A Large-Scale Model of Turtle Visual Cortex

This is a model of the visual cortex of freshwater turtles that is based upon the known anatomy and physiology of individual neurons. The model was published in three papers (Nenadic *et al*., 2003; Wang *et al*., 2005; Wang *et al*., 2006), which should be consulted for full details on its construction. The model has also been used in several papers (Robbins and Senseman, 2004; Du *et al*., 2005; Du *et al*., 2006). It is implemented in *GENESIS* (Bower and Beeman, 1998).

Background on turtle visual cortex. The visual cortex of turtles has been studied in turtles in three genera (*Pseudemys = Trachemys, Chrysemys, Emys*) within the family Emydidae. Freshwater turtles are used because it is possible to maintain their brains alive in an *in vitro preparation*. See Ulinski (1999) for a review of turtle visual cortex.

Turtle visual cortex has approximately 100,000 neurons organized into three layers. The majority of cells are pyramidal neurons with somata located in the intermediate layer 2. The outer layer 1 contains scattered interneurons. Layer 3 contains principally inhibitory interneurons that have horizontally oriented dendrites. The visual cortex corresponds to the cytoarchitectonic area D of Colombe and Ulinski (1999). It is divided into medial and lateral parts, D_M and D_L respectively, that are distinguished by the presence of large clusters of neurons in the lateral part and small clusters of neurons in the medial part. The pyramidal cells in the lateral and medial parts are morphologically different. A complete inventory of interneurons in the cortex is not available (see Colombe and Ulinski, 1999), but three populations of inhibitory interneurons (subpial cells in layer 1, stellate cells in layer 2 and horizontal cells in layer 3) have been documented and are included in the model.

The dorsal lateral geniculate complex (Ulinski and Nautiyal, 1988; Rainey and Ulinski, 1986) provides visual input to dorsal cortex. Geniculate axons run from lateral to medial across dorsal area bearing synapses *en passant* (Mulligan and Ulinski, 1990). They shift their positions as they run across dorsal area such that they intersect the somata and proximal dendrites of lateral pyramidal cells but the distal apical dendrites of

medial pyramidal cells. The model includes geniculate neurons, but does not include inputs from cholinergic, noradrenergic or serotonergic subcortical structures, which are present in the real cortex.

The receptive fields of superficial cells (probably subpial cells) and deep cells (probably pyramidal cells) were studied by Mazurskaya (1974). Both sets of cells have wide receptive fields that respond to small stimuli anywhere in visual space (see Wang *et al.*, 2006). Studies with both multielectrode arrays and voltage sensitive dyes demonstrate that visual stimuli generate waves of activity that propagate across the cortex from its rostral pole to its caudal pole (e.g. Senseman and Robbins, 2002).

Distribution of cells in the model. The model contains 201 geniculate neurons arranged in a row and 788 cortical neurons (368 lateral pyramidal cells, 311 medial pyramidal cells, 44 subpial cells, 45 stellate cells and 29 horizontal cells). The cortical neurons are distributed within a 1.6 mm x 1.6 mm rectangular area (see Wang *et al.*, 2005). The spatial distribution of the five types of cells in the model was determined by charting the density of neurons in layers 1, 2 and 3 in a set of coronal sections through the cortex of one turtle. These counts were used to establish the positions of cells in the model using an algorithm (Nenadic *et al.*, 2003) that preserves the relative numbers of cells in layers 1, 2 and 3 at each point of the cortex. The axons of geniculate neurons are modeled as delay lines that run across the cortex. Delays were calculated using the measured conduction velocities of geniculate axons (Colombe and Ulinski, 1999).

The different neuronal populations are created under separate neutral object roots:

- HOR_ROOT
- LAT_ROOT
- LGN_ROOT
- MED_ROOT
- STE_ROOT
- SUB_ROOT

These root names should be defined in the main model program. They can be changed, since the objects are only accessed through these root names. The names of the neuron objects are of the form {ROOT}/cell#. For example, if the value of LAT_ROOT is "/network_lateral", then the lateral neurons are referenced as /network_lateral/cell1, /network_lateral/cell2, …

Compartmental models. Geniculate neurons were modeled as simple one compartment spike generators. Visual stimuli are simulated by activating all of the geniculate neurons simultaneously to simulate a light flash, or clusters of geniculate neurons to simulate patterned stimuli.

Cortical neurons were modeled as multicompartment models. The morphology of the lateral and medial pyramidal neurons and stellate cells was based on samples of neurons drawn from Golgi preparations. The morphology of subpial cells was based on neurons that were characterized physiologically and then filled with *Neurobiotin*. Passive membrane parameters were determined using the responses of neurons in each population to intracellular current injections. Voltage gated conductances have not been well studied in cortical neurons, so the minimum number of conductances needed to reproduce the firing patterns of each population of cortical neurons were used. Conductances were implemented using the Hodgkin-Huxley formalism beginning with the parameters used in Traub's model of a CA3 pyramidal cells (Traub *et al.*, 1991). Kinetic parameters were then adjusted so that the spike latencies and rates of spike rate adaptation in the model cells matched those of the real cells. Calcium buffering was modeled using standard equations. The models include a fast sodium conductance, a delayed rectifier conductance, a high threshold calcium conductance, and a medium after hyperpolarization conductance. Details of the conductances are given in Nenadic *et al*., (2003) and Wang *et al*., (2006).

Interconnections between neurons. Neurons of each type were connected to other neurons in the same population, or to neurons in other populations using axonal domains based on the known anatomy of each population of neurons. Connections from

one neuron to itself were not allowed. The density of connections was modeled by spherical Gaussian functions in most cases (see Nenadic *et al*., 2003, for the details). The synapse targets and their names are specified in the files that create the synapses from the respective neurons. The objects representing the synapses are placed in the hierarchy of the target neurons under the specific compartment that is their target.

The basic physiology of excitatory synapses between geniculate afferents and cortical neurons and between cortical neurons, and of inhibitory synapses within the cortex is known. Geniculocortical synapses are exclusively AMPAergic which intracortical excitatory synapses have both AMPAergic and NMDAergic components. The voltage dependence of the NMDA components of excitatory synapses was modeled according to Jahr and Stevens (1990).

A general problem for large-scale models is that the number of synapses on each neuron is less than on cells in the real cortex because the model contains only a fraction of the total number of cells in the real cortex. It is, consequently, often necessary to scale up the strengths of the synapses to compensate for the smaller number of synapses. This was done in this model by adjusting the strengths of the synapses so that the propagation of the wave in the model cortex matches the parameters of wave propagation in the real cortex.

Idiosyncratic features of the cortex. One artifactual feature of the model is that the number of inhibitory neurons in the model is relatively small because inhibitory neurons make up only a fraction of the total number of cells in the real cortex. The distribution of inhibitory neurons is consequently patchy and some areas have relatively high ratios of inhibitory interneurons to pyramidal cells while other areas have relatively low ratios. This patchiness probably does not affect the general features of the waves in the model, but may produce inaccuracies in the responses to some patterned stimuli.

Several individuals were involved in constructing the model, and decisions made by one individual were not always consistent with those made by other individuals. For

example, all of the geniculate synapses onto pyramidal and stellate cells were effected on one compartment of the target neurons, while geniculate synapses were distributed on all of the compartments of subpial cells which were the subject of a detailed study of synaptic integration. It is unlikely that these differences have any effect on the performance of the large-scale model.

Authorship and Support

The model described here was developed as part of a larger collaboration that involves four principal investigators: Bijoy Ghosh (Texas Tech), Kay Robbins and David Senseman (University of Texas at San Antonio) and Philip Ulinski (University of Chicago). Zoran Nenadic and Wenxue Wang, who were both graduate students in the Ghosh laboratory, played the major roles in actually constructing the first draft of the model. Kay Robbins and David Senseman did a second draft, with input from David Beeman from the *Genesis* team. Preparation of this model was aided by support from the Learning and Intelligent Systems and Collaborative Research in Computational Neuroscience programs at the National Science Foundation.

Bibliography of References on Turtle Visual Cortex

Blanton MG, Kriegstein AR, Properties of amino acid neurotransmitter receptors of embryonic cortical neurons when activated by exogenous and endogenous agonists. *J Neurophys*, **67**: 1185 - 1200, 1992.

Blanton MG, Shen JM, Kriegstein AR, Evidence for the inhibitory neurotransmitter γ-aminobutyric acid in aspiny and sparsely spiny nonpyramidal neurons of the turtle dorsal cortex, *J Comp Neurol*, **259**: 277 – 297, 1987.

Boiko VP, Responses to visual stimuli in thalamic neurons of the turtle *Emys orbicularis*, *Neurosci Behav Physiol*, **10**: 183 – 188, 1980.

Bower JM, Beeman D, *The Book of Genesis*, 2nd ed., TELOS, New York.. 1998.

Colombe JB, Sylvester J, Block J, Ulinski PS, Subpial and stellate cells: Two populations of interneurons in turtle visual cortex, *J Comp Neurol*, **471**: 333 – 351, 2004.

Colombe JB,Ulinski PS, Temporal dispersion windows in cortical neurons, *J Comput Neurosci* **7**: 71 - 87, 1999.

Connors BW, Kriegstein AR, Cellular physiology of the turtle visual cortex: Distinctive properties of pyramidal and stellate neurons, *J Neurosci,* **6**: 164 - 177, 1986.

Desan PH The organization of the cerebral cortex of the pond turtle, *Pseudemys scripta elegans*. Ph.D. Thesis, Harvard University, Cambridge, MA, 1984.

Du X, Ghosh BK, Ulinski PS Encoding and decoding target locations with waves in the turtle visual cortex, *IEEE Trans Biomed Eng*, **52**: 566 - 577, 2005.

Du, X, Ghosh BK, Ulinski PS Encoding motion targets by waves in turtle visual cortex. *IEEE Trans Biomed Eng*, 53: 1688 – 1696.

Hall JA, Foster RE, Ebner FF, Hall WC, Visual cortex in a reptile, the turtle (*Pseudemys scripta* and *Chrysemys picta*), *Brain Res,* **130**: 197 – 216. 1997.

Heller SB, Ulinski PS, Morphology of geniculocortical axons in turtles of the genera *Pseudemys* and *Chrysemys*, *Anat Embryol,* **175**: 505 - 515, 1987.

Jahr CE, Stevens CF A qualitative description of NMDA receptor channel kinetic behavior. *J. Neurosci*. 10: 1830 – 1837.

Kenigfest NB, Repérant J, Rio J-P, Belekhova MG, Tumoanova NL, Ward R, Veselkin NP, Herbin M, Chkeidze DD, Ozirskaya EV Fine structure of the dorsal lateral geniculate nucleus of the turtle, *Emys orbicularis*. A Golgi, combined HRP tracing andGABA immunochemical study, *J Comp Neurol* , **356**: 595 - 614.

Kriegstein AR, Synaptic responses of cortical pyramidal neurons to light stimulation in the isolated turtle visual system, *J Neurosci* **7**: 2488 - 2492, 1987.

Kriegstein AR, Connors BW, Cellular physiology of the turtle visual cortex: Synaptic properties and intrinsic circuitry, *J. Neurosci,* **6**: 178 - 191, 1986.

Larson-Prior LJ, Ulinski PS, Slater NT, Excitatory amino acid receptor-mediated transmission in geniculocortical and intracortical pathways within visual cortex, *J Neurophysiol,* **66**: 293 - 306, 1991.

Mancilla JG, Fowler M, Ulinski PS, Responses of regular spiking and fast spiking cells in turtle visual cortex to light flashes, *Vis Neurosci,* **15**: 979 - 993, 1998.

Mancilla JG, Ulinski PS Role of $GABA_A$-mediated inhibition in controlling the responses of regular spiking cells in turtle visual cortex, *Vis Neurosci*, **18**: 9 – 24, 2001.

Mazurskaya PZ, Study of the projection of the retina to the forebrain of the tortoise *Emys orbicularis, J.Evol Biochem Physiol*, **8**: 550 – 555, 1972.

Mulligan KA,Ulinski PS, Organization of geniculocortical projections in turtles: Isoazimuth lamellae in the visual cortex, *J. Comp Neurol*, **296**: 531 – 547, 1990.

Nenadic Z, Ghosh BK, Ulinski PS, Modelling and estimation problems in the turtle visual cortex, *IEEE Trans Biomed Eng*, **49**: 753 - 762, 2002.

Nenadic Z, Ghosh BK,Ulinski PS, Propagating waves in visual cortex: A large-scale model of turtle visual cortex. *J Comput Neurosci*, **14**: 161 – 184, 2003.

Rainey WT, Ulinski PS, Morphology of neurons in the dorsal lateral geniculate complex in turtles of the genera *Pseudemys* and *Chrysemys*, *J Comp Neurol*, **253**: 440 – 465, 1986.

Reiner A, A comparison of neurotransmitter-specific and neuropeptide-specific neuronal cell types present in the dorsal cortex in turtles with those present in the isocortex in mammals: implications for the evolution of isocortex, *Brain Behav Evol*, **38**: 53 – 91, 1991.

Robbins KA, Senseman DM, Extracting wave structure from biological data with application to responses in turtle visual cortex, *J Comput Neurosci,* **16**: 267 – 298, 2004.

Senseman DM, Spatiotemporal structure of depolarization spread in cortical pyramidal cell populations evoked by diffuse retinal light flashes. *Vis Neurosci*, **16**: 65 – 79, 1999

Senseman DM,Robbins KA, High-speed VSD imaging of visually evoked cortical waves: Decomposition into intra- and intercortical wave motions, *J Neurophysiol,* **87**: 1499 – 1514, 2002.

Smith LM, Ebner FF,Colonnier M, The thalamocortical projection in *Pseudemys* turtles: A quantitative electron microscope study, *J Comp Neurol,* **190**: 445 - 461, 1980.

Traub RD, Wong RKS, Miles R, Michelson H (1991) A model of a CA3 hippocampal pyramidal cell incorporating voltage-clamp data on intrinsic conductances. *J. Neurophysiol*. 66: 635 – 650.

Ulinski PS, Organization of corticogeniculate projections in the turtle, *Pseudmys scripta*. *J Comp Neurol*, **254**: 529 – 542, 1986.

Ulinski PS, Neural mechanisms underlying the analysis of moving stimuli, In: Ulinski PS, Jones EG, Peters A, eds. *Cerebral Cortex, Vol. 13. Models of Cortical Circuitry*, Plenum Press, New York, pp. 283 – 399, 1999.

Ulinski PS, Nautiyal J, Organization of retinogeniculate projections in turtles of the genera *Pseudemys* and *Chrysemys*, *J Comp Neurol,* **276**: 92 – 112, 1988.

Wang W, Campaigne C, Ghosh BK, Ulinski PS, Two cortical circuits control propagating waves in visual cortex, *J Comput Neurosci*, **19**: 263 - 289, 2005.

Wang W, Ghosh BK, Ulinski PS Generation of the receptive fields of subpial cells in turtle visual cortex. *J. Integrative Neurosci*. 5: 1 - 32. 2006.

Zhu D, Lustig LH, Bifulco K, Keifer J, Thalamocortical connections in the pond turtle *Pseudemys scripta elegans*, *Brain Behav Evol,* **65**: 278 - 292, 2005.