 | 0.37 | 1 |
| CA3 Ivy | CA3 Basket CCK+ | 1.54 | 5.40 | 614.01 | 20.98 | 0.23 | 1 |
| CA3 Ivy | CA3 Bistratified | 2.16 | 6.24 | 660.48 | 22.69 | 0.17 | 1 |
| CA3 Ivy | CA3 Ivy | 1.39 | 5.51 | 675.54 | 17.72 | 0.31 | 1 |
| CA3 Ivy | CA3 Mossy Fiber-Associated ORDEN | 1.27 | 6.96 | 578.90 | 28.45 | 0.30 | 1 |
| CA3 Ivy | CA3 QuadD-LM | 1.18 | 6.89 | 563.47 | 26.15 | 0.30 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 Pyramidal | 0.88 | 7.15 | 496.05 | 20.62 | 0.12 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 Axo-Axonic | 2.12 | 4.55 | 762.60 | 21.45 | 0.16 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 Basket | 1.08 | 3.90 | 759.12 | 15.70 | 0.36 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 Basket CCK+ | 1.42 | 4.32 | 693.92 | 17.08 | 0.22 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 Bistratified | 2.00 | 4.96 | 776.57 | 17.27 | 0.17 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 Ivy | 1.35 | 5.39 | 712.27 | 21.22 | 0.30 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 Mossy Fiber-Associated ORDEN | 1.16 | 5.53 | 642.10 | 22.52 | 0.29 | 1 |
| CA3 Mossy Fiber-Associated ORDEN | CA3 QuadD-LM | 1.10 | 5.52 | 637.95 | 21.01 | 0.29 | 1 |
| CA3 QuadD-LM | CA3 Pyramidal | 0.77 | 9.11 | 382.14 | 24.79 | 0.11 | 1 |
| CA3 QuadD-LM | CA3 Axo-Axonic | 1.91 | 5.17 | 635.01 | 22.34 | 0.15 | 1 |
| CA3 QuadD-LM | CA3 Basket | 1.00 | 4.29 | 663.25 | 16.42 | 0.34 | 1 |
| CA3 QuadD-LM | CA3 Basket CCK+ | 1.31 | 4.83 | 596.50 | 17.78 | 0.21 | 1 |

**Table 5 Firing rates and activity sparseness during resting-state behaviors as recorded in our model and those recorded *in vivo* for the neuron types included in our network model. Firing rates are expressed as mean** ± **s.d.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Neuron Type** | **Synchronous Model Firing Rate (Hz) and Activity Sparseness (%)** | **Asynchronous Model Firing Rate (Hz) and Activity Sparseness (%)** | **Immobility Firing Rate (Hz) and Activity Sparseness (%)** | **Animal** | **Animal State** | **Reference** |
| Pyramidal | 0.27 ± 0.58  2.61 ± 0.01 | 0.27 ± 0.58  2.61 ± 0.01 | 0.2  --- | Rat | Awake; freely-moving | [43] |
| 0.5  --- | Rat | Awake; freely-moving | [67] |
| 0.72 ± 0.51  --- | Rat | urethane-anesthetized | [58] |
| CA3a: 0.4  CA3b: 0.3  --- | Rat | Awake; freely-moving | [68] |
| 1.74 ± 1.45  --- | Mice | Awake; freely-moving | [69] |
| Axo-Axonic | 5.71 ± 1.31  52.69 ± 0.36 | 5.72 ± 1.30  52.73 ± 0.20 | 22.8 ± 3.1  --- | Rat | urethane-anesthetized | [55] |
| Basket | 4.34 ± 1.69  38.97 ± 0.69 | 4.38 ± 1.69  39.19 ± 0.63 | 20 ± 7  --- | Rat | urethane-anesthetized | [54] |
| 17±7  --- | Rat | isoflurane-anesthetized | [70] |
| 8.2 ± 5.6  --- | Rat | Awake; head-fixed | [71] |
| Basket CCK+ | 0.25 ± 0.29  2.46 ± 0.09 | 0.25 ± 0.29  2.48 ± 0.11 | 0.99  --- | Rat | urethane-anesthetized | [58] |
| Bistratified | 4.44 ± 0.74  41.41 ± 0.25 | 4.46 ± 0.74  41.54 ± 0.32 | 0.9 ± 0.26\*  --- | Rat | urethane-anesthetized | [72] |
| 30.4\*  --- | Rat | Awake; Freely moving | [73] |
| Ivy | 1.66 ± 0.88  16.31 ± 0.24 | 1.67 ± 0.88  16.38 ± 0.19 | 1.7 ± 0.3\*  --- | Rat | urethane-anesthetized | [56] |
| 3.0 ± 3.6\*  --- | Rat | Awake; freely-moving |
| MFA-ORDEN | 1.05 ± 0.68  10.43 ± 0.17 | 1.05 ± 0.67  10.41 ± 0.20 | N/A  --- | --- | --- | --- |
| QuadD-LM | 3.94 ± 0.97  37.80 ± 0.20 | 3.94 ± 0.97  37.85 ± 0.19 | 6.14 | Rat | urethane-anesthetized | [58] |

\*These values are from recordings in CA1

**Table 6 Preferred firing phases by neuron type for the baseline and archetype networks for synchronous (1,000) and asynchronous (10,000) random Pyramidal cell activation**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Neuron type | Synchronous | | | | Asynchronous | | | |
| Baseline | | Archetype | | Baseline | | Archetype | |
| Phase (°) | MRVL | Phase (°) | MRVL | Phase (°) | MRVL | Phase (°) | MRVL |
| CA3 Pyramidal | 152 | 0.89 | 157 | 0.97 | 151 | 0.89 | 174 | 0.99 |
| CA3 Axo-Axonic | 218 | 0.91 |  |  | 218 | 0.91 |  |  |
| CA3 Basket | 192 | 0.97 | 191 | 0.99 | 192 | 0.97 | 194 | 0.99 |
| CA3 Basket CCK+ | 256 | 0.92 |  |  | 265 | 0.81 |  |  |
| CA3 Bistratified | 180 | 0.97 |  |  | 180 | 0.97 |  |  |
| CA3 Ivy | 270 | 0.84 |  |  | 270 | 0.85 |  |  |
| CA3 MFA-ORDEN | 277 | 0.85 | 222 | 0.94 | 276 | 0.85 | 214 | 0.93 |
| CA3 QuadD-LM | 255 | 0.87 |  |  | 254 | 0.87 |  |  |

**Table 7 Preferred firing phases by neuron type for the MF-Like - CA3 network**

|  |  |  |
| --- | --- | --- |
| Neuron Type | Phase (°) | MRVL |
| CA3 Pyramidal | 173 | 0.99 |
| CA3 Axo-Axonic | 218 | 0.89 |
| CA3 Basket | 276 | 0.96 |
| CA3 BC CCK+ | 134 | 0.64 |
| CA3 Bistratified | 210 | 0.92 |
| CA3 Ivy | 229 | 0.76 |
| CA3 MFA ORDEN | 261 | 0.63 |
| CA3 QuadD-LM | 235 | 0.80 |

**Table 8 Conceptual Elements for Building Full-Scale Network Models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Conceptual Element | Limitations if Modeled or Rationale for Exclusion | Advantages of the Element |
| Modeled | Neuron types | Eight neuron types were included in our model as representatives of the majority of supertypes in CA3. However, we have not included all 25 defined neuron types in the subregion. | Provides strong explanatory power as to how cells classified by morphology, primary neurotransmitter, and molecular markers contribute to the network dynamics. |
| Population sizes for each neuron type | Each included neuron type adopts the population size of the represented supertype. | Provides strong mechanistic constraints regarding the relative proportions of neuron types within the modeled circuit. |
| Input-output relationships for each neuron type | See ‘Diversity of input-output relationships’ and ‘Input-output relationships modeled through a multi-compartment formalism’ below. | Employing Izhikevich models for each neuron type allows for lower computational cost while preserving the realistically diverse firing patterns observed experimentally. |
| Connection probabilities between neuron types | Hippocampome.org provides probabilities for all local-circuit axonal-dendritic connections. We employed reasonable assumptions to estimate long-range and perisomatic connections. | Realistic connection probability estimates strongly constrain activity pattern propagation through the network. |
| Short-term synaptic dynamics based on fast receptor currents | N/A | Inclusion of short-term synaptic dynamics accounts for synaptic depression and facilitation observed in hippocampal networks, as well as the failure rate of transmitter release. |
| Conductance delays | Conductance delays were computed based on the somatic distances of axons within the individual CA3 layers and an assumed conductance velocity. These delays were rounded at the precision of 1 ms, whereas intra-layer conductance delays may be shorter. | Estimates of conductance delays allow for activity patterns to propagate through the network following similar constraints as imposed in a real mouse hippocampus. Conductance delays may be important to binding of neurons into cell assemblies [74]. |
| Excluded | Long-term plasticity (LTP) | We do not have connection type specific data to constrain estimates for LTP, nor information about connection type specific learning rules. Thus, we used fixed rather than plastic synaptic weights in our network models. | LTP in network models allows for new information to be stored, updated, or removed via synaptic weight changes. An understanding of how LTP works across individual connection types or classes could be crucial to understanding hippocampal memory processes. |
| Diversity of input-output relationships (i.e., including multiple firing patterns for defined neuron types) | We do have multiple Izhikevich parameter sets for the Pyramidal and Bistratified cells but opted not to include them to simplify the interpretation of network dynamics. We plan to include these parameter sets in future modeling work. | Neurons of the same type can vary in their spiking response to the same input pattern. Incorporating this diversity in network models may clarify the mechanism of different network activity states. |
| Input-output relationships modeled through a multi-compartment formalism | We do have Izhikevich parameter sets optimized for multiple compartments but opted not to include them to limit computational cost. We plan to include these parameter sets in future modeling work. | Neurons consist of multiple structural elements: a soma, dendrites, and an axon. Network models that contain multi-compartment based neurons may be important for replicating hippocampal functions observed *in vivo*, such as theta-nested gamma oscillations during memory storage and retrieval [62,75]. |
| Short-term synaptic dynamics based on both fast and slow receptor currents (e.g., NMDA and GABAB) | We do not yet have enough data available to constrain the slow components of short-term synaptic signals. | Network models that incorporate both fast (e.g., AMPA and GABAA) and slow (e.g. NMDA and GABAB) current types could better reproduce distinct network oscillations. |
| Neuromodulatory effects on synaptic dynamics | We do not yet have enough data available to incorporate the effects of neuromodulation at each connection type. | Hippocampal neurons express receptors for serotonin, dopamine, acetylcholine, and other neuromodulators [76]. These receptors influence synaptic gain and plasticity [77]. Network models that employ connection type specific neuromodulation could thus be critical to elucidate those operations. |
| Higher order connectivity motifs | We do not yet have estimates for the frequencies of occurrence of connectivity motifs at the level of individual neurons. | Incorporating realistic connectivity motifs between neurons [78] could lead to more robust network models of pattern completion [79]. |
| Embedding of network in more than one spatial dimension | We do not yet have data to constrain the connection probabilities between neuron types in greater than one dimension. | Models that can account for the 3D embedding of hippocampal neurons and their connectivity could better capture functional dynamics [80]. |