

# PhD Dissertation

Randal A. Koene. *Functional requirements determine relevant ingredients to model for on-line acquisition of context dependent memory* PhD thesis, McGill University, 2001: [[Compressed Postscript](#)], [[PDF](#)].

(Formatting and layout particulars, such as the location of paragraphs on pages and page numbers, may differ due to differences in the typesetting of the character fonts used in the Postscript and PDF documents generated from the LaTeX source text.)

**Abstract:** Biophysical simulations of memory must choose which aspects of known neurophysiology and neuroanatomy to model. Relevant aspects were constrained by functional requirements determined for on-line acquisition in context dependent memory, memory that is retrieved by contextual cues. In an on-line task, the protocol of data presentation and the times at which encoding or retrieval in memory is needed are not predetermined. A sequence of neuronal spike patterns representing items may be presented only once. Yet, episodic memory of the sequence immediately encodes the temporal context of familiar items, a process known to depend on hippocampal function. For this, interference caused by overlapping spike patterns must be avoided, a requirement that suggested the relevance of coincidental spiking. Overlap in the input to the hippocampus was reduced by recruiting such spikes in a model of encoding in dentate gyrus. Durable encoding is required in the hippocampus, since hippocampal damage can cause retrograde amnesia in context dependent memory that spans years. Long-lasting synaptic changes involved modeling relevant neurophysiology concerning protein production elicited by the spaced reactivation of spike patterns. The likelihood of reactivation was increased by the well-known process of long-term potentiation of synaptic transmission. Such potentiation is elicited when a presynaptic spike precedes a postsynaptic spike within a specific time window repeatedly. The intervals in a sequence of spike patterns must be compressed and the sequence repeated, requirements that were achieved with a model of short-term memory based on persistent spiking. Retrieval may be concurrent with these encoding processes due to effects of different phases of a brain rhythm at theta frequency (3-12 Hz) that modulate transmission and plasticity. A model of short-term memory by Lisman and Idiart (Science 267:1512-15), extended by Jensen *et al.* (Learning and Memory 3:243-287), was a suitable framework for rapid sequence acquisition. Each functional requirement of on-line acquisition was met by adding relevant neurophysiology and neuroanatomy to the framework. Subsequent simulations had more parameters, but values were selected independently for each function. When simulating biological systems, a top-down focus on functional requirements deals with the problem that more components lead to more complex behaviour.

**Oral Defense Presentation:** [Powerpoint](#), [compressed postscript](#), [presentation notes](#) ([compressed novelties postscript](#) and my own [compressed comments postscript](#) with paragraph references as numbered in the pre-defense version of the Ph.D. thesis dissertation) and [HTML](#).

**Complementary materials to the thesis dissertation, as noted in Appendix B.**

The Generic Enhanced Spiking Neuron models library, [GESNlib](#), provides C++ software functions of modeling components used in experiments, with the goal of optimization for accuracy and computational efficiency. Recent developments involve [Event-Predictive Emulation](#), rooted in spline-decomposition of neurobiological functions. As this optimization improves, simulations of more extensive and realistic neuronal circuitry become feasible.

## [JLILTM] Improvements in Recall Behaviour of a Model Combining Oscillatory Short Term Memory and Long Term Potentiation-Depression

- (2.2) **Fig.2.1d:** Neuronal circuitry simulation program [corrected](#) (C program) with [basic.ini](#) (simulation initialization file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).
- (2.3.1) **Fig.2.2 and Fig.2.3:** Numerical simulation [jensencomp.m](#) (Octave script) in [Octave](#).
- (2.3.2) **Fig.2.4 and Fig.2.5:** Neuronal circuitry simulation program [corrected](#) (C program) with [cued-low-GABA-reverberation](#) (simulation configuration and initialization files), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).
- (2.3.3) **Fig.2.6:** Neuronal circuitry simulation program [corrected](#) (C program) with [overlap4](#) (simulation configuration and initialization files), evaluated in [Octave](#) with [jlioutput.m](#)

(Octave script).

- **(2.3.4) Fig.2.7:** Neuronal circuitry simulation program [corrected](#) (C program) with [overlap4](#) (simulation configuration and initialization files), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).

## JLILTM: Continued Research

Further advances have been made in the design and evaluation of the STM model in the context of research conducted at Michael Hasselmo's Computational Neurophysiology laboratory at Boston University.

The STM model has been reimplemented with more detailed integrate-and-fire neurons that include explicit membrane capacitances and response dynamics that are computed from the changing potential differences over receptor channel conductances. This dual-oscillation short-term memory has been incorporated in a [Catacomb](#) model of a [virtual rat](#), with learning and behaviour in a simulated environment directed by prefrontal cortex, entorhinal (ECII, ECIII) and hippocampal (CA3, CA1) networks ([Cannon, Hasselmo and Koene, 2002](#); [Koene, Cannon and Hasselmo, 2002](#)).

Research detailing a plausible first-in-first-out (FIFO) item replacement mechanism for the STM queue that relies on the conditional and synchronized activation of a population of interneurons, as well as detailed derivations of the dependencies between parameter constraints in the STM model are nearing completion and are scheduled for presentation.

## [Connectivity] Localized Distribution of Connectivity and GABA<sub>B</sub> Control of Learning and Recall Modes in an Oscillatory Model of Memory

- **(3.1.2) Fig.3.1:** Numerical simulation [gabab.m](#) (Octave script) in [Octave](#).
- **(3.2) Fig.3.4d:** Neuronal circuitry simulation program [corrected](#) (C program) with [basic.ini](#) (simulation initialization file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).
- **(3.3.1) Fig.3.5 and Fig.3.6:** Neuronal circuitry simulation program [connectivity](#) (C program, version 0.9.5) with [connectivity2](#) (simulation configuration and initialization files), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).

## Connectivity: Continued Research

Additional details about the mossy fibre connections between dentate gyrus and CA3 and the role of presynaptic LTP (Maccaferri, Toth and McBain, Science, 1998) at those large synapses are being investigated. The experimental results may add support to the hypothesis that separate regions of the hippocampus are specialized for autoassociative and heteroassociative learning involving the same selected sparse encoded representations.

[ITM]

## Sparse Hippocampal Memory Encoding. Attentional Gain-Control of Memory Formation with Multiple Instantiation

- **(4.3) Fig.4.2:** Neuronal circuitry simulation program [connectivity](#) (C program, version 0.9.5) with [interference](#) and [interleaved](#) (simulation configuration and initialization files) and model preparation with [proccfg](#) (C++ preprocessor version 0.8.5, generates model neuronal circuitry from a configuration file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).
- **(4.3) Fig.4.3:** Neuronal circuitry simulation program [connectivity](#) (C program, version 0.9.5) with [minststm](#) and [minststm2](#) (simulation configuration and initialization files) and

model preparation with [proccfg](#) (C++ preprocessor version 0.8.5, generates model neuronal circuitry from a configuration file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).

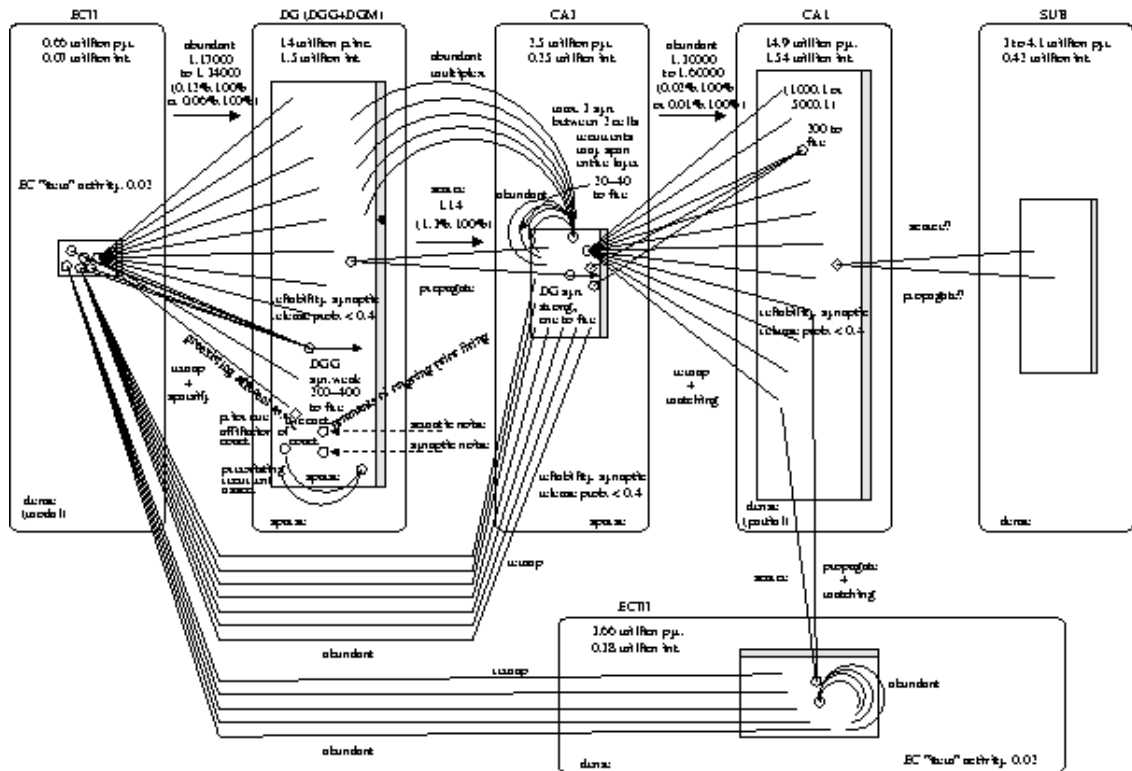
- **(4.3) Fig.4.4:** Neuronal circuitry simulation program [connectivity](#) (C program, version 0.9.5) with [minstitm](#) (simulation configuration and initialization files) and model preparation with [proccfg](#) (C++ preprocessor version 0.8.5, generates model neuronal circuitry from a configuration file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).
- **(4.3) Fig.4.5:** Neuronal circuitry simulation program [connectivity](#) (C program, version 0.9.5) with [minstitm2](#) (simulation configuration and initialization files) and model preparation with [proccfg](#) (C++ preprocessor version 0.8.5, generates model neuronal circuitry from a configuration file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).
- **(4.3) Fig.4.6:** Neuronal circuitry simulation program [connectivity](#) (C program, version 0.9.5) with [minstitm3](#) (simulation configuration and initialization files) and model preparation with [proccfg](#) (C++ preprocessor version 0.8.5, generates model neuronal circuitry from a configuration file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).

[LTM]

## Sparse Hippocampal Memory Consolidation. Formation of Long-Term Memory Traces under Attentional Guidance

- **(5.1.1) Fig.5.1:** Numerical simulation [ltpltm.m](#) (Octave script) in [Octave](#).
- **(5.3.1) Fig.5.5:** Numerical simulation [ltmexp1.m](#) (Octave script) in [Octave](#).
- **(5.3.1) Fig.5.6:** Numerical simulation [ltmexp2.m](#) (Octave script) in [Octave](#).

## [DenseLTM] Dense Neocortical Memory Consolidation. Selective Transfer from Hippocampus with Multiple Instantiation through Recruitment



Notes - Connectivity values in brackets do not indicate synaptic coupling, since coupling will always be completely adjacent, but they do give a fairly good impression of the dynamics of connectivity. Eg. with a ratio of 0.04% 100% it is not difficult for a pattern in ECT1 to synapse on a pattern in DG, thereby enabling a complete w/coupling.

ECT1 to ECT1 is based... it is quite possible that the sparse, orthogonal function is only necessary in DG as a precursor to rapid synaptic acquisition, which perhaps occurs autoassociatively. This learning can occur in ECT1 during sensory presentation. Unlike the sparse w/coupling flow connections in DG which are for autoassociative pattern formation, there would need to support such a possibility. If this is so, then the CA3 to DG connectivity may be used to upgrade the DG specialization through the availability of sparse candidate connections in the distribution of patterns in CA3, rather than as an attractor network as we consider.

The importance of using either for human entorhinal cortex and hippocampus when we do high-resolution hippocampal function rather than using values found in the rat is underlined by the differences in connectivity and structure values found by West et al. [WEST.ENT, WEST.ENTCORR]. A single pyramidal cell may cause intracellular firing [GUL.SINGLE], a single sensory fibre can cause pyramidal cell firing.

While some state that the connectivity from CA3 to CA1 is 1000, the ratio of CA3 cells to CA1 cells and a connectivity of 1,00000 or 1,00000 from CA3 to CA1 would indicate between 3000 and 10000 connections from CA3 entering at each CA1 pyramidal cell. Perhaps the 10000 cells indicate how many different CA3 cells contact a CA1 cell, so that each CA3 cell may make 5 to 10 synapses on a contact CA1 cell. In that case, the 300 EPSPs required to fire a CA1 cell could originate in a CA3 pattern composed of only 30 to 40 CA3 cells. Note that this corresponds to the number of w/coupling EPSPs needed in CA3! For 50000 L1, CA3 patterns would be 300 cells or more.

When drawing this for the paper, in order to properly demonstrate the values, first use the above with and adjust the high to correspondingly.

Figure B-6.1: Human neuronal cell population and connection numbers used as a template for the ratios in modeled circuitry from entorhinal cortex layers through the hippocampal layers to the subiculum.

- (6.2.1) Fig.6.3: Neuronal circuitry simulation program [connectivity](#) (C program, version 1.0) with [denseltn1](#) (simulation configuration and initialization files) and model preparation with [proccfg](#) (C++ preprocessor version 1.0, generates model neuronal circuitry from a configuration file), evaluated in [Octave](#) with [jlioutput.m](#) (Octave script).
- (6.2.1) Fig.6.4: Numerical simulation [denseltn2.m](#) (Octave script) in [Octave](#).
- (6.2.5) Fig.6.8: Numerical simulation [reactivationshift.m](#) (Octave script) in [Octave](#).
- (6.3.3) handwritten note reference: ``early development possible model for adult neurogenesis''.

### DenseLTM: Continued Research

(6.2.1)

(6.2.3)

Further related simulation program files may be found in the archival collection ``[simulations-additional](#)'' . These were used in addition to or in preparation of the experiments shown in the results. Several also connect to ongoing research.

The neuronal circuitry simulations included are:

- connectivity
- connectivity3
- corrected-cue
- corrected-cue2
- corrected-max
- denselstm-hyp2-1
- fullSTM-nonoise
- hierarchyhetero
- jensen-max
- jensen-max2
- jensen.overlap-1
- jensen.overlap-2
- multiple1
- original-cue
- overlap
- overlap2
- overlap3
- pairednegator
- recall-full-gij
- stminterference

The numerical simulations included are:

- ADPtest.m
- ADPtest.evolutionary-tuning.m
- iris.m
- irisback.m
- sahptest.m
- learnwindow.m
- tpspi.m
- vmvthres.m

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