Neuronal Cell Death and Synaptic Pruning driven by Spike-Timing Dependent Plasticity

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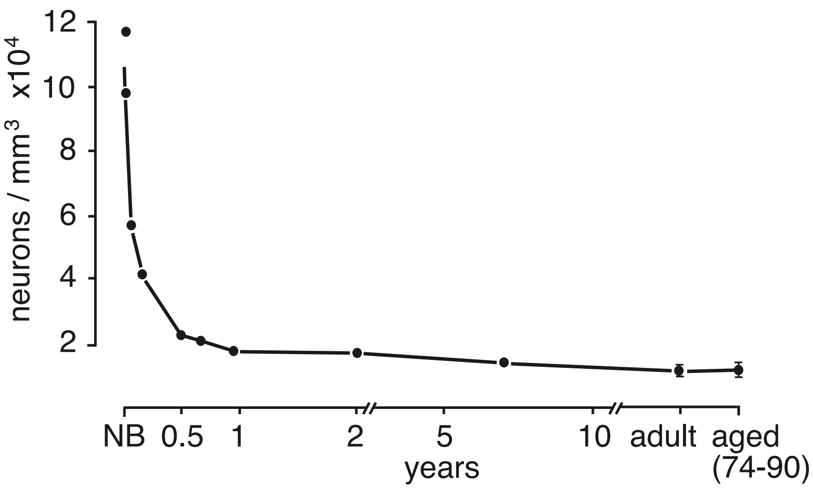
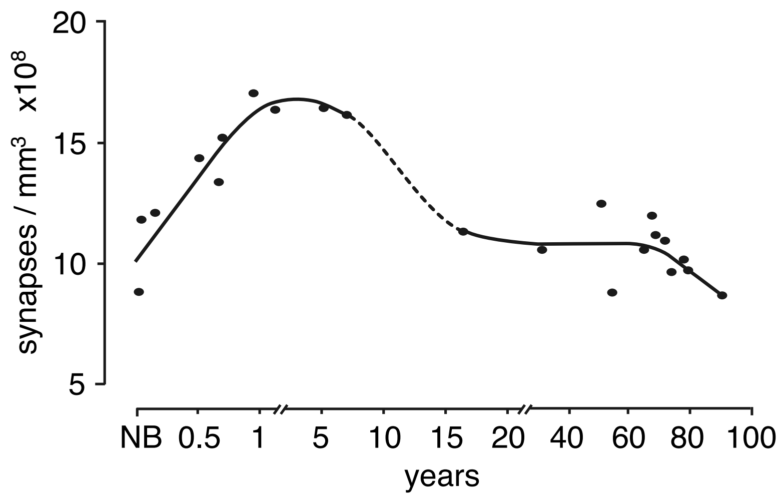
introduction: synaptogenesis and synaptic pruning





modified from Huttenlocher, *Synaptic density in human frontal cortex – developmental changes and effects of aging*, Brain Research, 163:195–205, 1979

- The memory performance of a network is optimally maximized if, under limited metabolic energy resources restricting their number and strength, synapses are first overgrown and then pruned.

Chechik *et al.*, *Synaptic pruning in development: A computational account*, Neural Computation, 10(7):1759–77, 1998

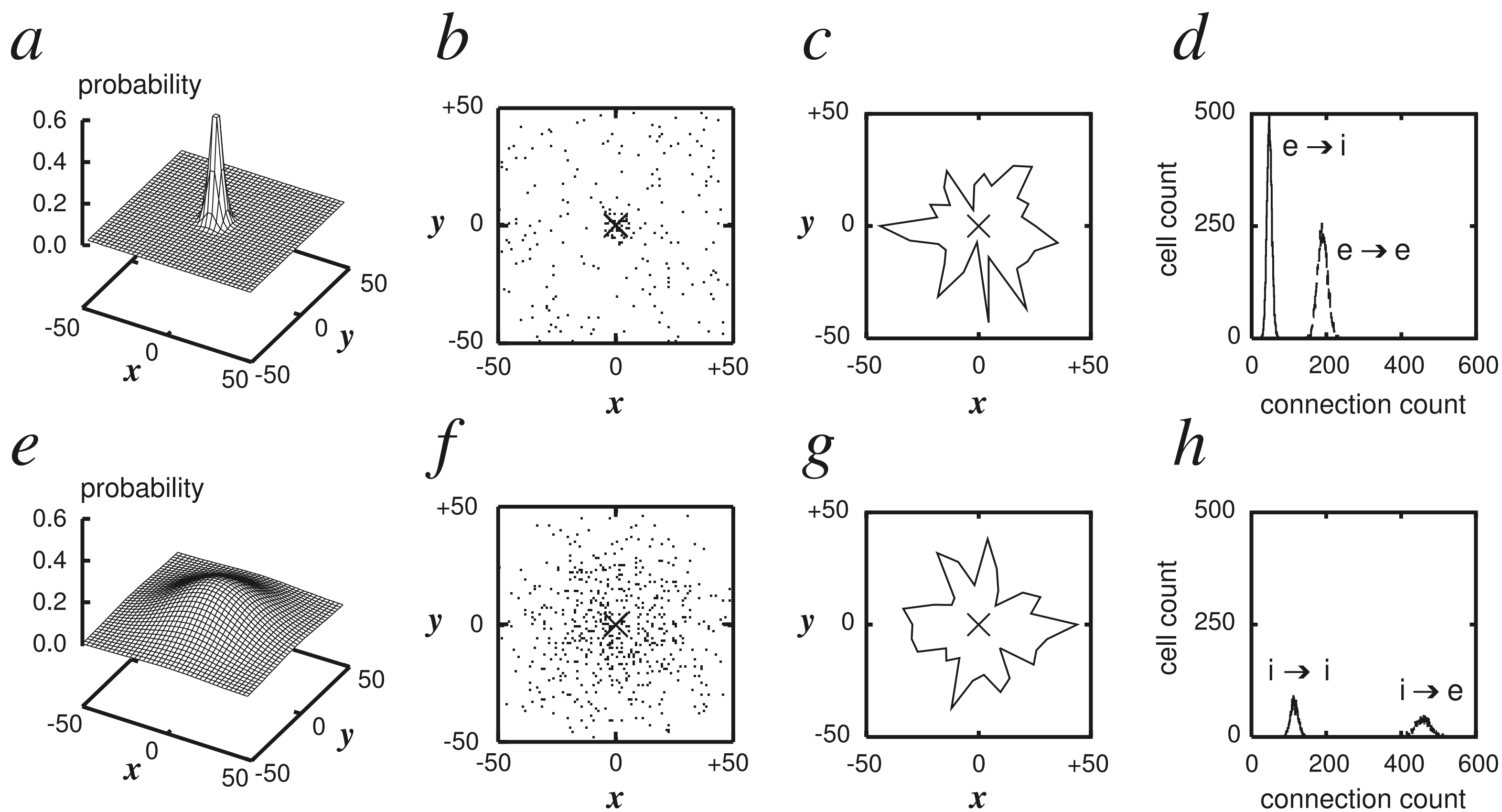
- Neuronal regulation might maintain the memory performance of networks undergoing synaptic degradation.

Horn *et al.*, *Memory maintenance via neuronal regulation* Neural Computation, 10(1):1–18, 1998

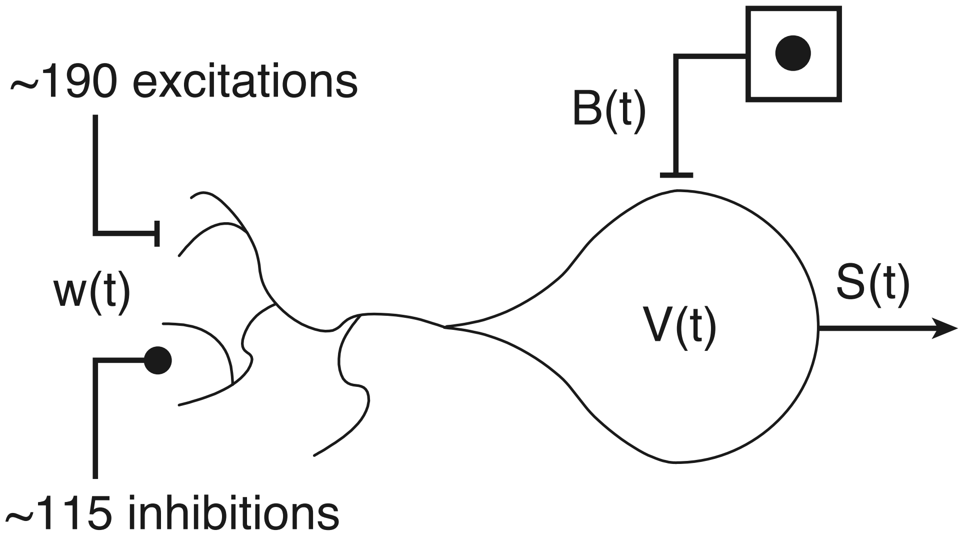
- STDP has been shown to maintain the postsynaptic input field.

Abbott *et al.*, *Synaptic plasticity: taming the beast* Nature Neuroscience, 3:1178–83, 2000

model: network



Iglesias *et al.*, *Dynamics of Pruning in Simulated Large-Scale Spiking Neural Networks*, Biosystems, 79(1-3):11-20, 2005



Type I	=	excitatory 80%	
Type II	=	inhibitory 20%	
V_{rest}	=	-76	[mV]
θ_i	=	-40	[mV]
τ_{mem}	=	15	[ms]
t_{refract}	=	exc:3 inh:2	[ms]
λ_i	=	5	[spikes/s]
n	=	50	

$$V_i(t{+}1) = V_{\text{rest}[q]} + (1 - S_i(t)) \cdot ((V_i(t) - V_{\text{rest}[q]}) \cdot k_{\text{mem}[q]}) + \sum_j w_{ji}(t) + B_i(t)$$

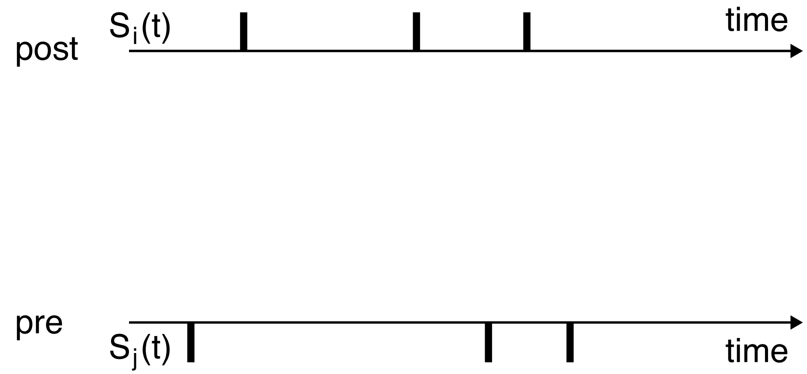
$$S_i(t) = \mathcal{H}(V_i(t) - \theta_{q_i})$$

$$w_{ji}(t+1) = S_j(t) \cdot A_{ji}(t) \cdot P_{[q_j, q_i]}$$

$$B_i(t+1) = \mathcal{P}_{reject}(\lambda_{q_i}) \cdot n \cdot P_{[q_1, q_i]}$$

model: STDP and pruning

$$
\begin{aligned}
L_{ji}(t+1) = \quad & L_{ji}(t) \cdot k_{\mathrm{act}[q_j, q_i]} \\
& +(S_i(t) \cdot M_j(t)) \\
& -(S_j(t) \cdot M_i(t))
\end{aligned}
$$



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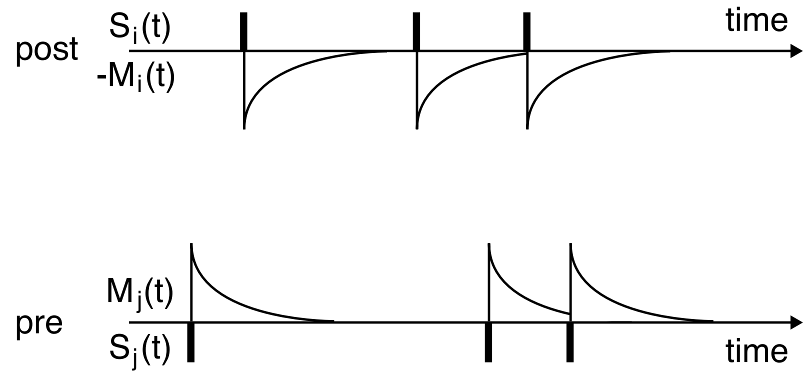

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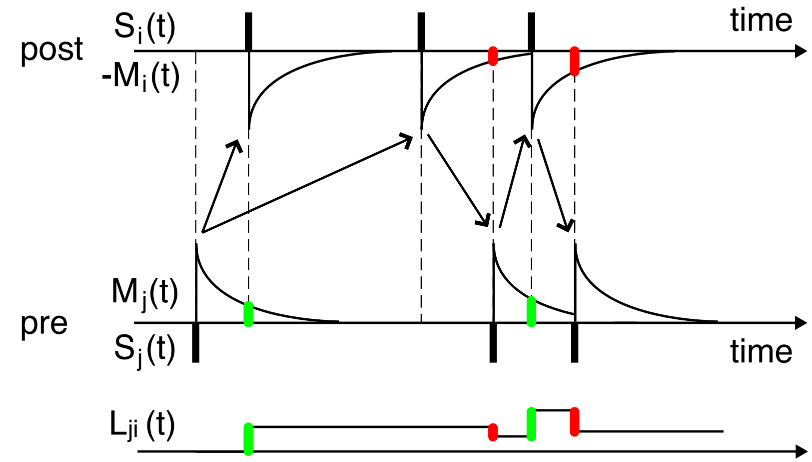
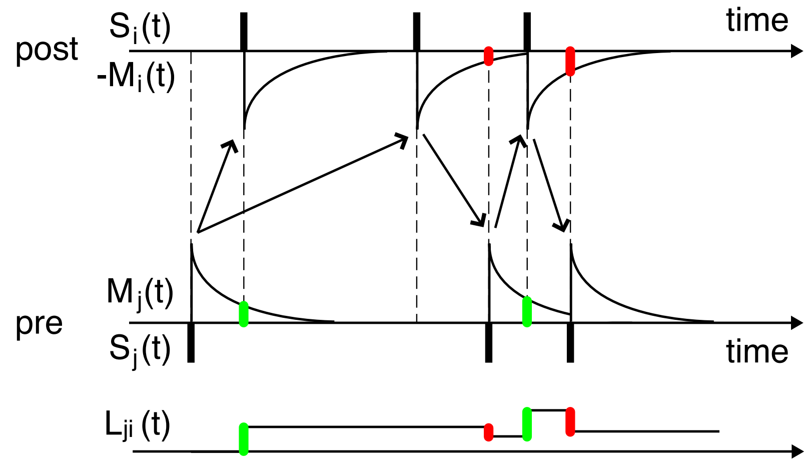
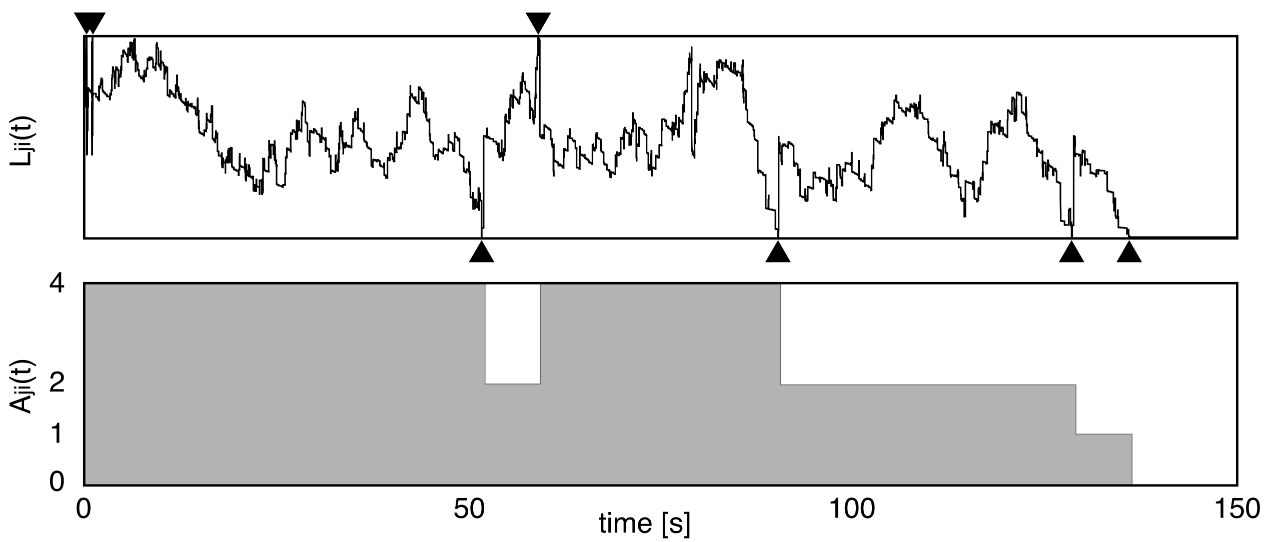


model: STDP and pruning

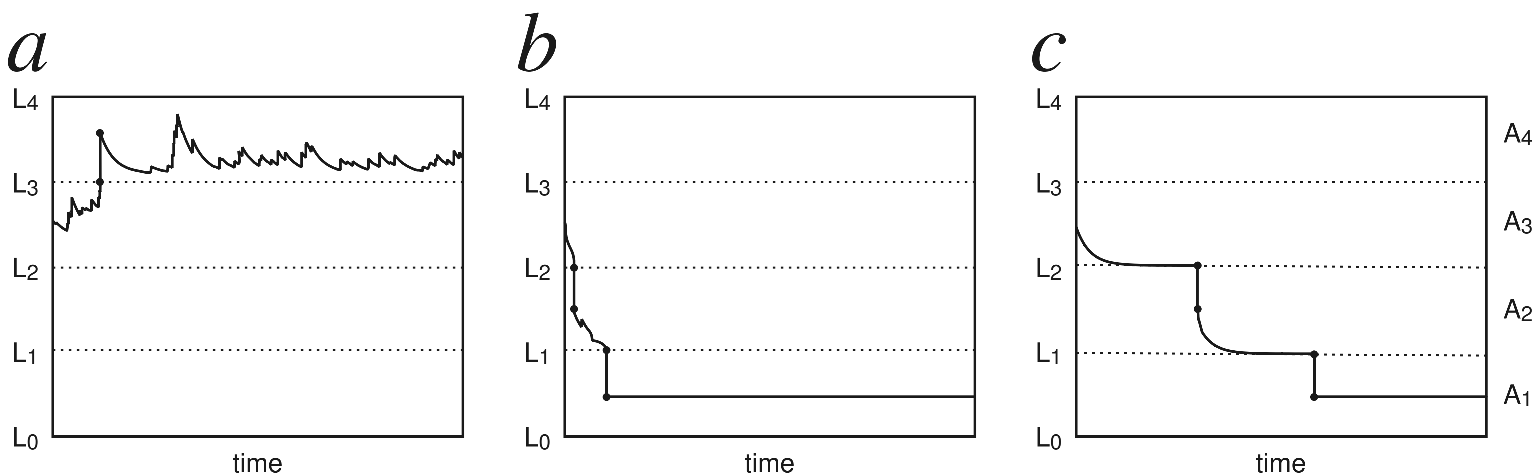
$$L_{ji}(t+1) = \begin{aligned} & L_{ji}(t) \cdot k_{\mathrm{act}[q_j,q_i]} \\ & +(S_i(t) \cdot M_j(t)) \\ & -(S_j(t) \cdot M_i(t)) \end{aligned}$$





$$w_{ji}(t+1) = S_j(t) \cdot A_{ji}(t) \cdot P_{[q_j,q_i]}$$

model: synaptic adaptation examples



Strongly Interconnected (SI) units

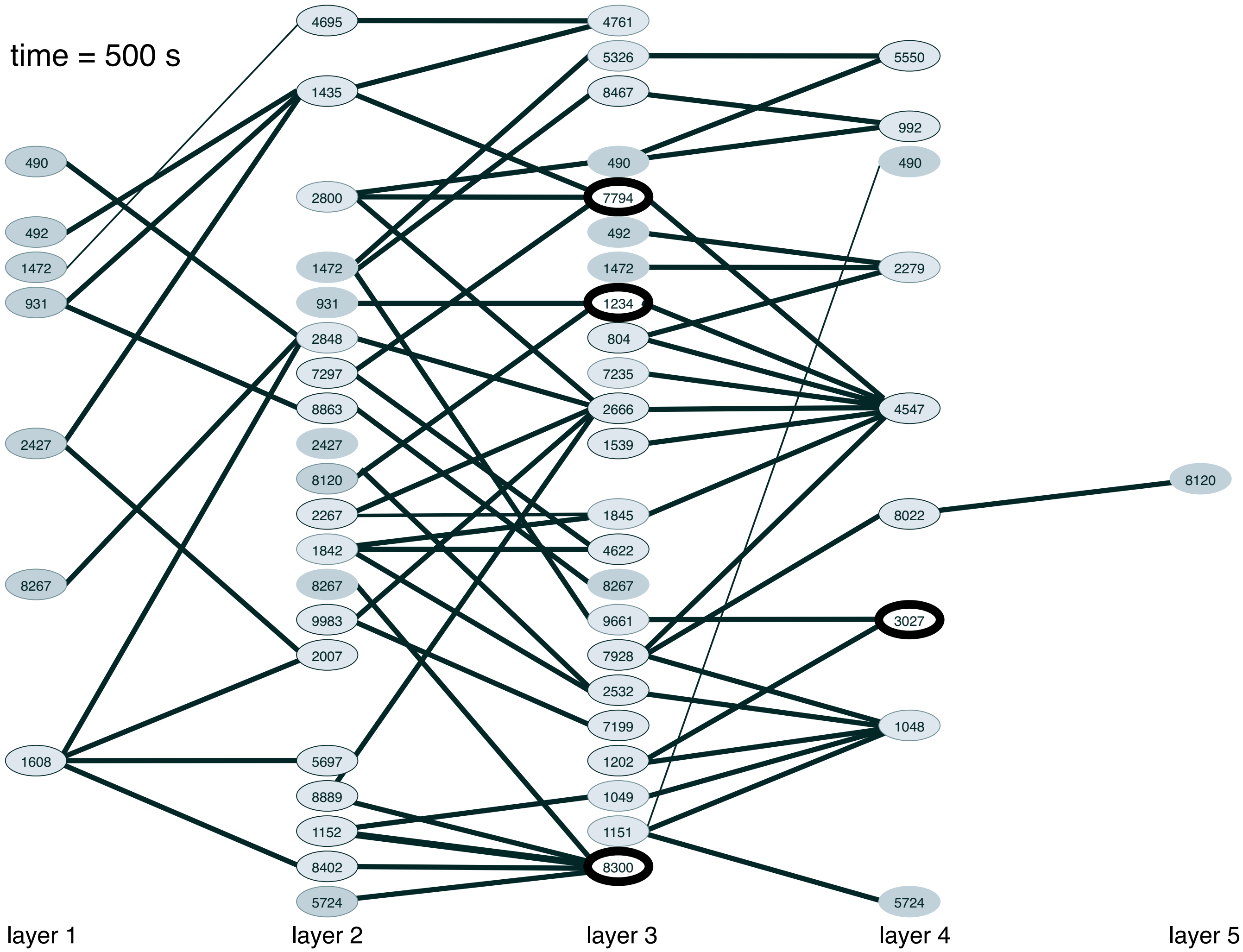
at the end of the simulation
set of cells (discarding input units)
maintaining $k_{out} \geq 3$ and $k_{in} \geq 3$
with strongest activation level ($A_{ji}(t) = 4$)
with units with the same properties.

Neighbourhood

all excitatory units (including input units)
with at least one projection to or from SI-units.

results: circuit

Iglesias *et al.*, *Emergence of Oriented Cell Assemblies Associated with Spike-Timing-Dependent Plasticity*, LNCS 3696:127-132, 2005



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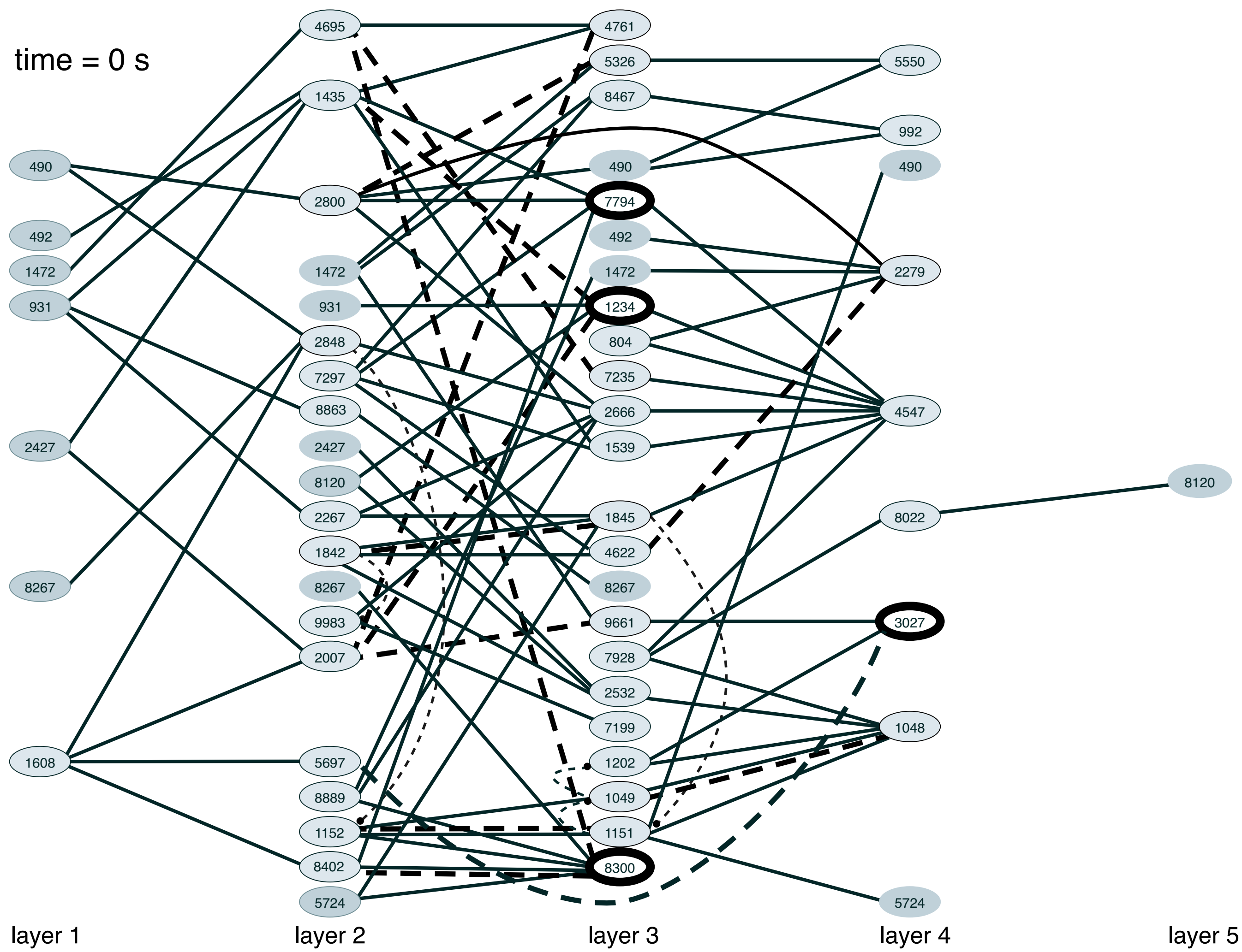
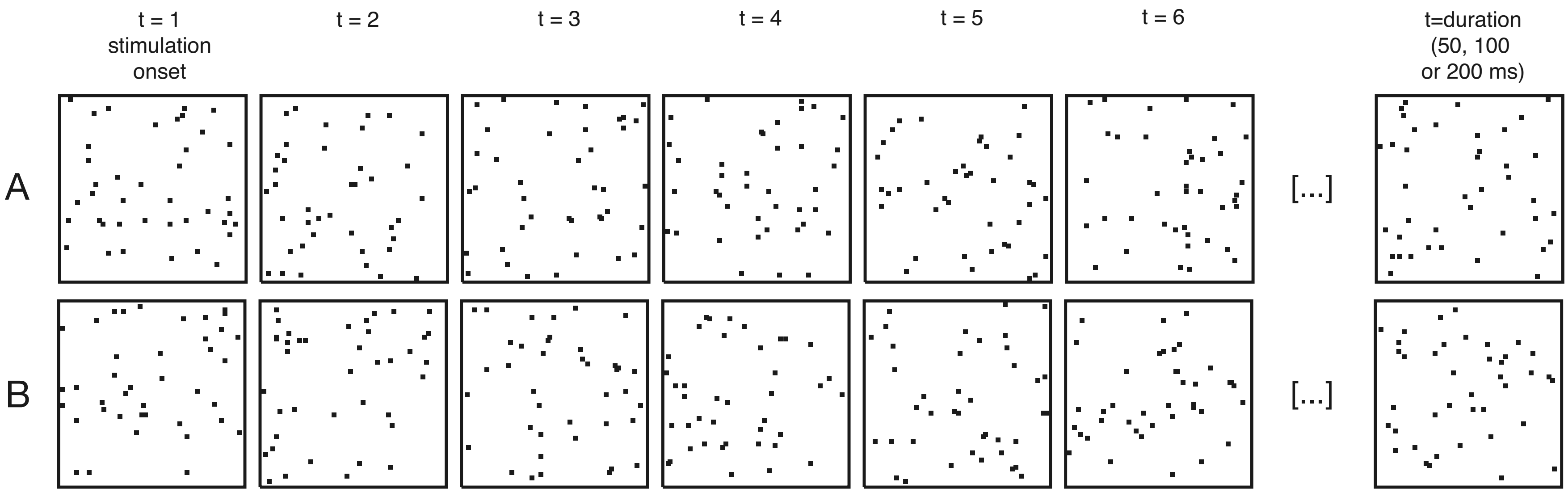


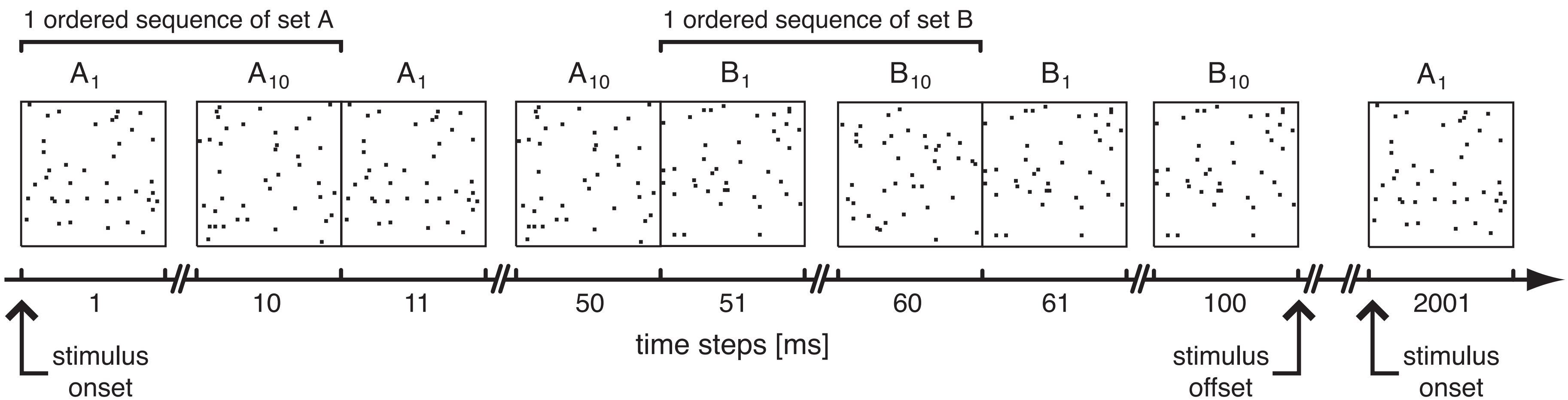
model: stimulus



every 2 seconds
10 groups of 40 units activated in sequence (10% input units)
during 100 time steps ($5 \times A + 5 \times B$ or $5 \times B + 5 \times A$)

Animated sequences are available for both stimuli A and B.

model: stimulus (cont.)



- **apoptosis induced by excessive firing rate**

  50 ms running window

  firing rate threshold:

  $\theta_\nu^{exc} = 245$ sp/s for excitatory units

  $\theta_\nu^{inh} = 250$ sp/s for inhibitory units

  death probability function: $\mathcal{P}_{\mathrm{apopt}}(t) = \frac{0.5 \cdot t^2 - 4.5 \cdot 10^{-6} \cdot t^3}{44 \cdot (2.5 \cdot 10^6 + 6 \cdot 10^{-3} \cdot t^2)}$

  $\mathcal{P}_{\mathrm{apopt}}(t = 100) = 4.5 \cdot 10^{-5}$

  $\mathcal{P}_{\mathrm{apopt}}(t = 700) = 2.2 \cdot 10^{-3}$

  $\mathcal{P}_{\mathrm{apopt}}(t = 800) = 2.9 \cdot 10^{-3}$

- **apoptosis induced by lack of excitatory afferents**

  loss of all excitatory inputs due to:

  apoptosis of pre-synaptic unit

  STDP driving to $A_{ji}(t) = 0$

- $0 \leq t < \{700, 800\}$ ms (initial phase)

  apoptosis induced by excessive firing rate

- $\{700, 800\} \leq t < 10^5$ ms

  Spike-Timing Dependent Plasticity

  $\Rightarrow$ synaptic pruning

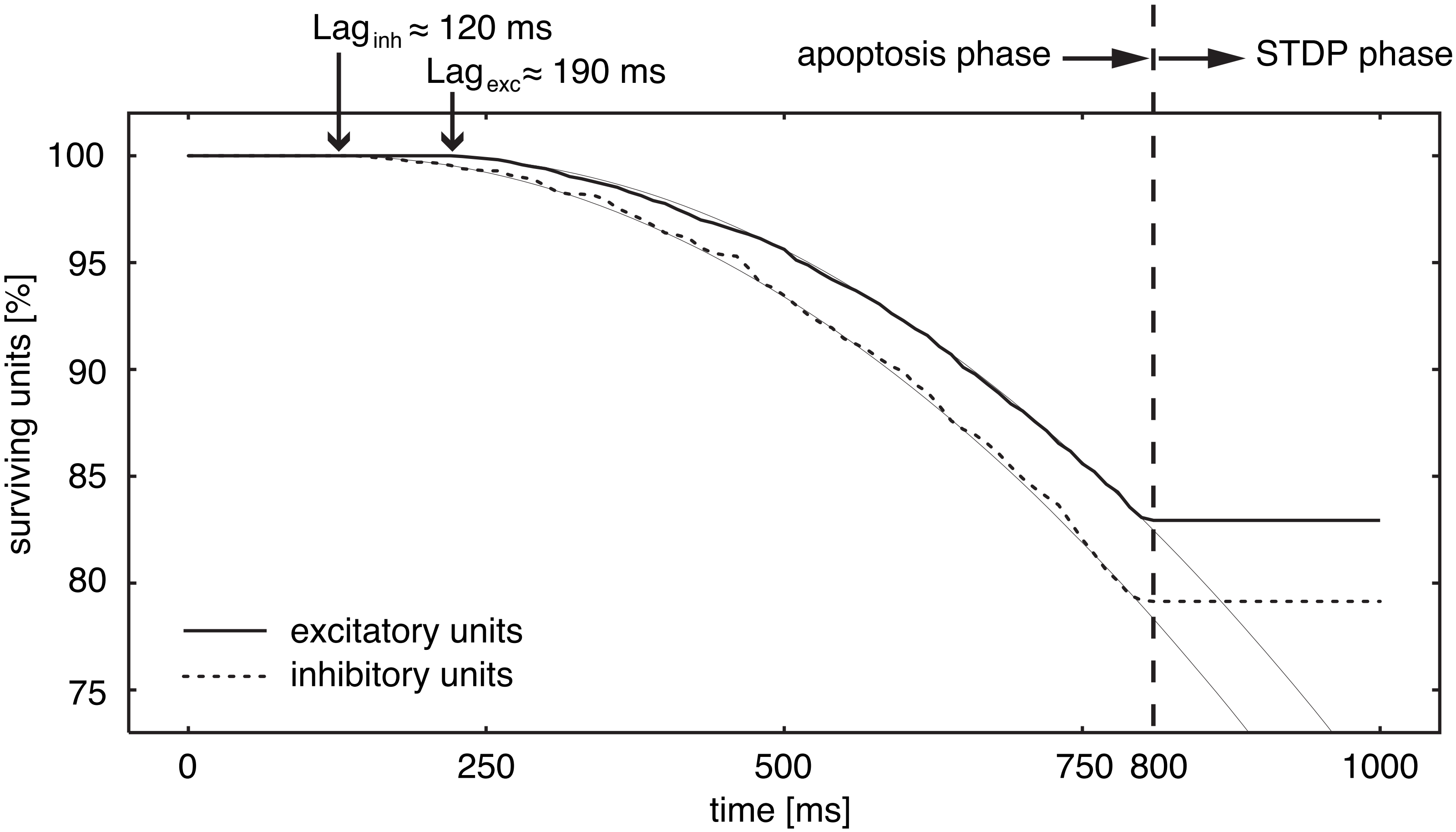
  $\Rightarrow$ apoptosis induced by lack of excitatory inputs

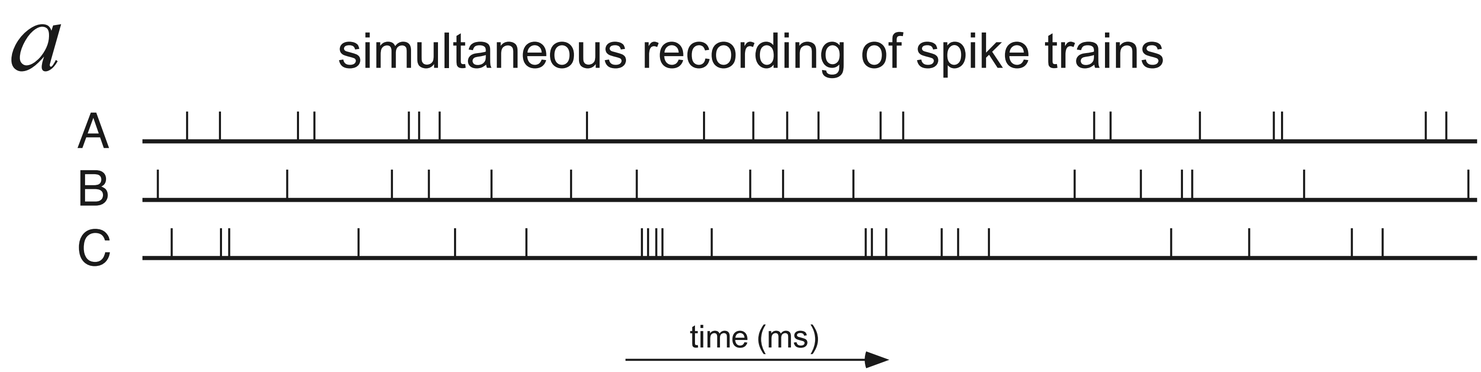
- $t = \{1000, 3000, 5000, \ldots\}$ ms

  100 ms lasting stimuli

  50 presentations (random mix: 50% AB and 50% BA)

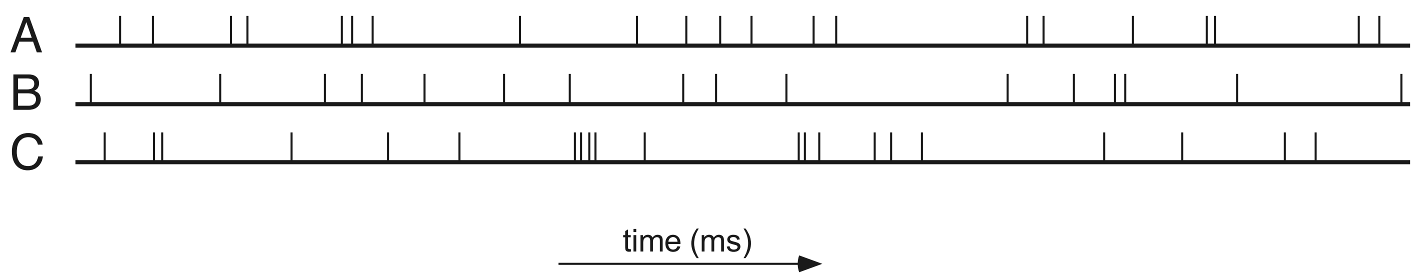
results: excitatory *vs.* inhibitory cell death




a
simultaneous recording of spike trains
A
B
C
time (ms)

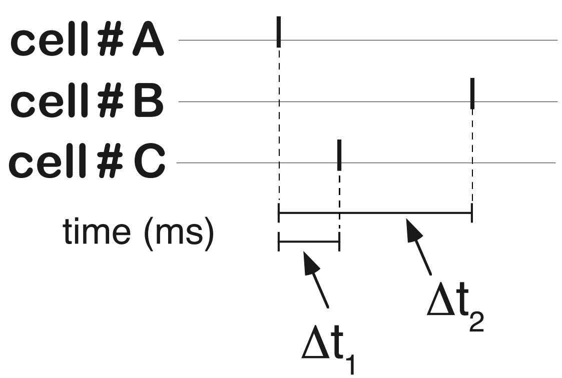
introduction: detection of spatiotemporal patterns of activity

a simultaneous recording of spike trains



b detection of statistically significant spatiotemporal firing patterns

$<A,C,B;\ \Delta t_1,\Delta t_2>$

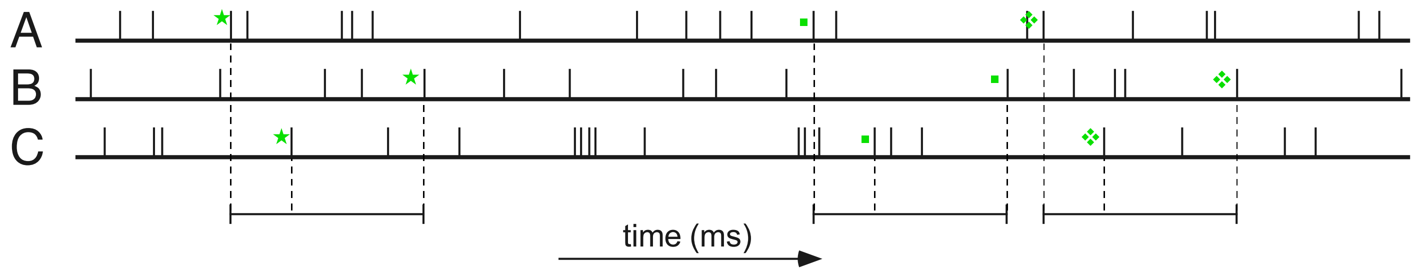


patterns found n=3

expected count N=0.02

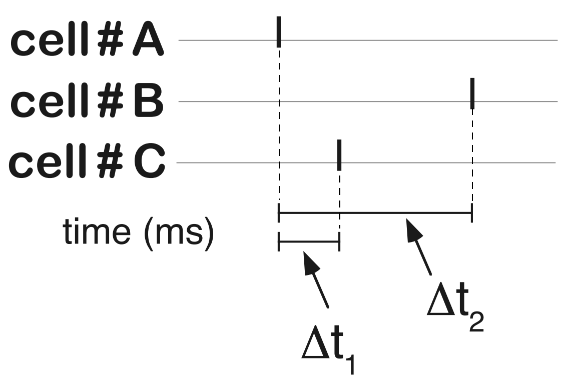
significance of this pattern
pr(3, 0.02) $\approx 1.3 \cdot 10^{6} < 0.001$

a simultaneous recording of spike trains



b detection of statistically significant spatiotemporal firing patterns

<A,C,B; Δt_1,Δt_2>



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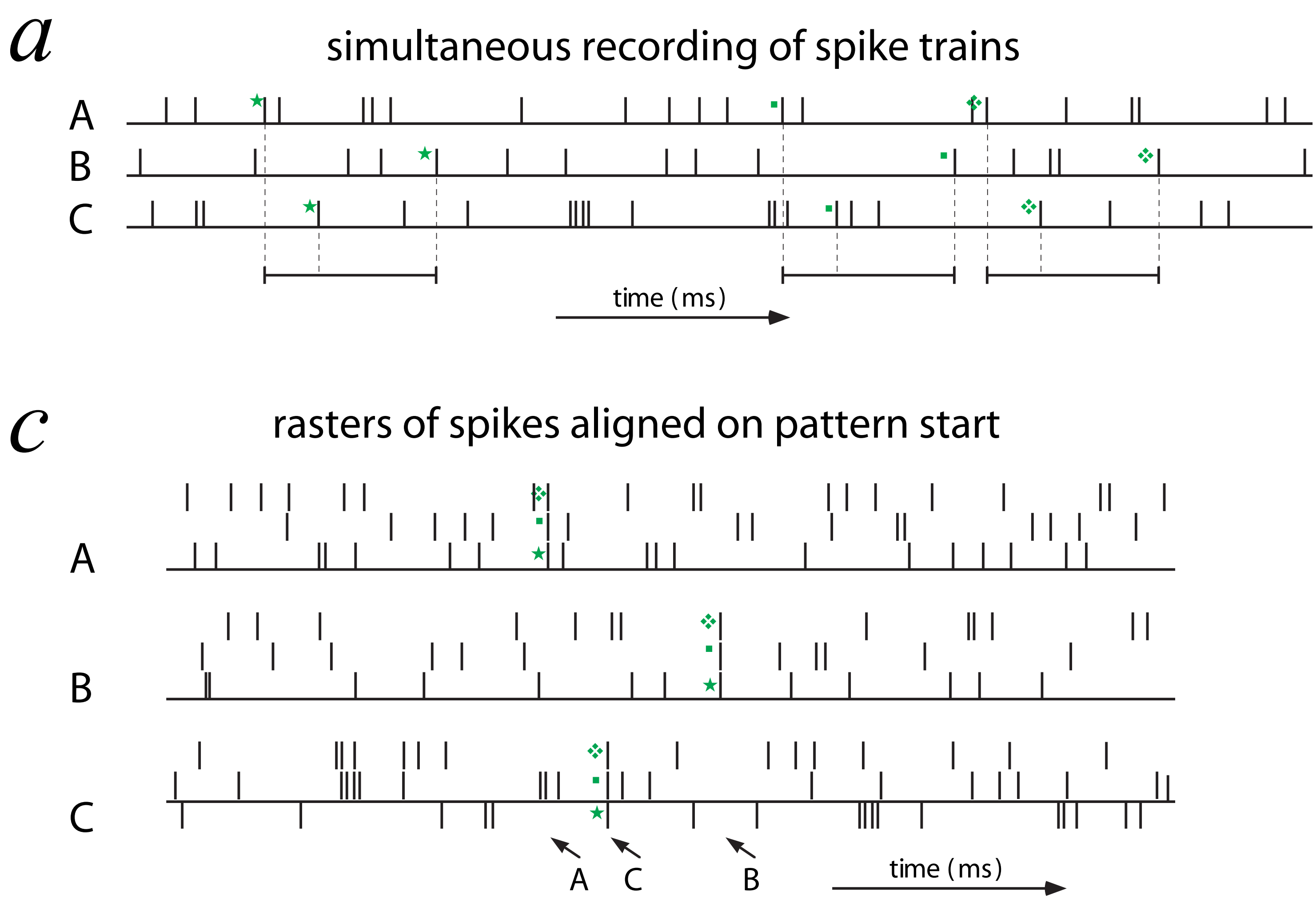
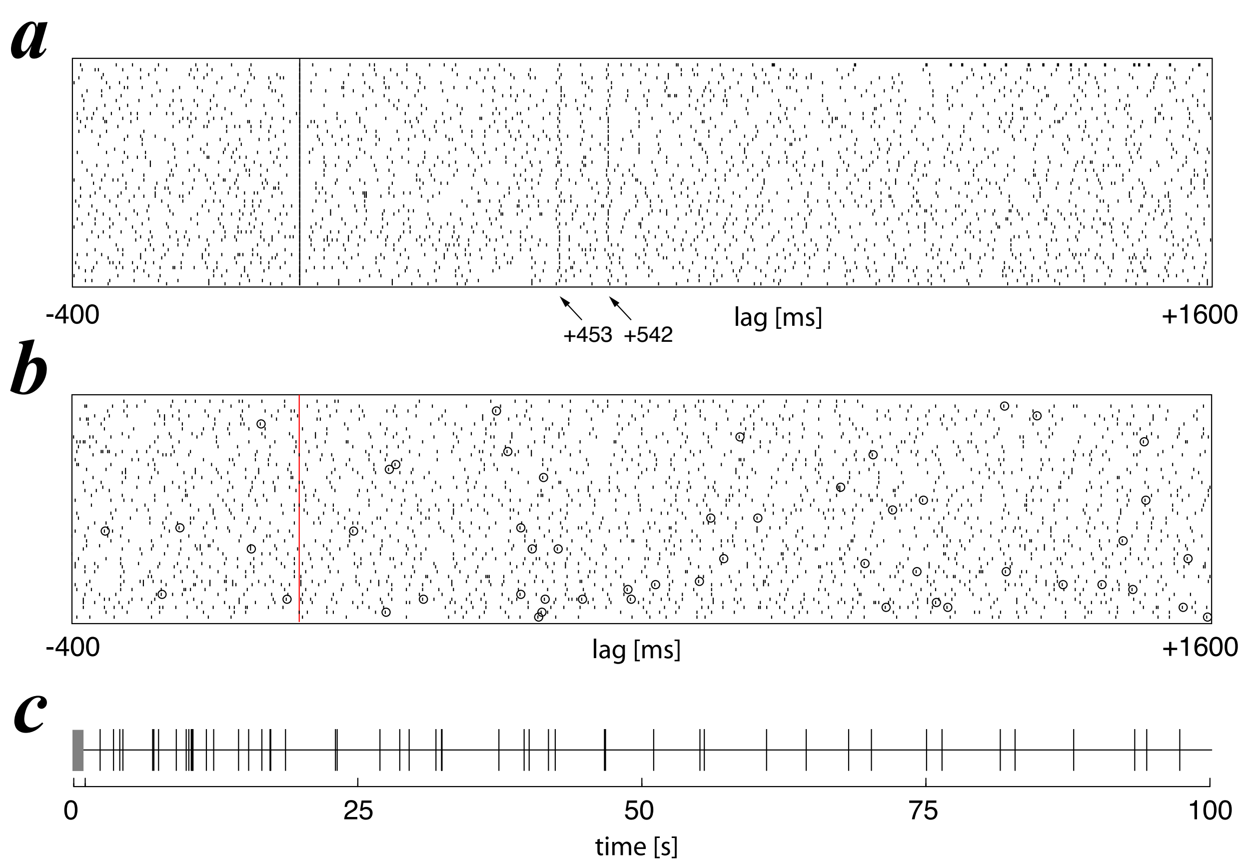
for methods, see Villa *et al.*, 1999; Tetko and Villa, 2001


a
simultaneous recording of spike trains
A
B
C
time (ms)
c
rasters of spikes aligned on pattern start
A
B
C
A
C
B
time (ms)

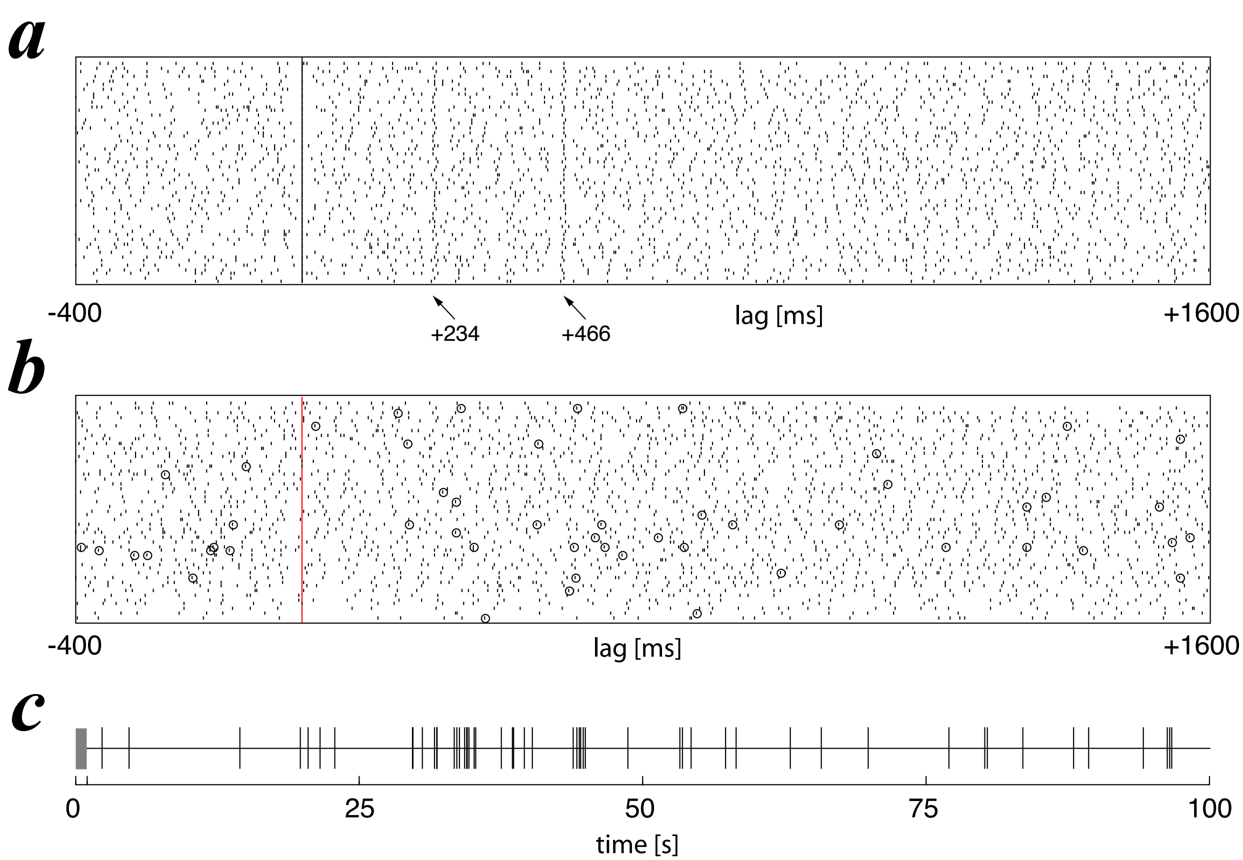
stopping firing rate-induced apoptosis at t=700ms

$<79, 79, 79; 453\pm3.5, 542\pm2.5>$



stopping firing rate-induced apoptosis at t=800ms

$<13, 13, 13; 234\pm3.5, 466\pm4.5>$



- inhibitory units enter apoptosis
  about 70 ms before excitatory units

- death dynamics of both populations followed
  the probability function to die $\mathcal{P}_{\mathrm{apopt}}(t)$

- addition of cell death to the model
  improved stability of the network

  stopping apoptosis at 700 ms lead to
  larger number of surviving units with lower mean firing rate

  stopping apoptosis at 800 ms lead to
  smaller number of surviving units with greater mean firing rate

- maintained ability to let emerge cell assemblies
  associated to preferred firing sequences