Laboratório de Sistemas Neurais

SisNe

NeuroMat

Planeta by León Ferrari

IS THERE COUPLED NETWORKS BETWEEN PYRAMIDAL CELLS IN THE HIPPOCAMPUS AND CORTEX? A COMPUTATIONAL APPROACH

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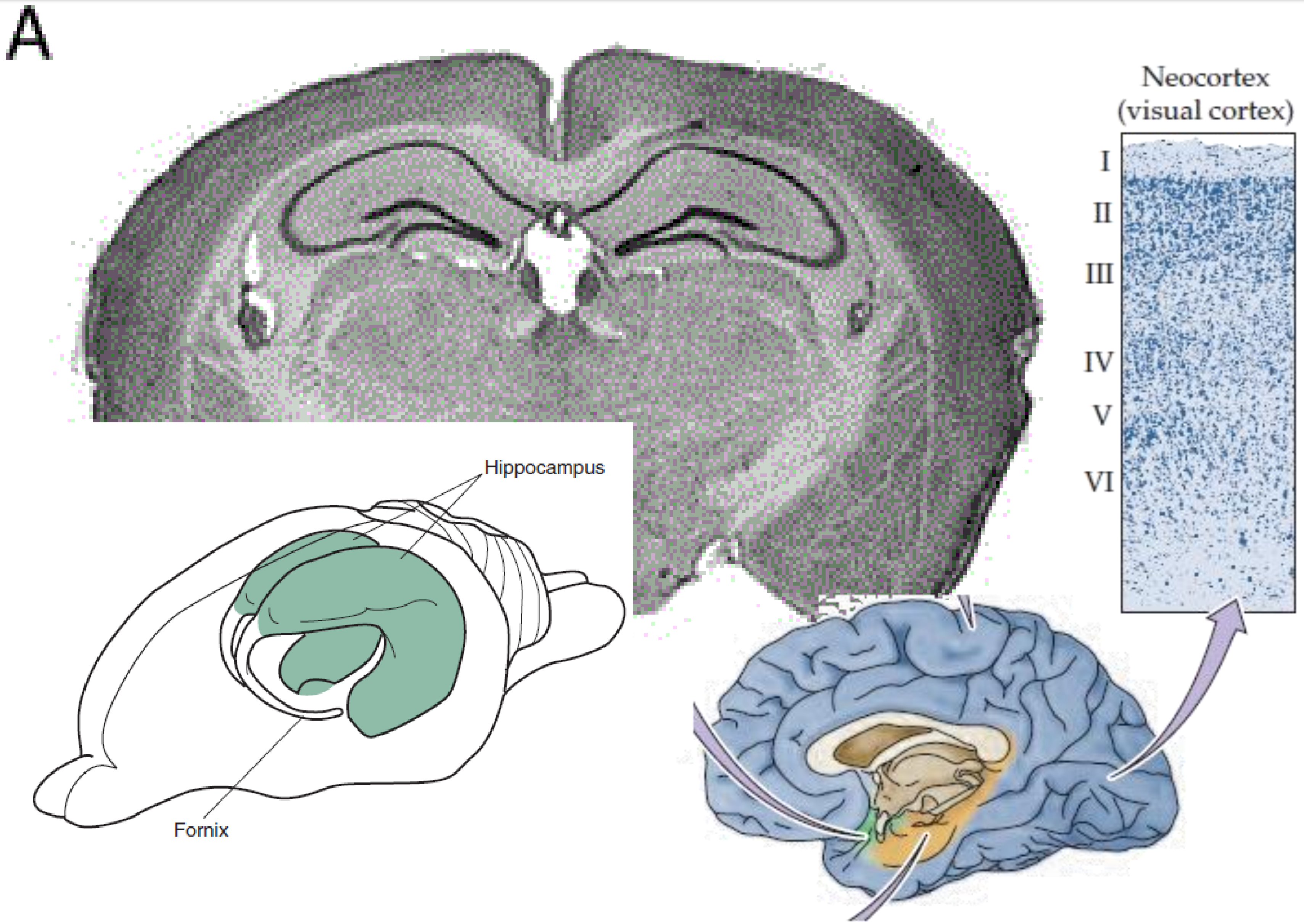
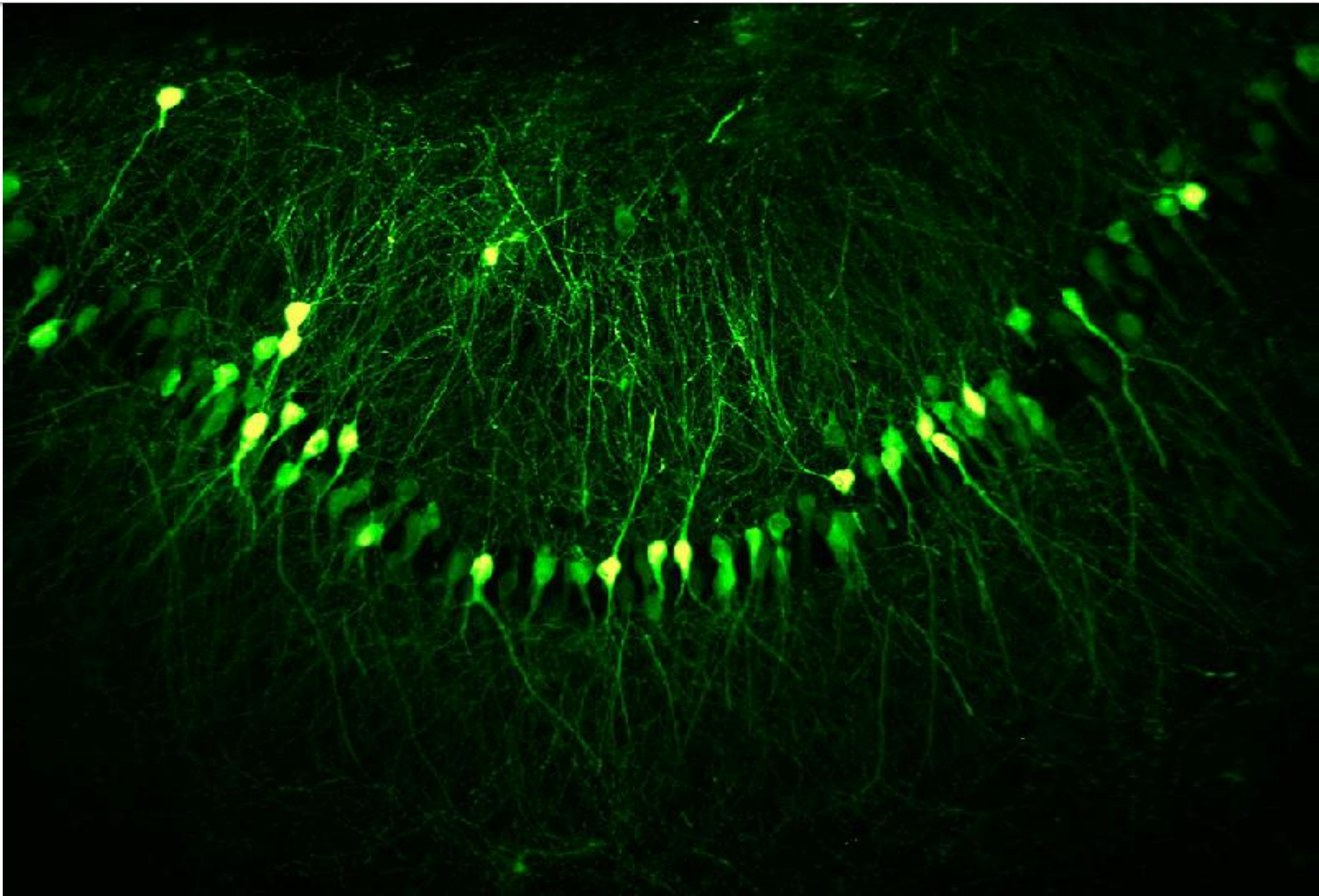
Hippocampus and Cortex – Neurons are in layers



Pyramidal cells: Somas, dendrites and axons



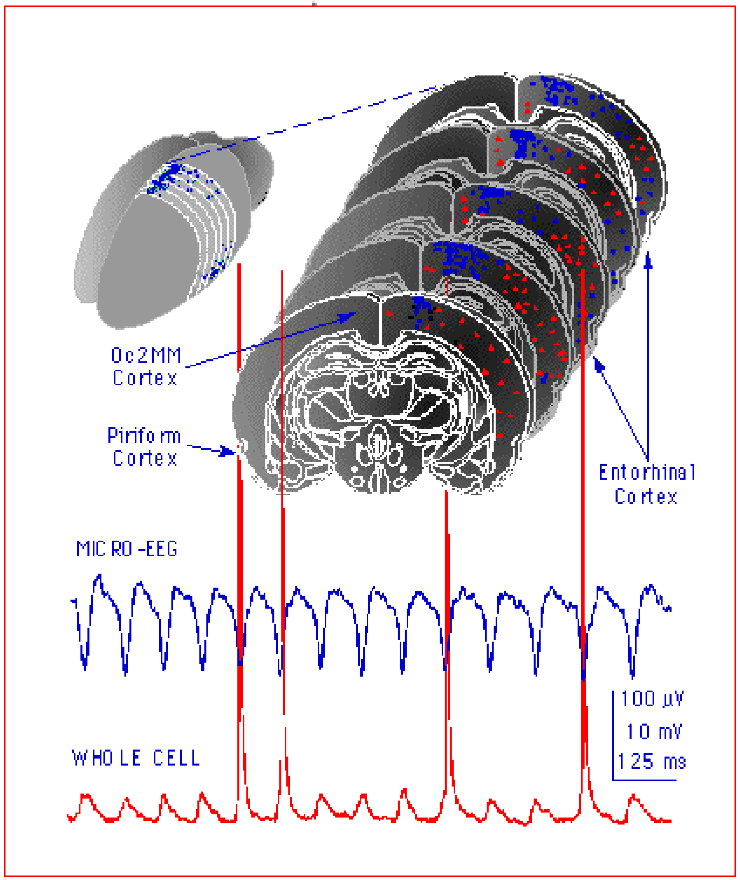
High frequency oscillations (HFO)

HFO have been recorded in the hippocampus and the cortex

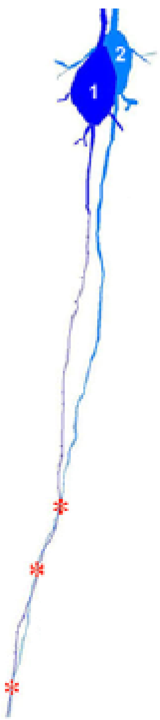
Chemical synapses are not necessary for HFO

Electrical synapses blockers vanish HFO

Thus, it has been suggested that HFO are generated by networks of coupled pyramidal cells



Coupled networks

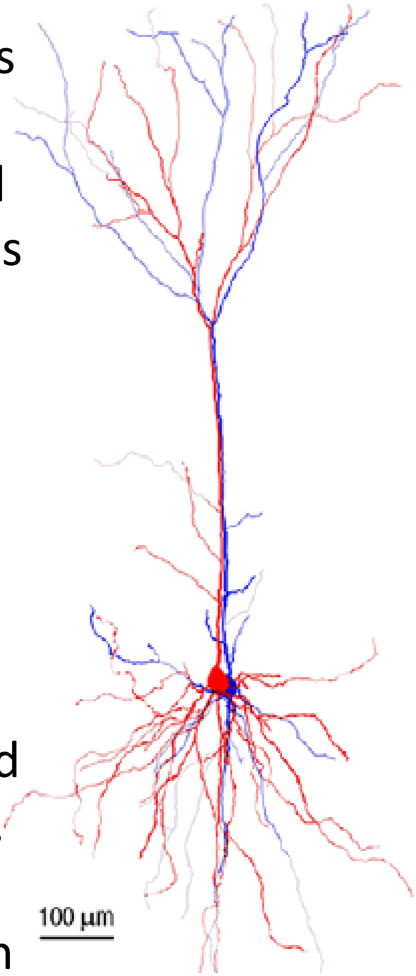


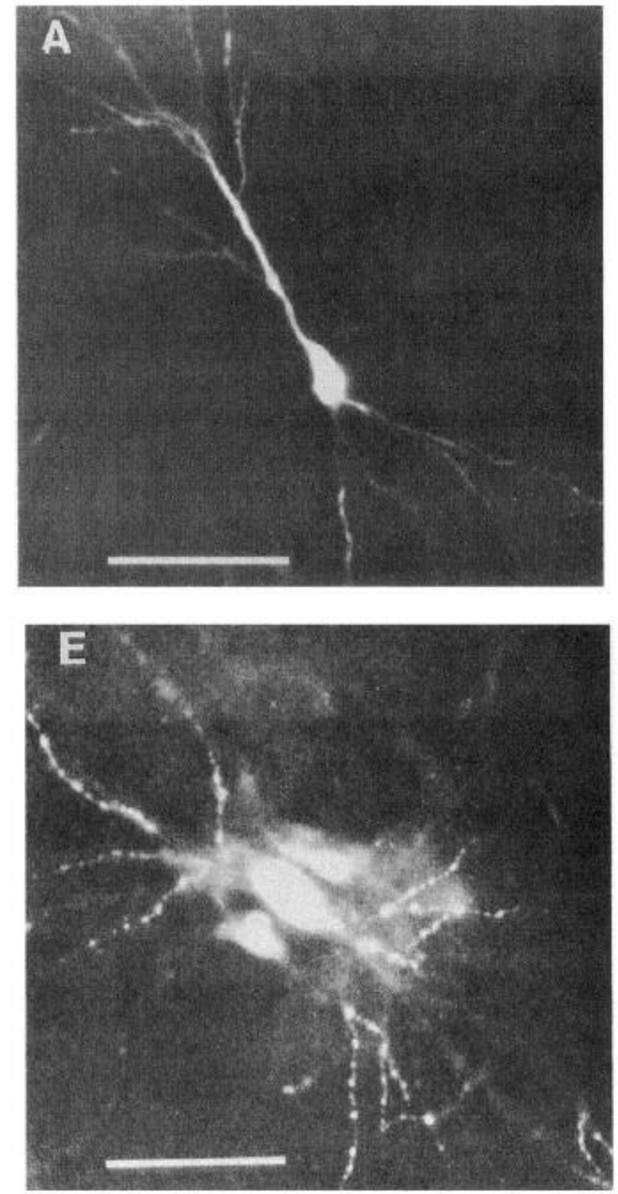
Computational simulations have demonstrated that large networks of coupled pyramidal cells in the axons might support the generation of HFO.

It exists experimental evidence that pyramidal cell axons are coupled.

Pyramidal cells are coupled in clusters of 2-3 neurons.

Neurons appart more than 50 μm are not coupled.

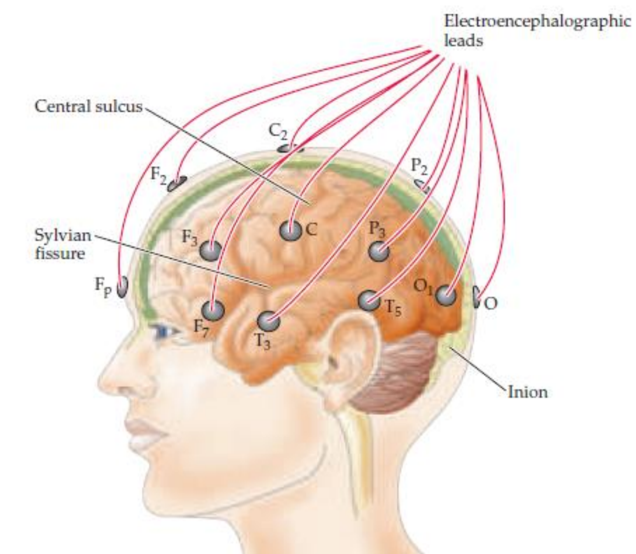


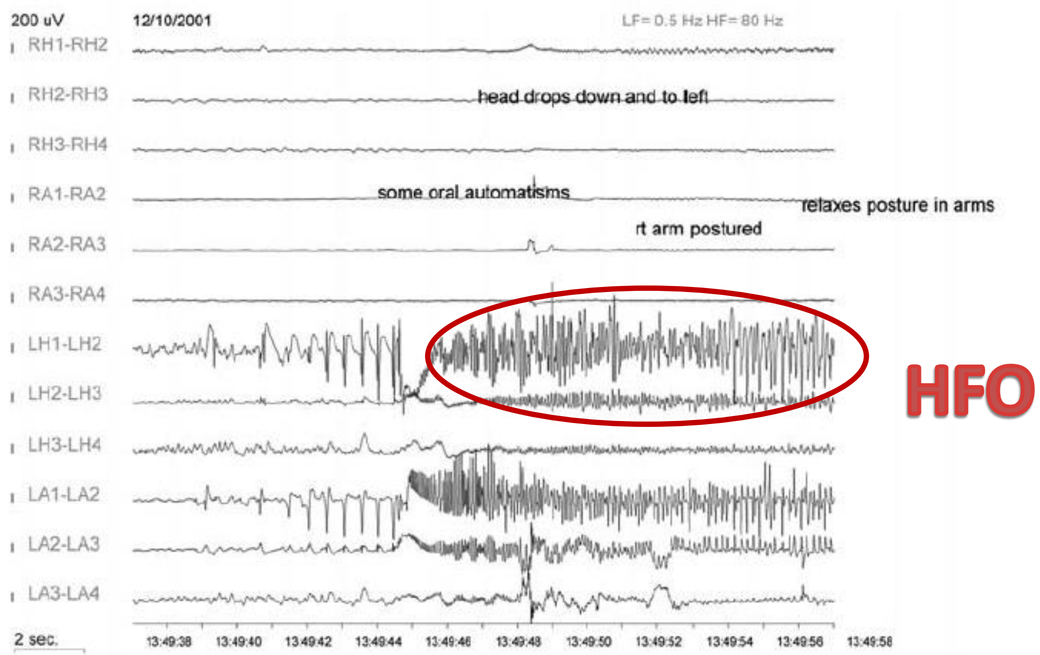


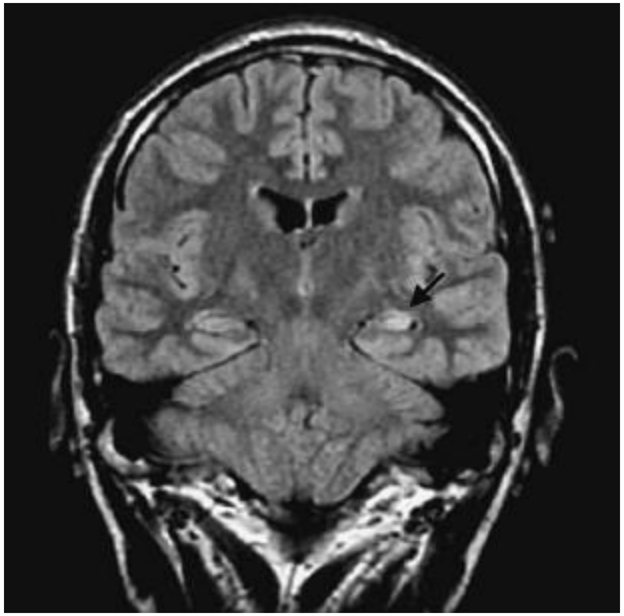
Surgery for intractable epilepsy

Electrode recordings localized the seizure focus.

There is thus a strong correlation between resection of a epileptic focus tissue and cure of the epilepsy.

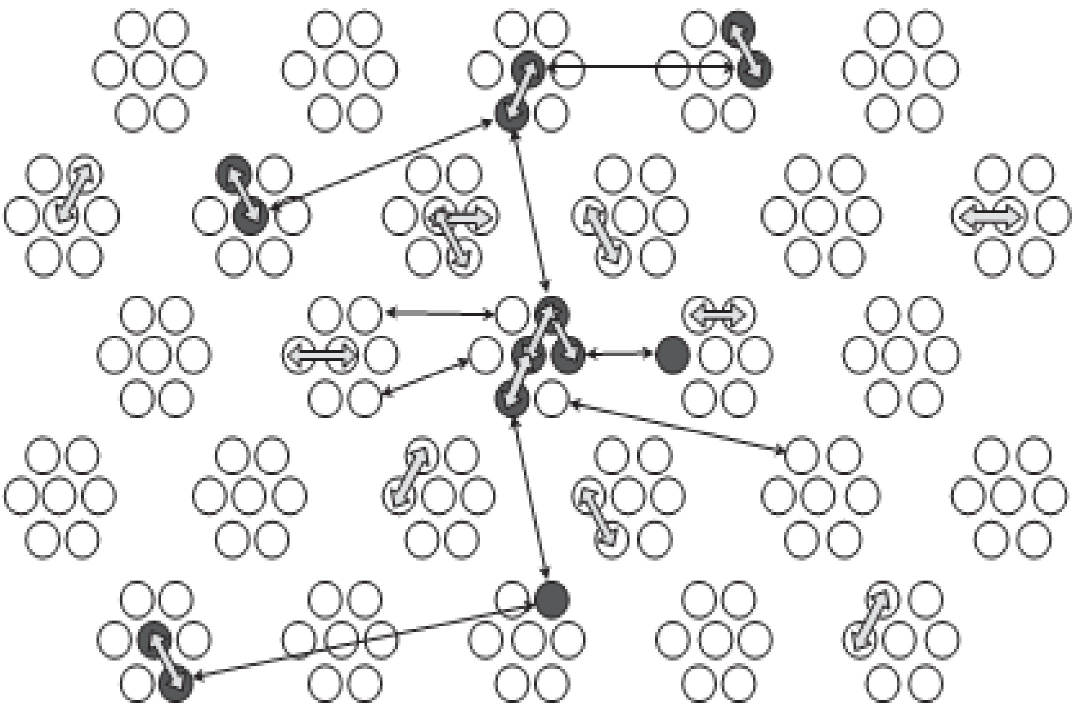






Computational models of HFO generation

Large networks of coupled axons allow the propagation of spontaneous spikes (Traub et al., 1999; Munro & Borgers, 2010)



The existence of such coupled networks is assumed.

There is no experimental evidence supporting that assumption.

Objective and Justification

Objective:

Establish the connectivity rules that might allow the generation of large coupled networks in the hippocampus and cortex.

Justification

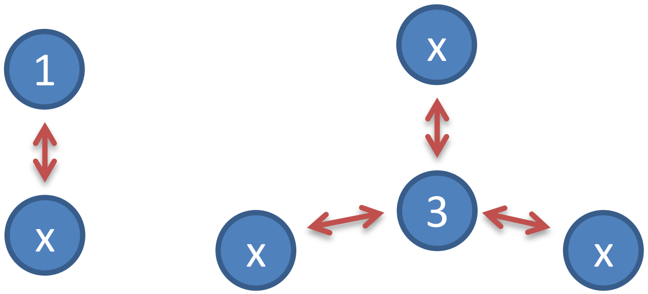
Currently, it is extremely difficult to establish the topology of sparse networks through experimental tecniques.

It is necessary to establish the existence of large networks that might support the hypotheses that electrical coupling among pyramidal cells might support the generation of HFO.

This work interacts with NeuroMat in the sense that it provides a computational framework for the study of large networks of electrically coupled neurons

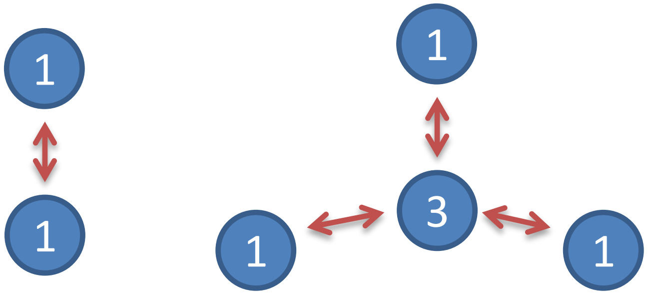
Theoretical analyses

Neurons were distributed homogeneously in a 3D space and randomly connected. Coupled motifs might be:



Where x can be 1 or 3

Motifs that represent small isolated clusters that do not contribute to the formation of large networks are:



Coupling with 1 neighbor isolates !!!

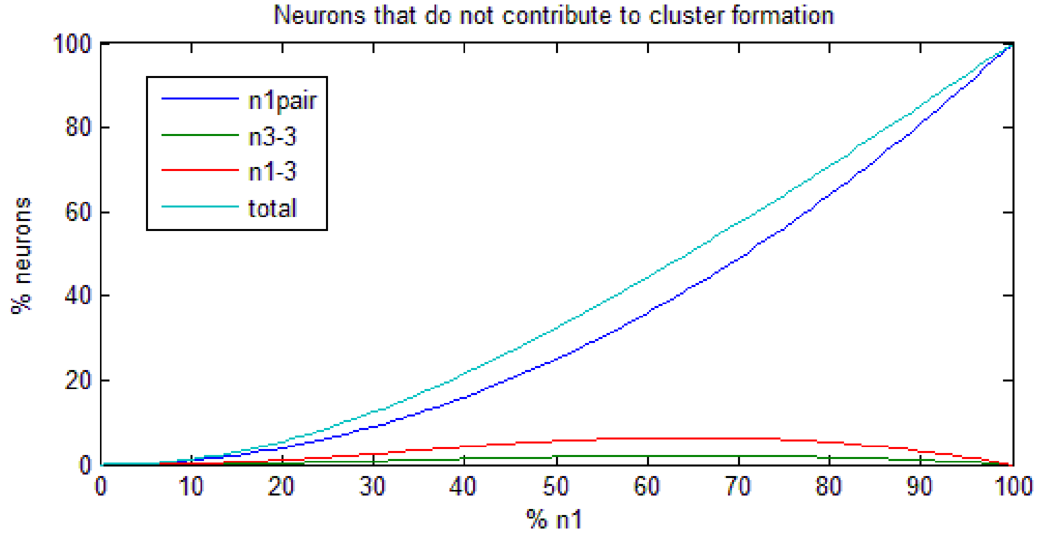
Results

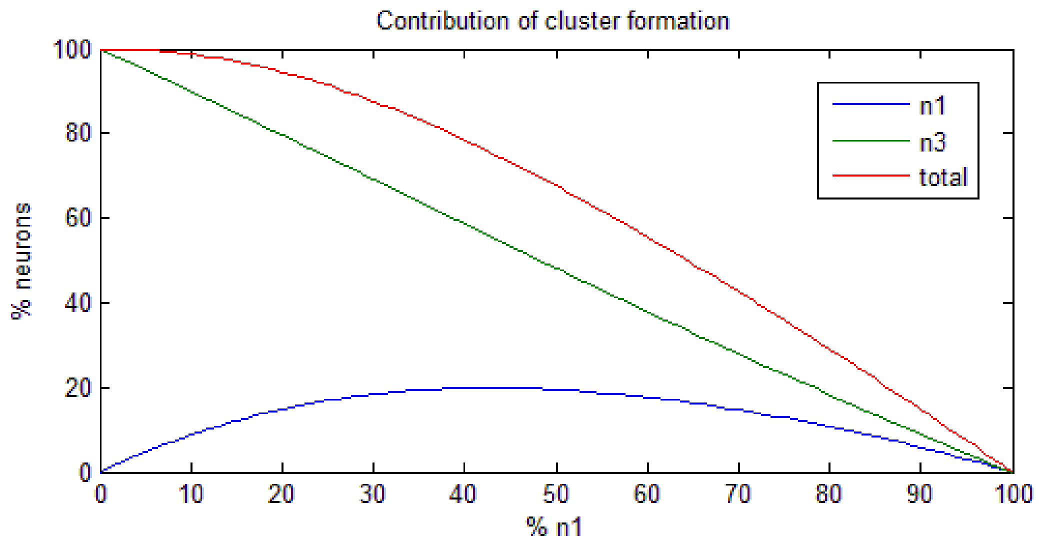
%N1 = % of neurons coupled with 1 neighbor

N1-N1 pairs increases with the increase of %N1

N1s are less than %20 in large clusters.

N3 are the majority in the large cluster.





Methodology – Computational simulations

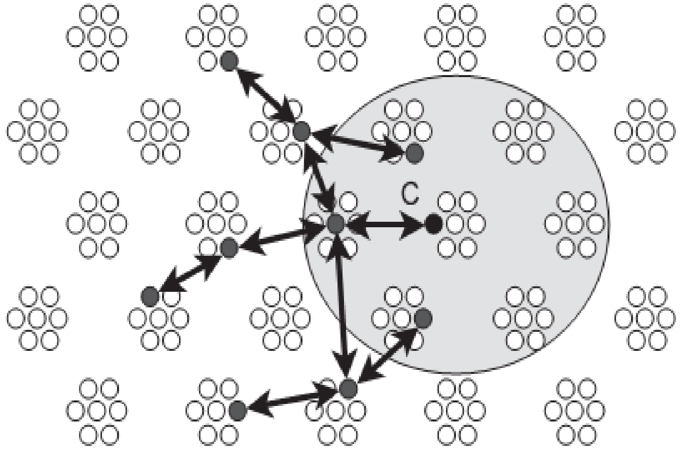
	Neuronal density (neurons/mm3)	Axonal initial segment length (µm)
Hippocampus	300.000	50
Cortex	50.000	40

Each neuron coupled with 1 or 3 other neurons within a radius r.

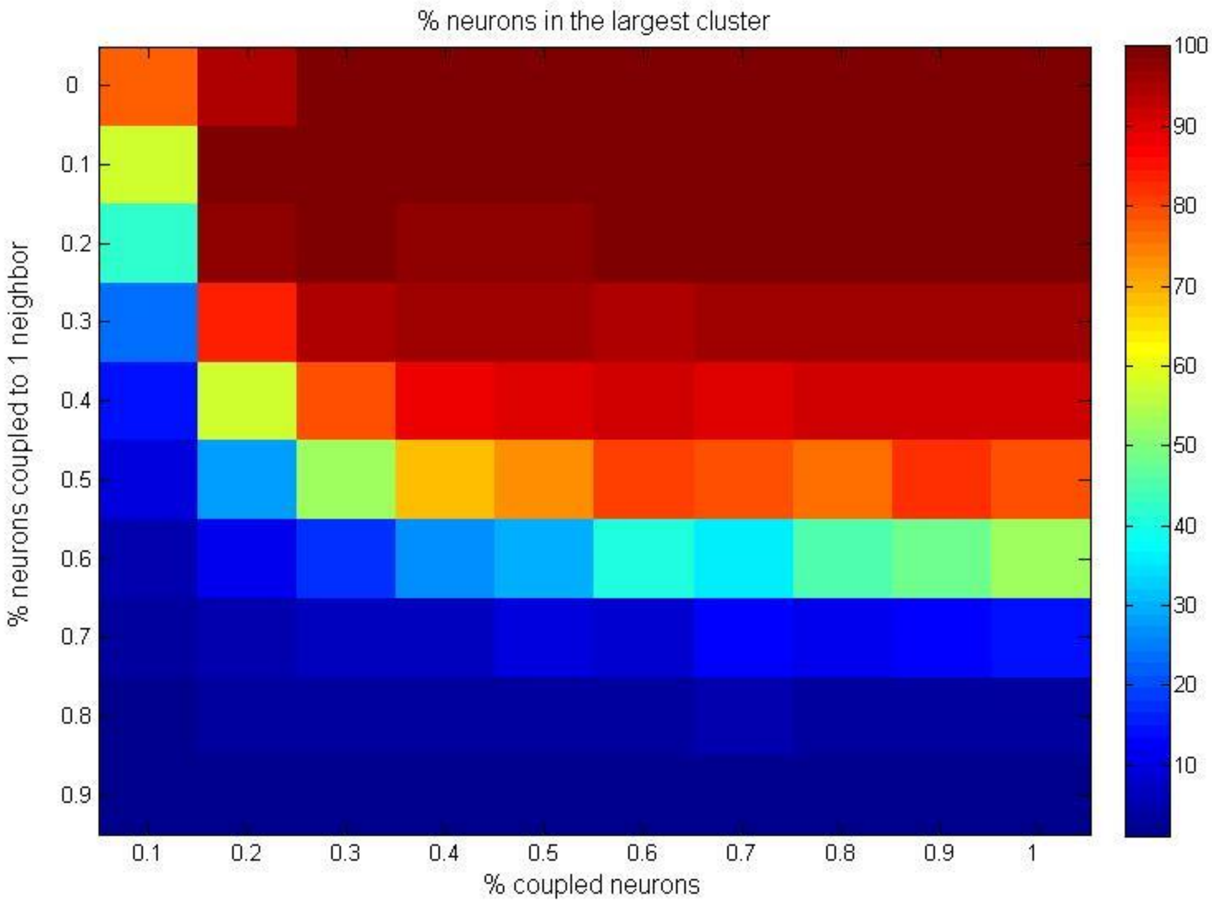
r = axon initial segment length

Neurons were distributed homogeneously (neuronal density) in a 3D space and randomly connected.

Volume: 100 µm x 300 µm x 300 mm

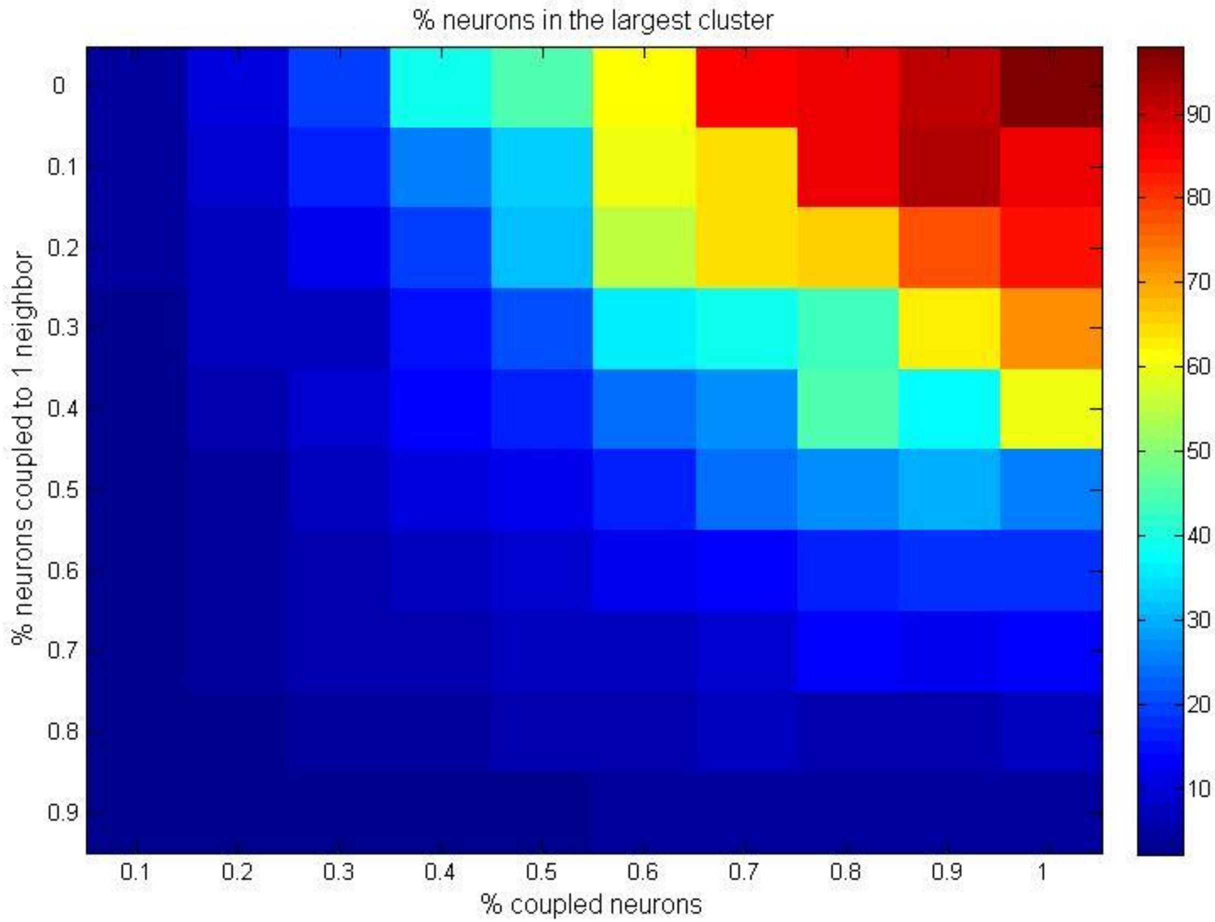


Results - Hippocampus



The network made of only neurons coupled with 3 neighbors always form a large cluster containing almost 100% of the neurons, even when only 10% of the neurons are coupled.

Results - Cortex



It is necessary more than 50 % of coupled neurons and more than 50 % of neurons coupled with 3 neighbors to generate large clusters.

Conclusions

1 - Neurons coupled with 1 neighbor are annihilator of large clusters

2 - Neurons coupled with 3 neighbor are creators of large clusters

3 - Increasing the density of coupled neurons increases the chance for the formation of large clusters

4 – Increasing the % of neurons coupled with 3 neighbors or diminishing the % of neurons coupled with 1 neighbors increases the size of the largest cluster

5 – Syncytium is plausible in the hippocampus but not in cortex

References

Draguhn, A., Traub, R. D., Schmitz, D., & Jefferys, J. G. R. (1998). **Electrical coupling underlies high-frequency oscillations in the hippocampus in vitro**. *Nature*, *394*(6689), 189-192.

Schmitz, D., Schuchmann, S., Fisahn, A., Draguhn, A., Buhl, E. H., Petrasch-Parwez, E., ... & Traub, R. D. (2001). **Axo-axonal coupling: a novel mechanism for ultrafast neuronal communication**. *Neuron*, *31*(5), 831-840

Traub, R. D., Schmitz, D., Jefferys, J. G., & Draguhn, A. (1999). **High-frequency population oscillations are predicted to occur in hippocampal pyramidal neuronal networks interconnected by axoaxonal gap junctions**. *Neuroscience*, *92*(2), 407-426.

Mercer, A., Bannister, A. P., & Thomson, A. M. (2006). **Electrical coupling between pyramidal cells in adult cortical regions**. *Brain cell biology*, *35*(1), 13-27.

Church, J. and Baimbridge, K. G. (1991). **Exposure to high-pH medium increases the incidence and extent of dye coupling between rat hippocampal CA1 pyramidal neurons *in vitro*.** J. Neurosci. *11*, 3289–3295

Perez-Velazquez, J. L., Valiante, T. A., & Carlen, P. L. (1994). **Modulation of gap junctional mechanisms during calcium-free induced field burst activity: a possible role for electrotonic coupling in epileptogenesis**. *The Journal of neuroscience*, *14*(7), 4308-4317.

Munro, E. & Borgers, C. (2010) **Mechanisms of very fast oscillations in networks of axons coupled by gap junctions**.J. Comput. Neurosci., 28, 539– 555.