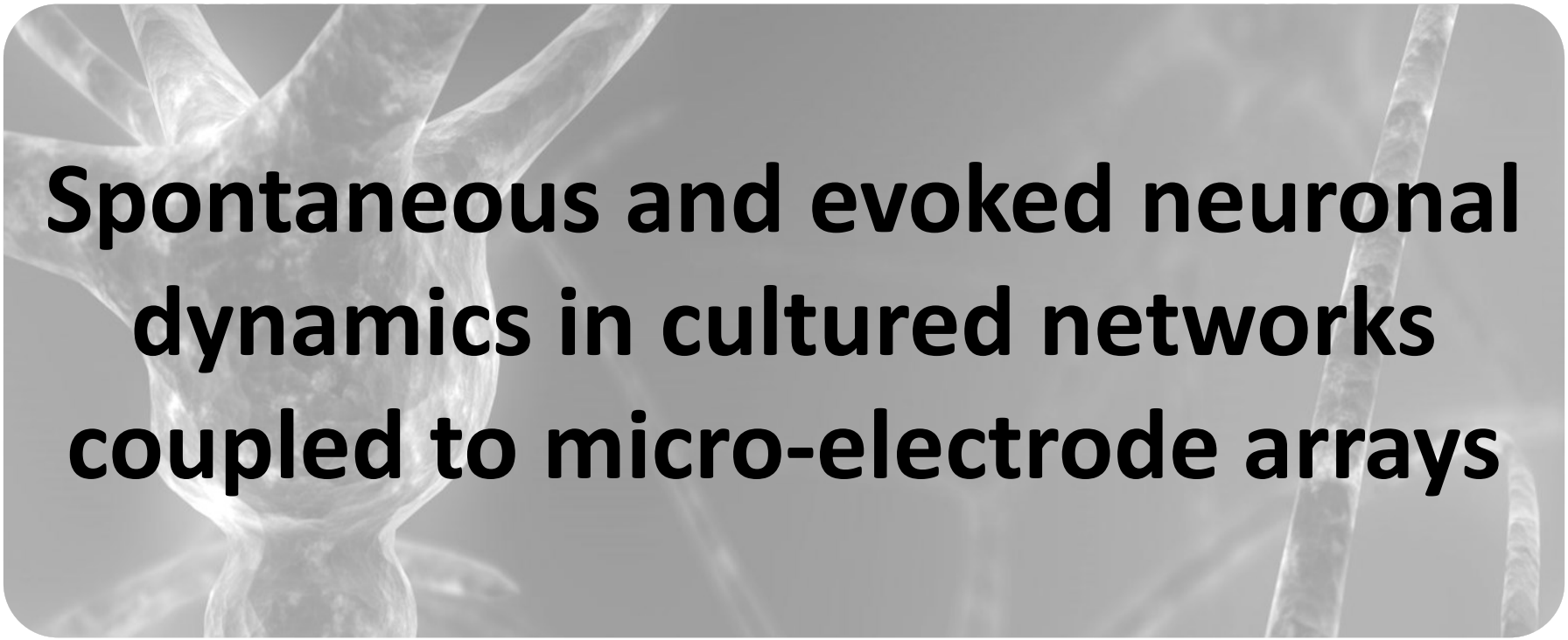

Spontaneous and evoked neuronal dynamics in cultured networks coupled to micro-electrode arrays

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Complexity of the brain

10^{11}

100.000.000.000

Connections

10^{14}

100.000.000.000.000

(1000:10000 connections each cell)

Information flow

Reverse engineering the brain

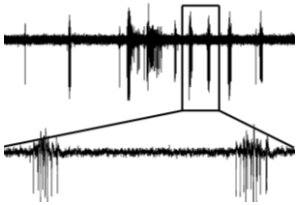
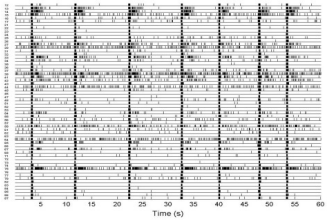
Why is it important to decode the neuronal information ?

Paralysed woman moves robot with her mind

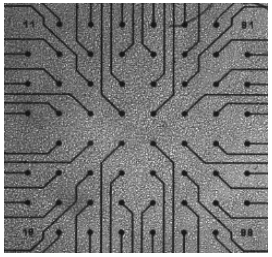
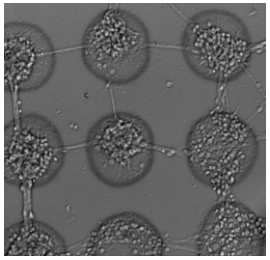
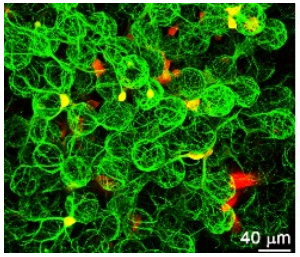
Video 1
https://www.youtube.com/watch?v=ogBX18maUiM

Outline

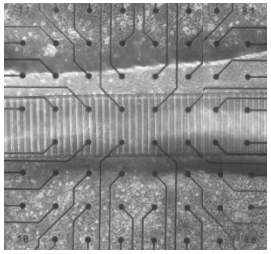
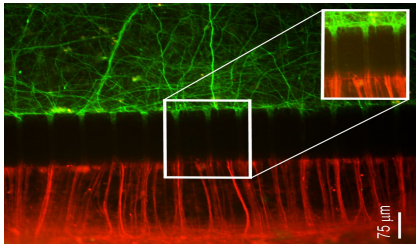
1. **Neuronal networks coupled to Micro-electrode arrays (MEAs)**

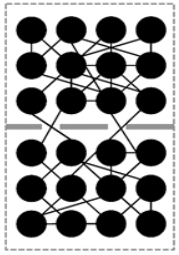




2. **Engineered networks coupled to MEA display complex and specific dynamics**

3. **Interplay between connectivity and network dynamics**

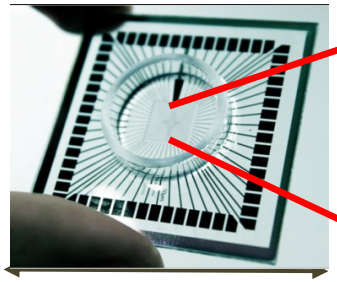


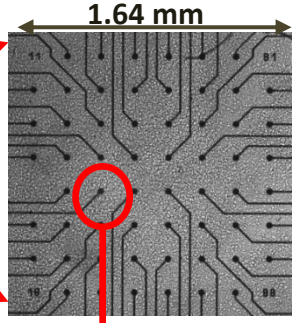
4. **Electrical stimulation on MEA evokes network plasticity**

Neuronal networks coupled to MEA

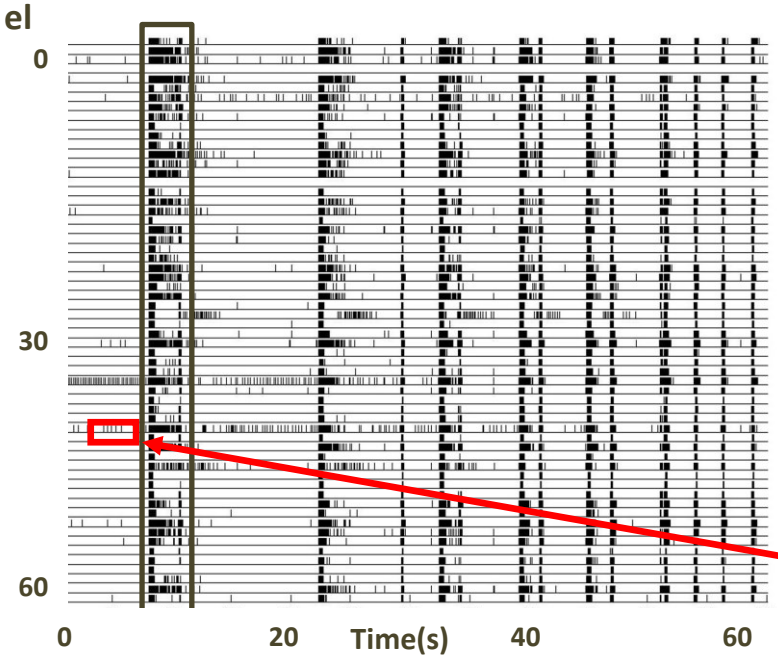
Primary cultures of rat neurons

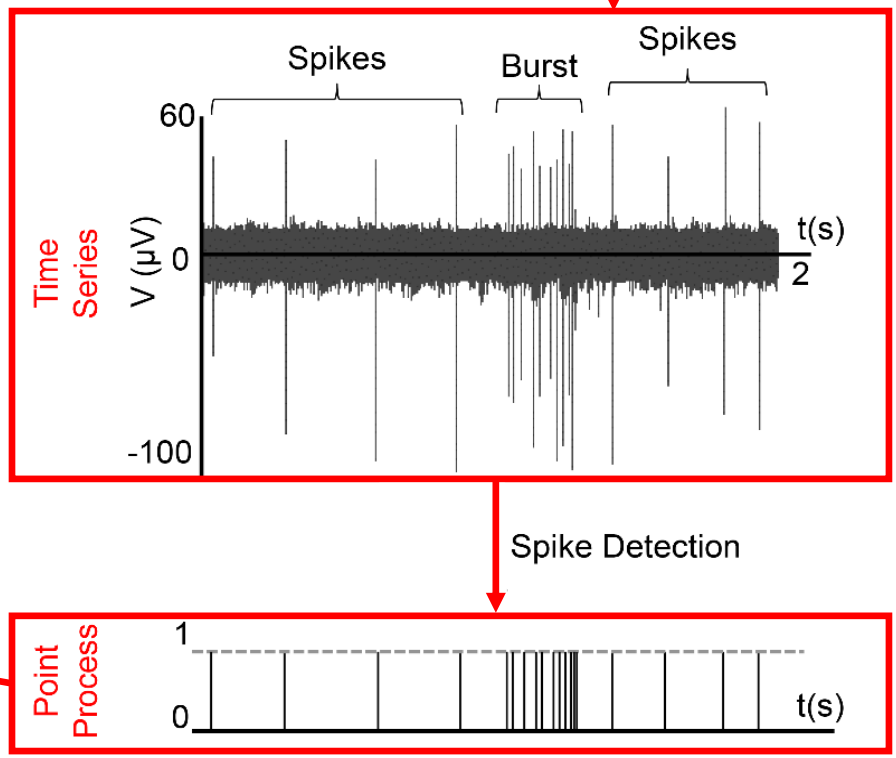
Micro-Electrode Arrays (MEAs)





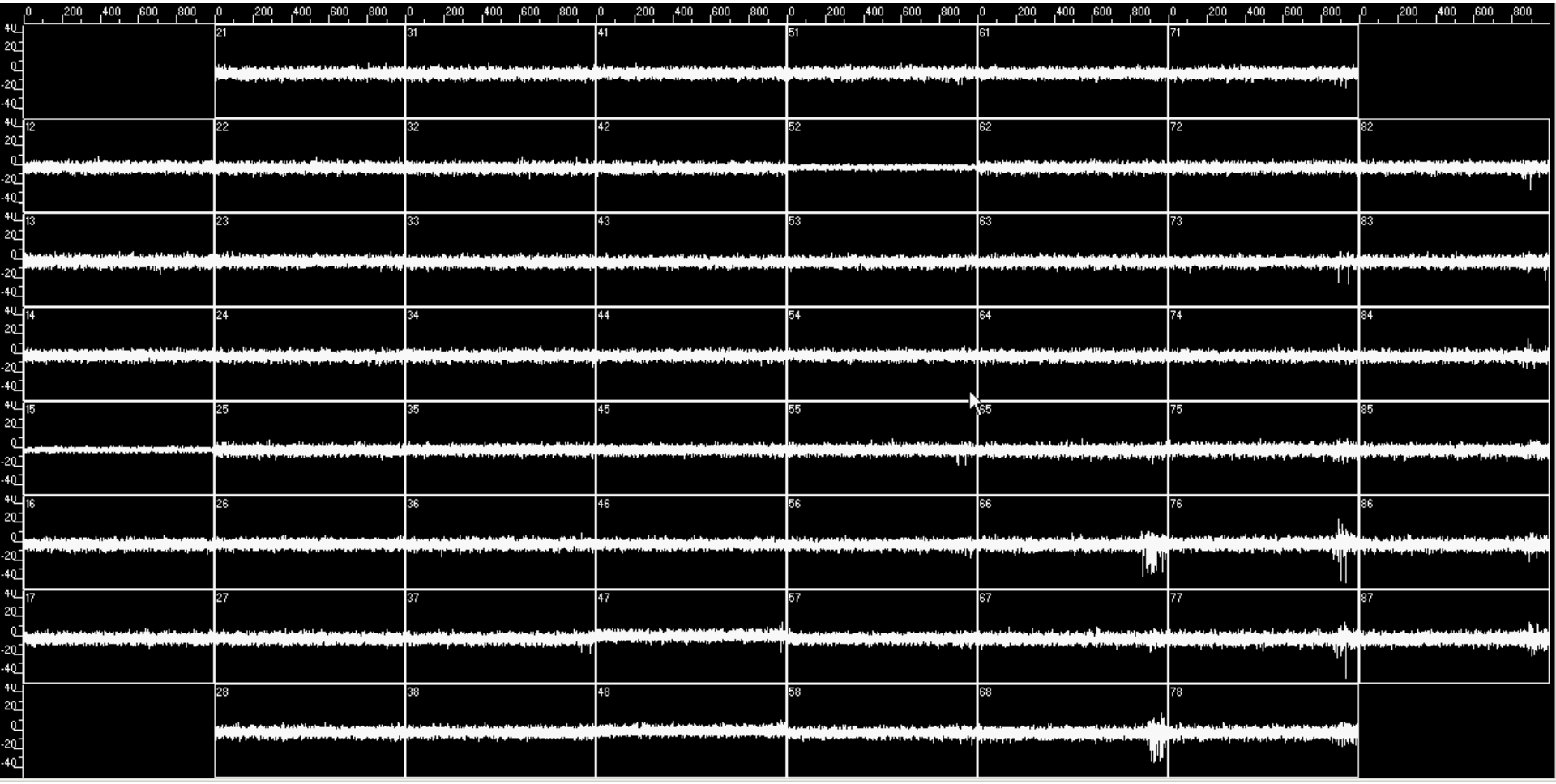
Network burst / Network Spike / Up state





Adapted from Poli et al., Frontiers in Neural Circuits, 2015

Electrophysiological activity of neuronal networks coupled to micro-electrode array



Rat neurons grown on a computer chip fly a simulated aircraft

Video 2
https://www.youtube.com/watch?v=1w41gH6x_30

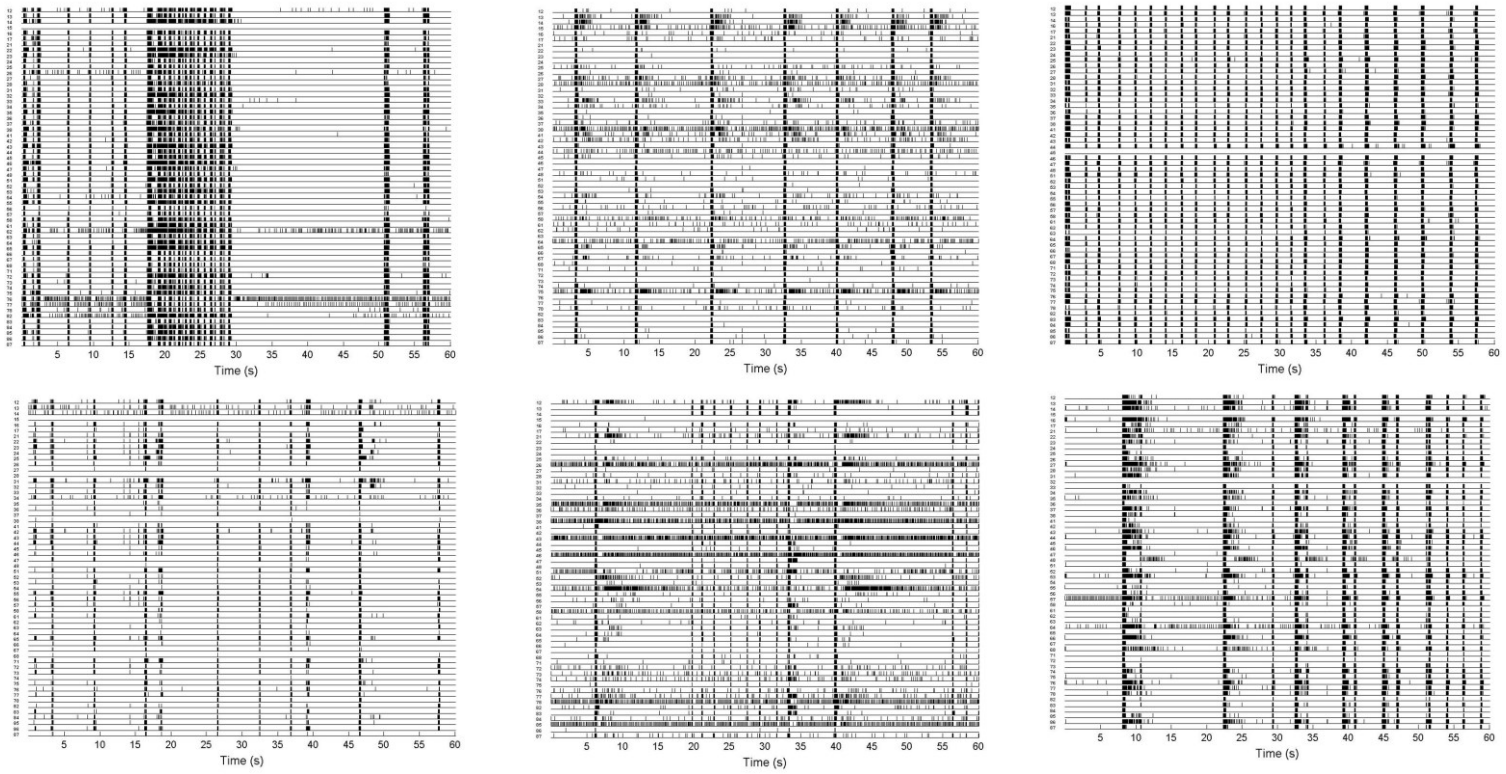
Robot controlled by neurons

https://www.youtube.com/watch?v=NZihD9QGqMs

Great variability of activity patterns

Experimental Evidence:

Cortical networks exhibit different patterns of activity at the same degree of development

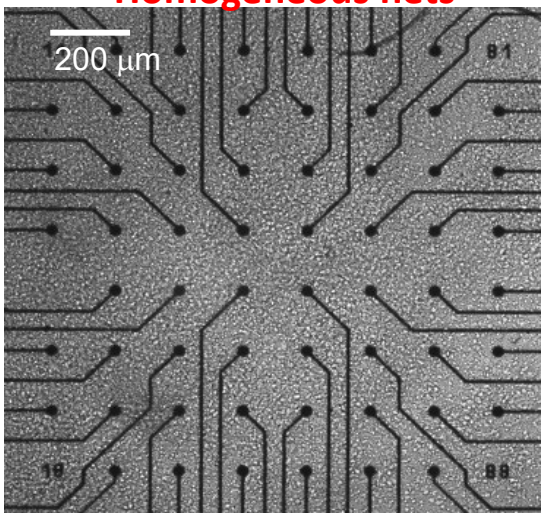


Scientific Question:

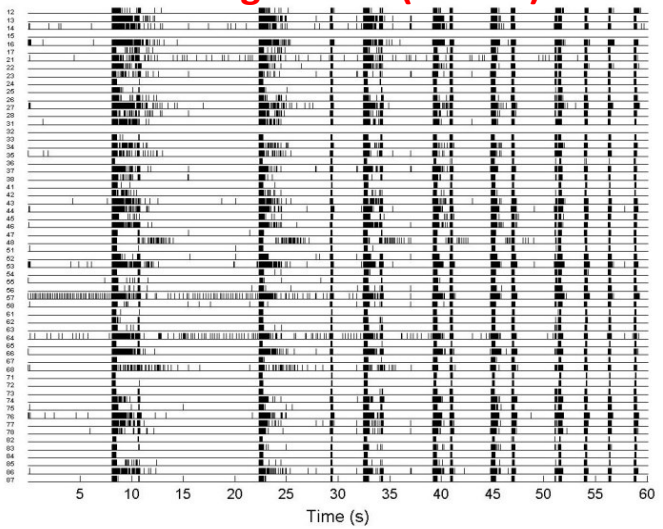
How neuronal connectivity shapes dynamics (and vice-versa) ?

Homogeneous vs. Interconnected networks

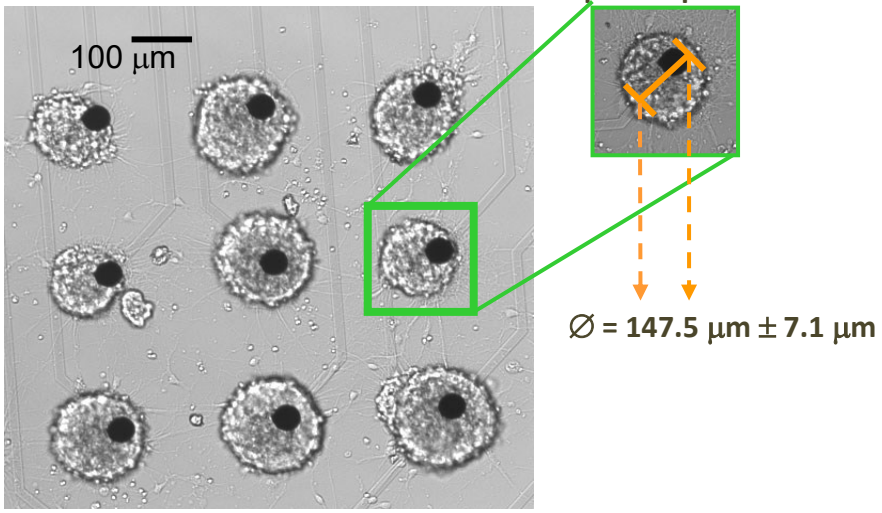
Homogeneous nets



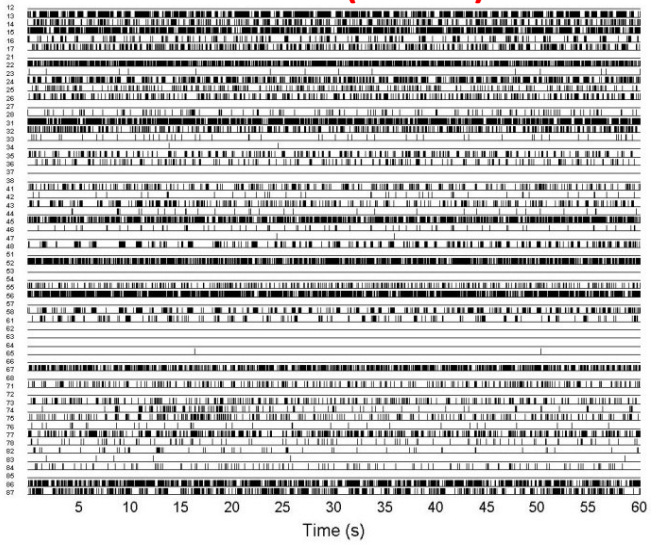
Homogeneous (DIV 21)



Interconnected nets

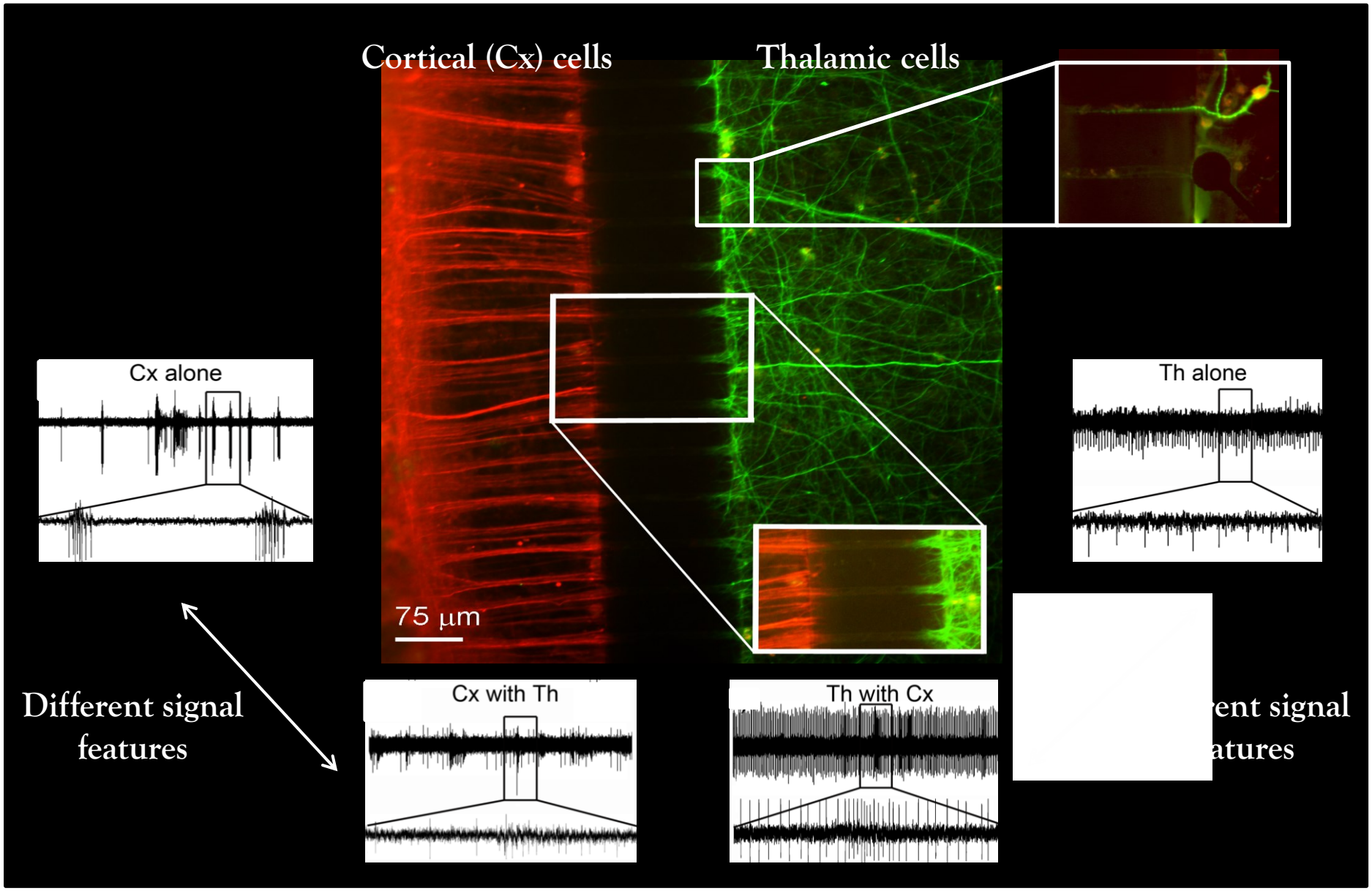


Patterned (DIV 21)



Macis E. et al., J. Neurosci. Meth., 2007
Massobrio & Martinoia, J. Neural Eng., 2008

Homogeneous vs. Heterogeneous networks



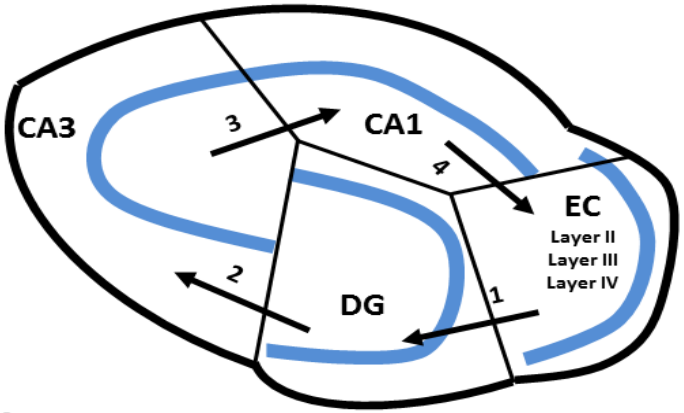
Kanagasabapathi T. et al., J. Neural Eng., 2012

The history behind the b-27 media system

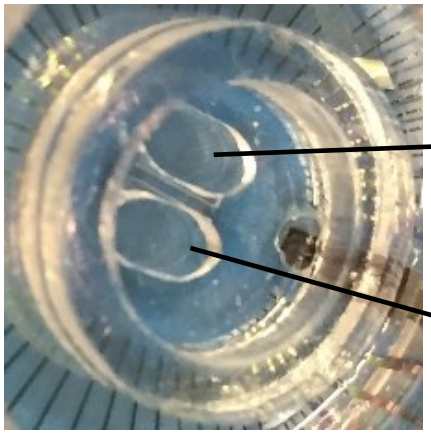
Video 3
https://www.youtube.com/watch?v=xQBkyo0yuzM

Coding of memory in engineered heterogeneous and interconnected neuronal networks reconstructed from hippocampus

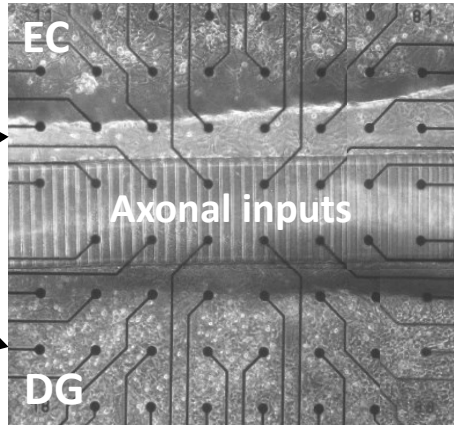
Hippocampal tri-synaptic loop



Two-chambers on MEA60

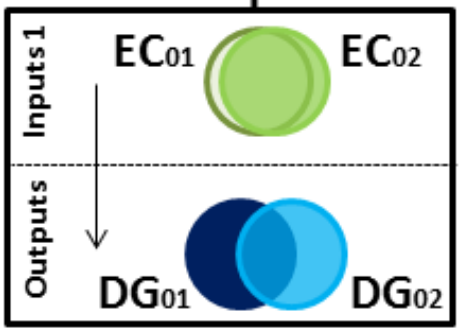


Co-cultured neurons

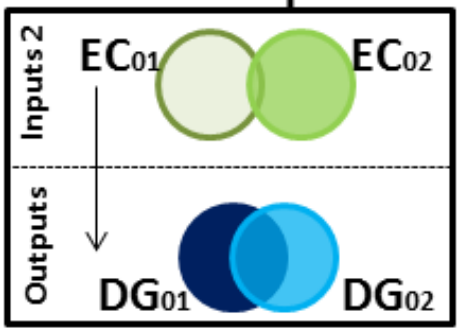


DG as a pattern separator

Pattern Separation

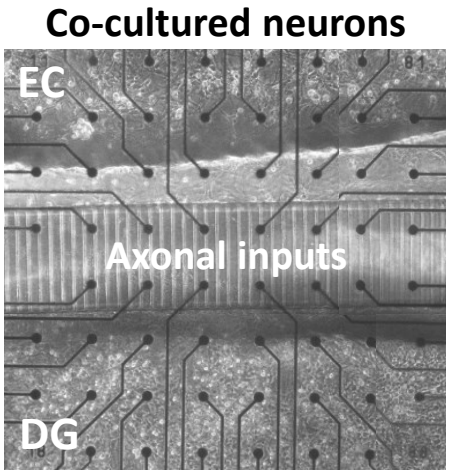


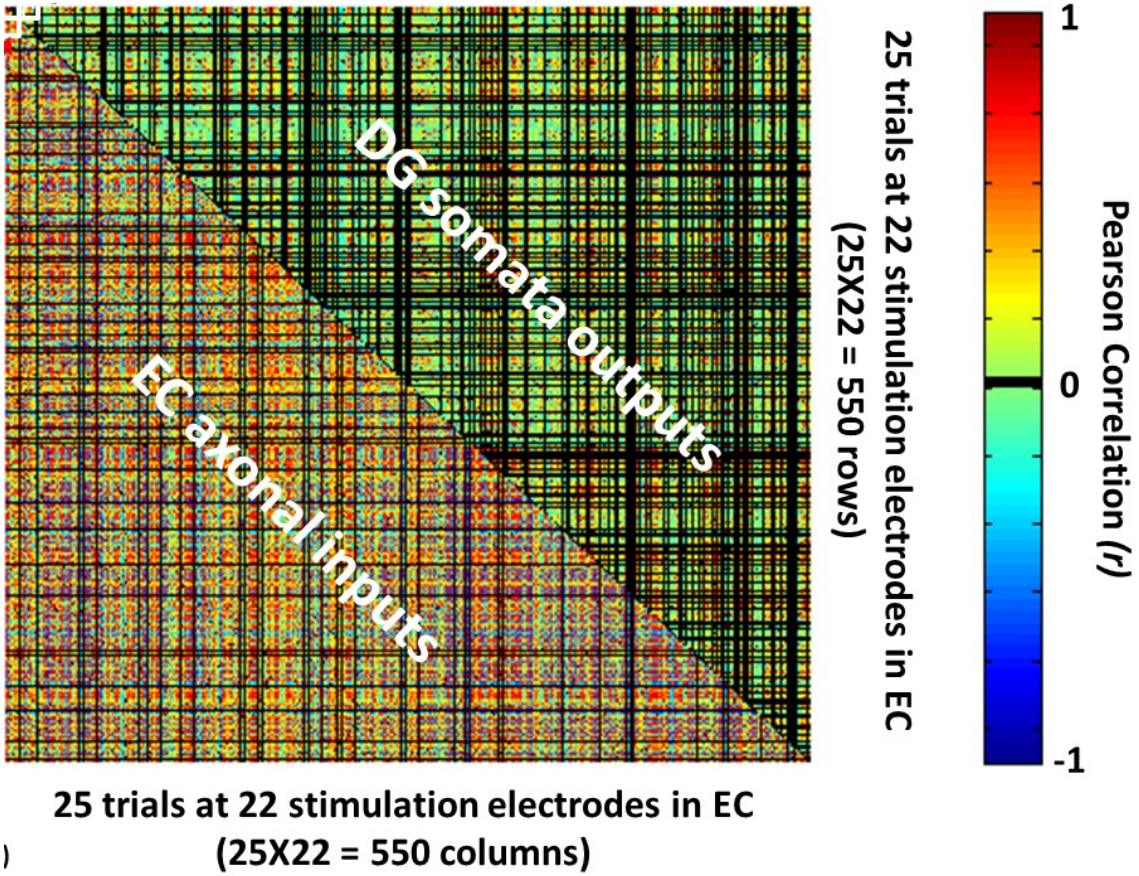
Pattern Completion



Poli D. et al., J. Neural Eng., 2018

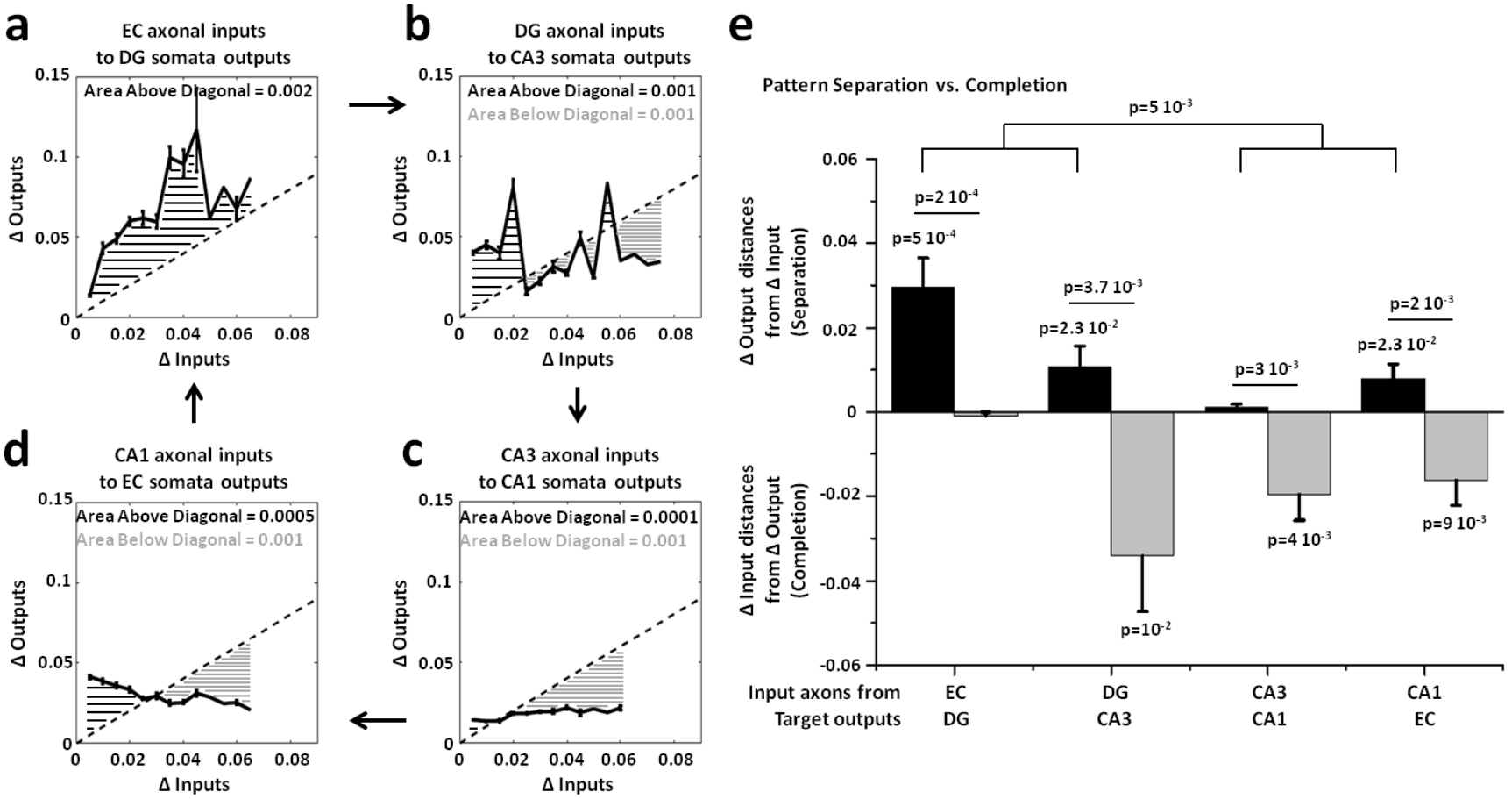
In vitro hippocampal networks ascribe functions for encoding episodic memories: Pattern Separation of EC axonal inputs transmitted via microtunnels into DG





Poli D. et al., J. Neural Eng., 2018

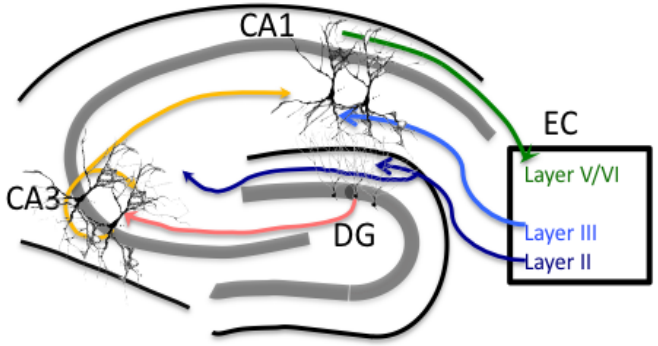
Pattern Separation of EC axonal inputs and Pattern Completion in CA3



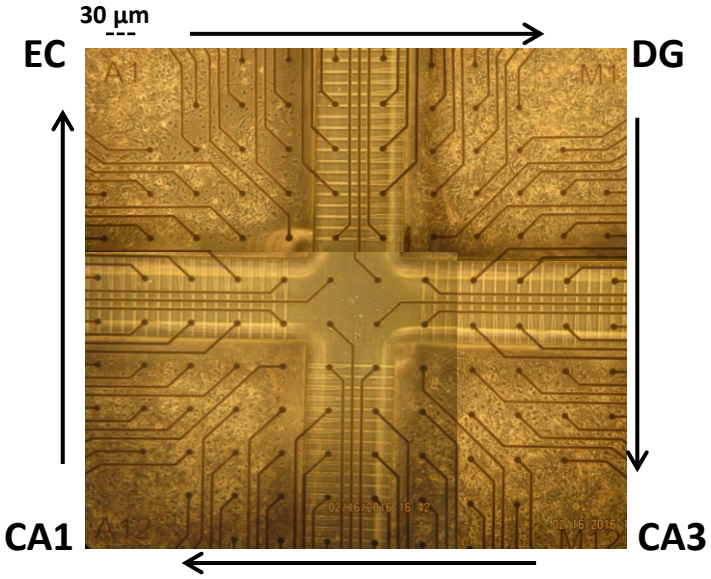
Poli D. et al., J. Neural Eng., 2018

Axonal transmission between each pair of four stages of the EC-DG-CA3-CA1 circuit

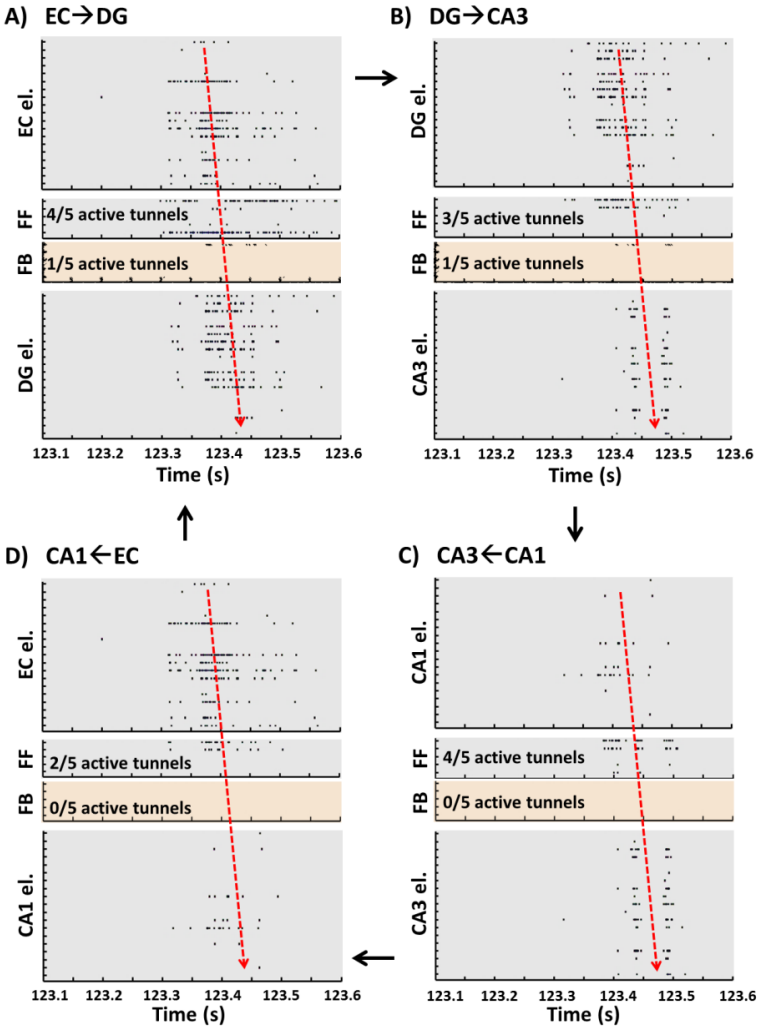
Hippocampal tri-synaptic loop



Four-chambers on MEA120

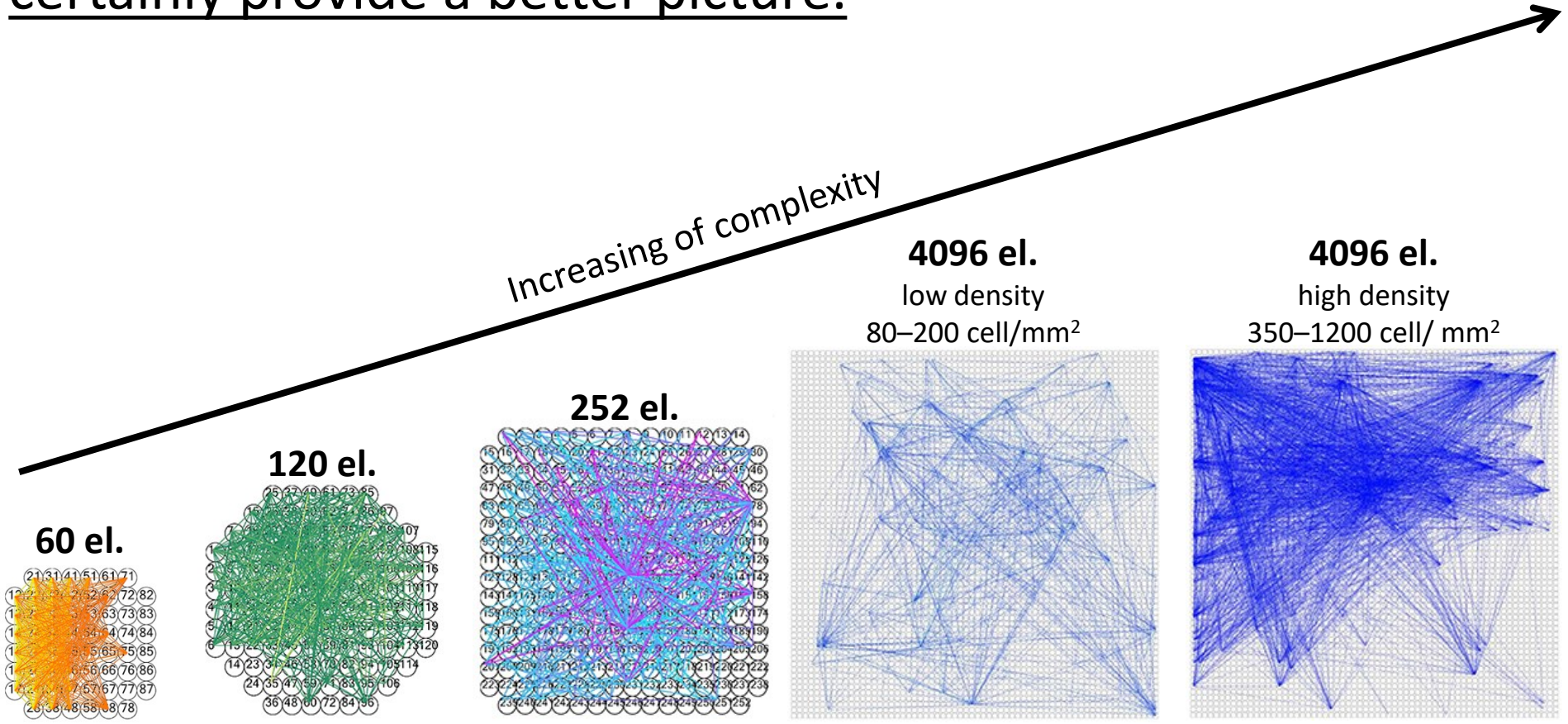


Spontaneous Activity (500 ms)



Poli D. et al., GNB 2018

High-density MEAs with large number of electrodes would certainly provide a better picture.



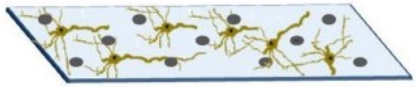
The high spatial resolution of high-density MEAs, would allow a more thorough investigation of the topological architectures of neuronal assemblies

1 mm

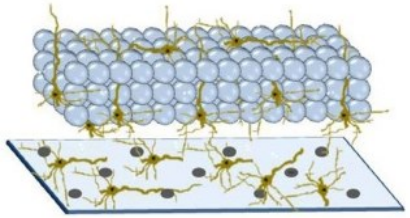
Pastore et al., Frontiers in Neuroinformatics, 2016

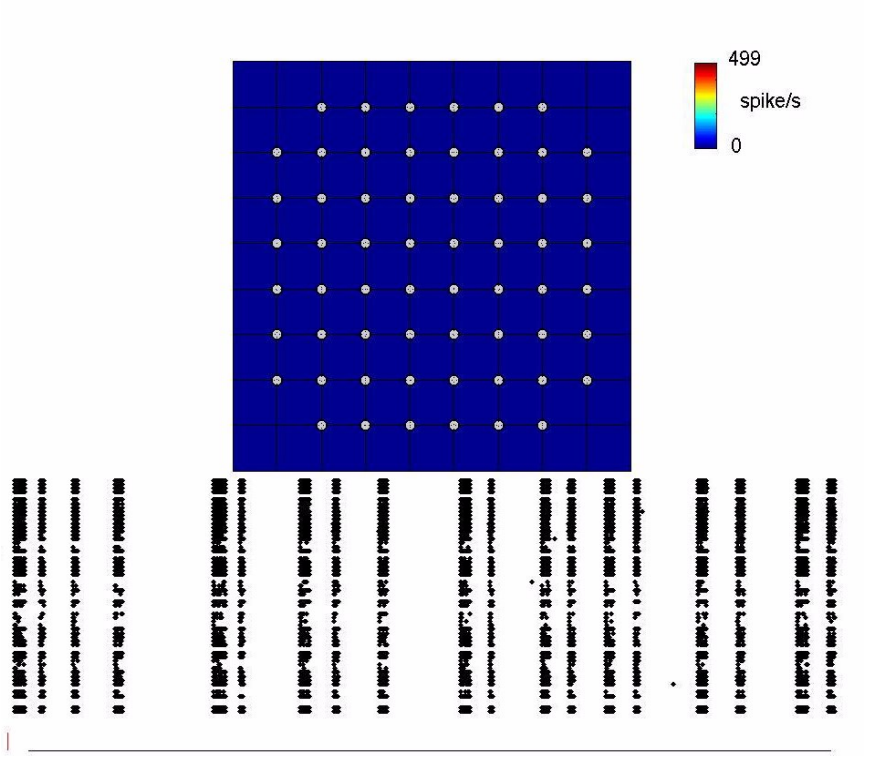
2D vs. 3D neuronal assemblies (1)

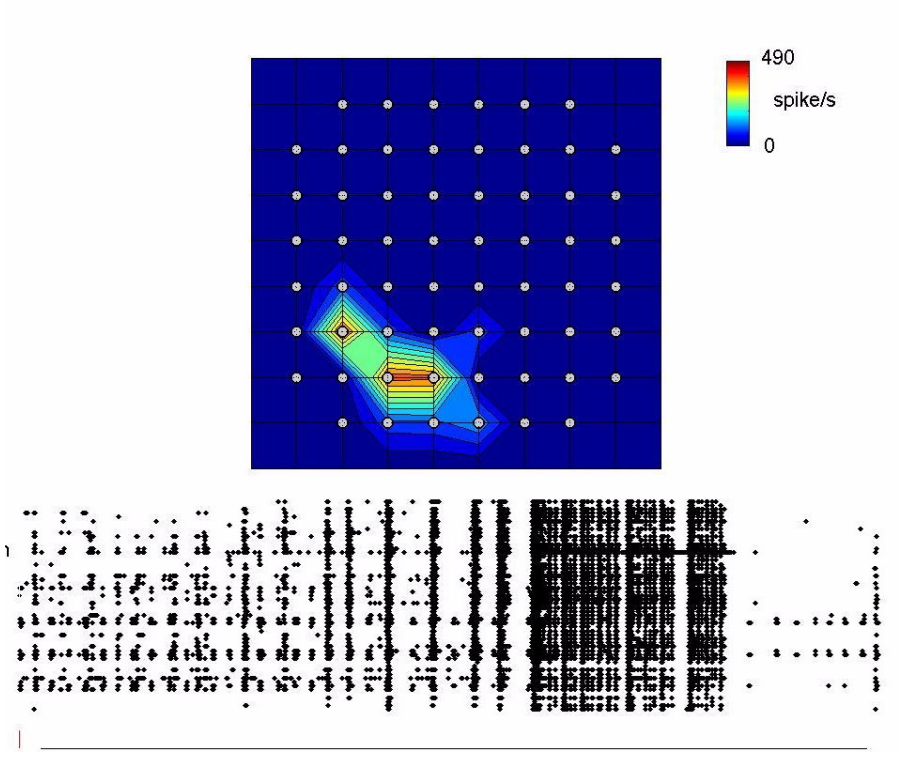
2D network on MEA



3D network on MEA

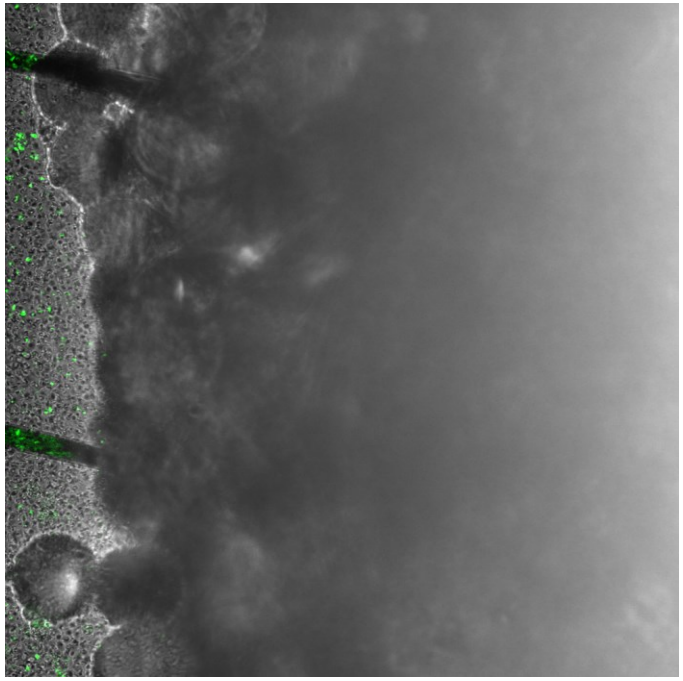


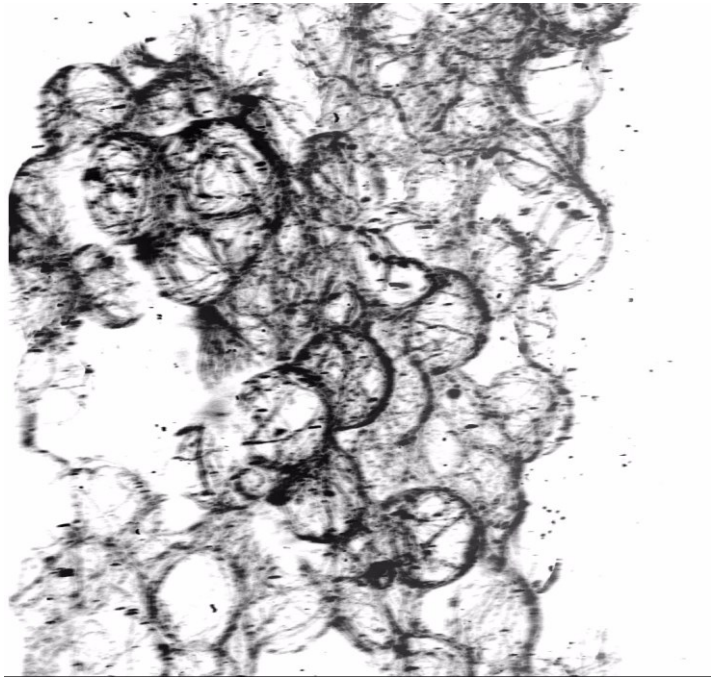




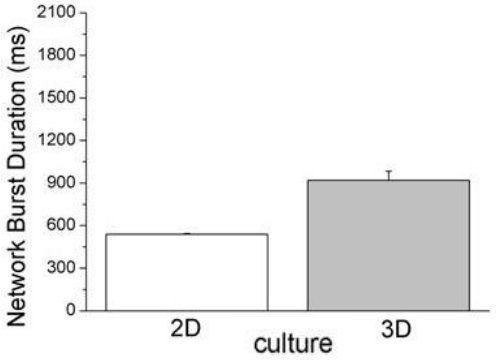
Frega M. et al., Sci. Rep. 2014

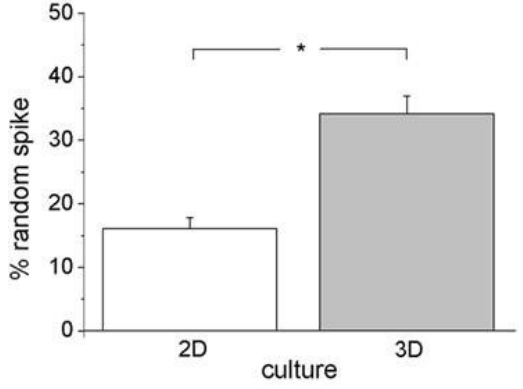
2D vs. 3D neuronal assemblies (2)





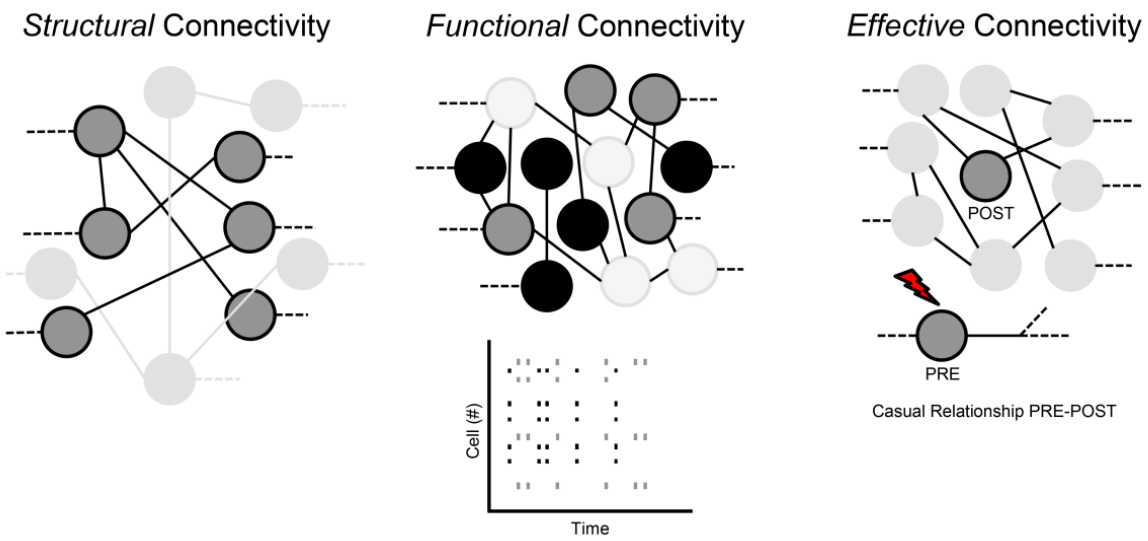
3D neuronal assemblies show network burst and random spikes: In vivo like!

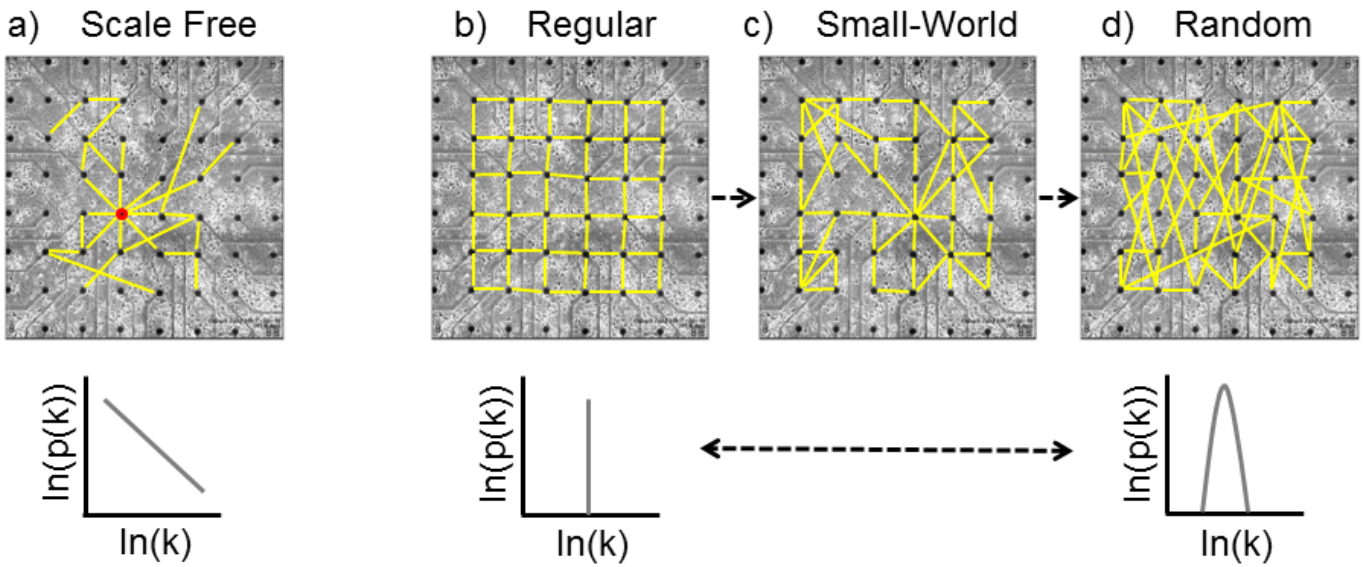




Frega M. et al., Sci. Rep. 2014

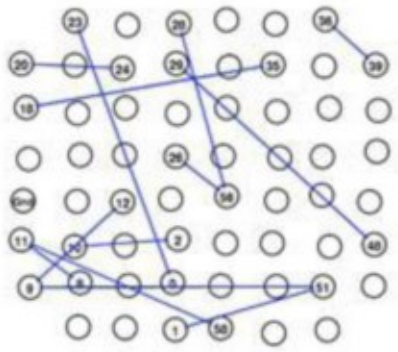
Interplay between connectivty and network dynamics



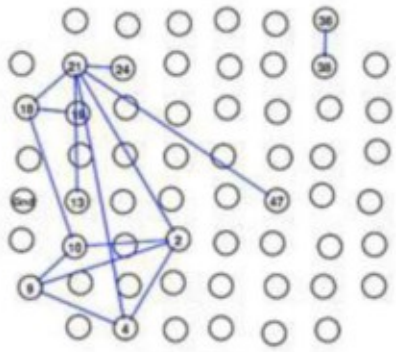


Poli et al., Frontiers in Neural Circuits, 2015

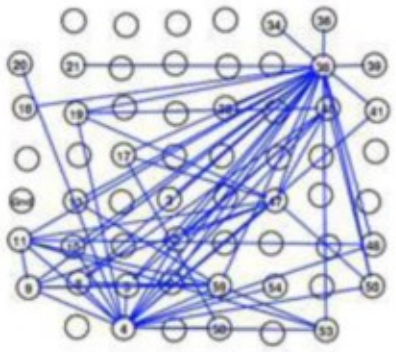
Topological network properties during development



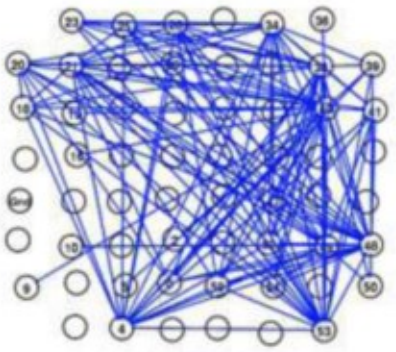
DIV 14



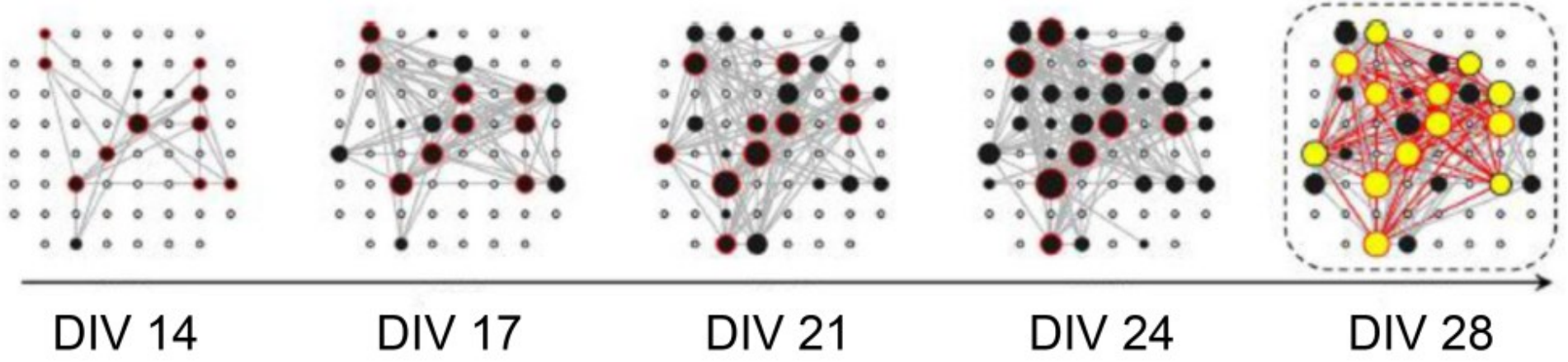
DIV 21



DIV 28



DIV 35



DIV 14 DIV 17 DIV 21 DIV 24 DIV 28

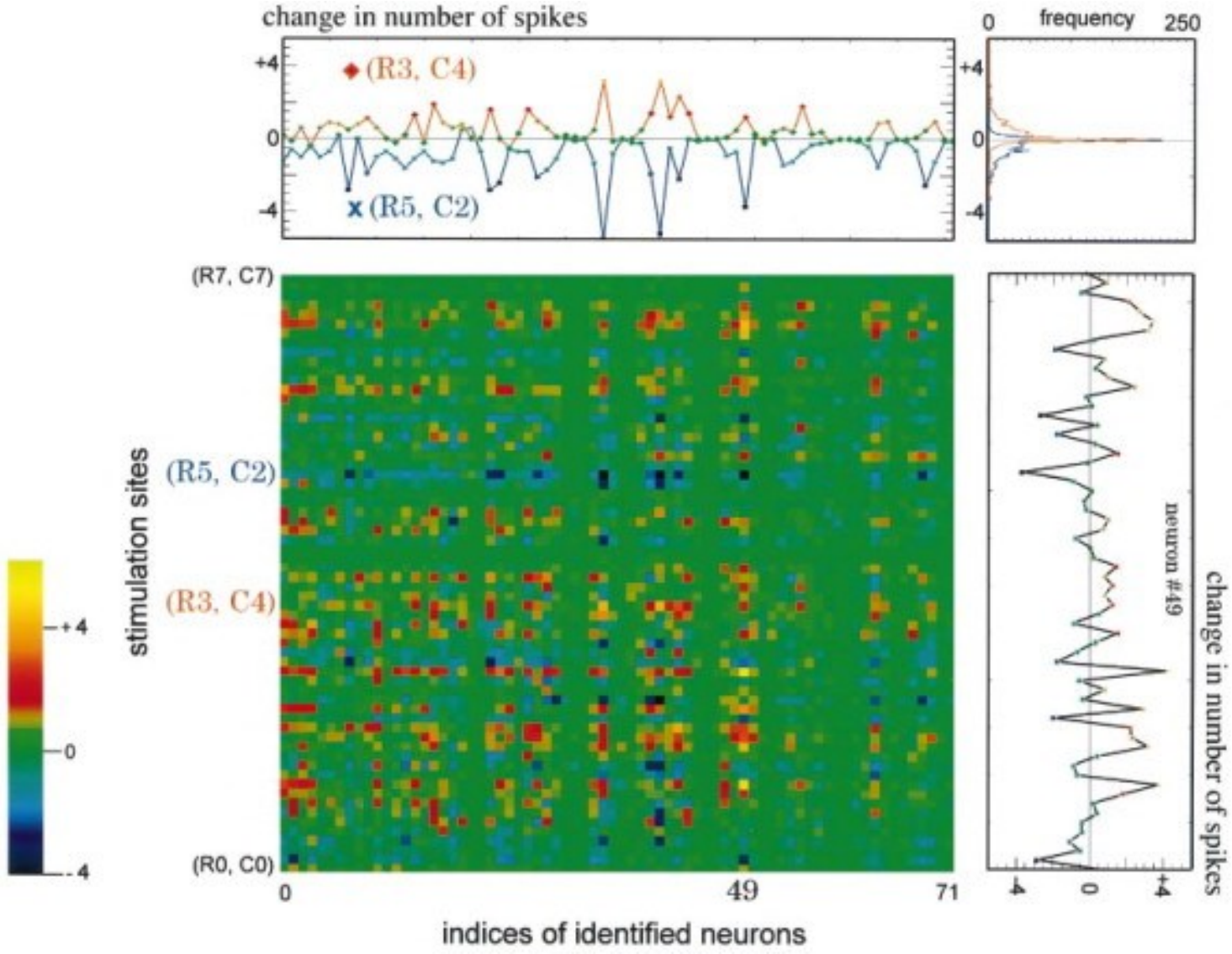
Poli et al., Frontiers in Neural Circuits, 2015

Neuronal dynamics evoked by electrical stimulation for studying signal processing and network plasticity

MEA technology can displays specific evoked network responses (#1)

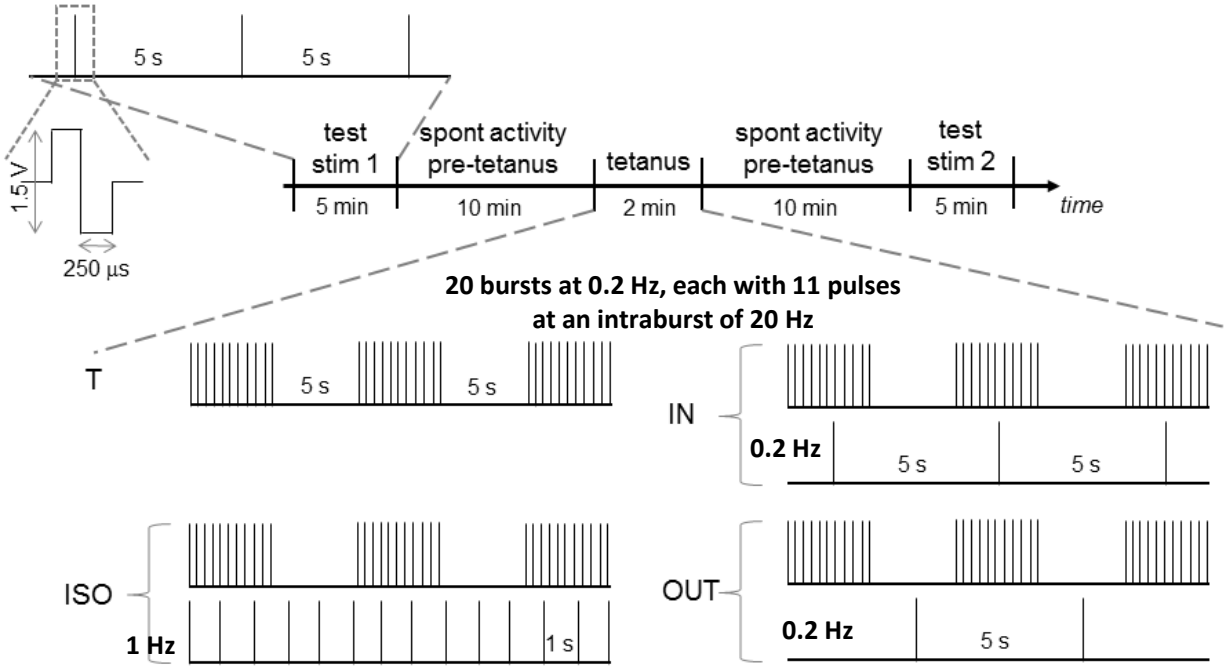
Video 4
https://www.youtube.com/watch?v=eyfN6TPlLts

Neuronal dynamics evoked by high-frequency stimulation (single tetanus) show a mixture of increased and descreased activity

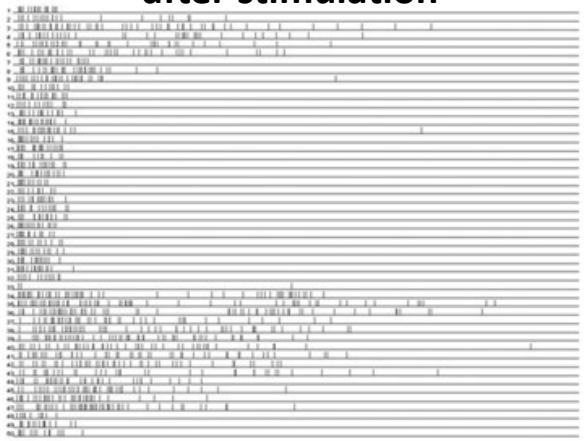


Jimbo et al., Biophysical Journal, 1999

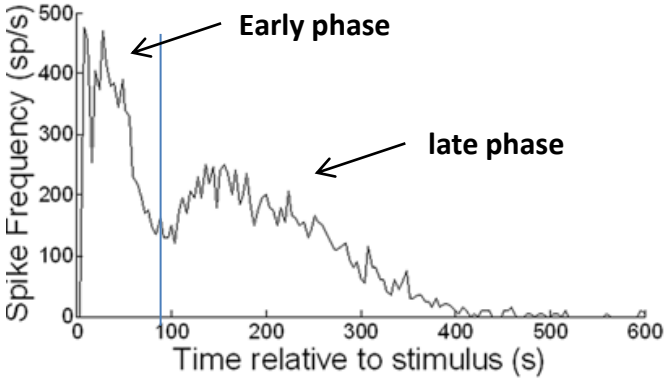
What about different protocols of tetanic stimulation?



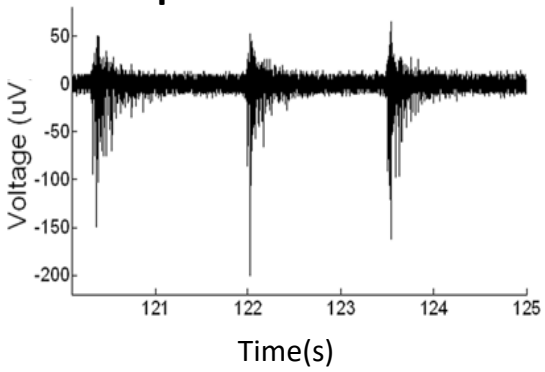
Activity evoked by 50 stimuli (test stim.1) at on electrode in 600 ms after stimulation



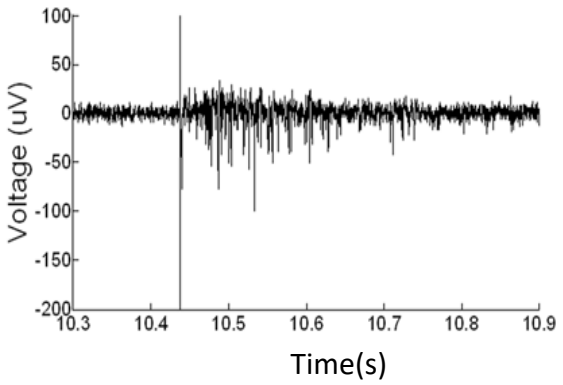
PSTH (600 ms after stimulation) for the same channel (top)



Spontaneous activity pre-test stim.1



Activity evoked by test stim.1



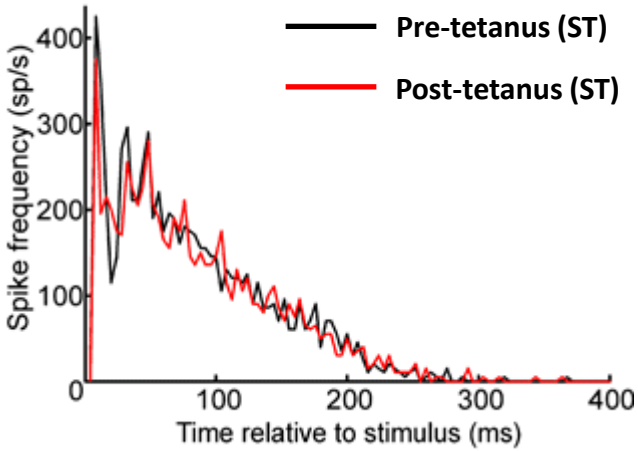
Poli and Massobrio, Physical Biology, 2018

Chiappalone et al., European_Journal_of_Neuroscience , 2008

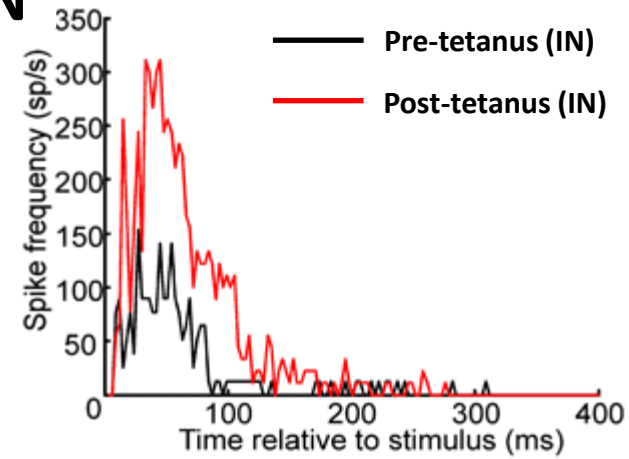
Different protocols of tetanic stimulation evoke network plasticity (depression or potentiation)

PSTHs from one channel example for each protocol

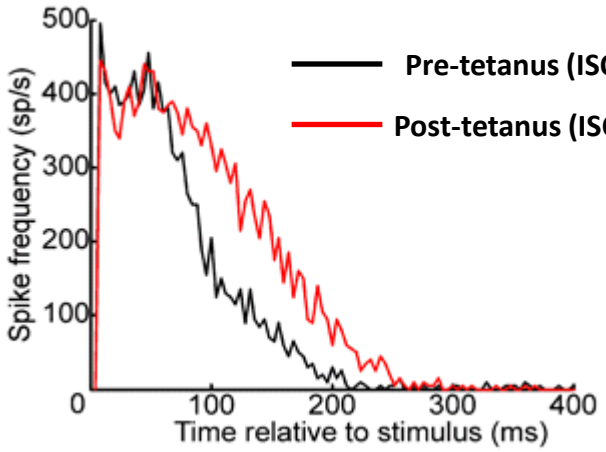
ST



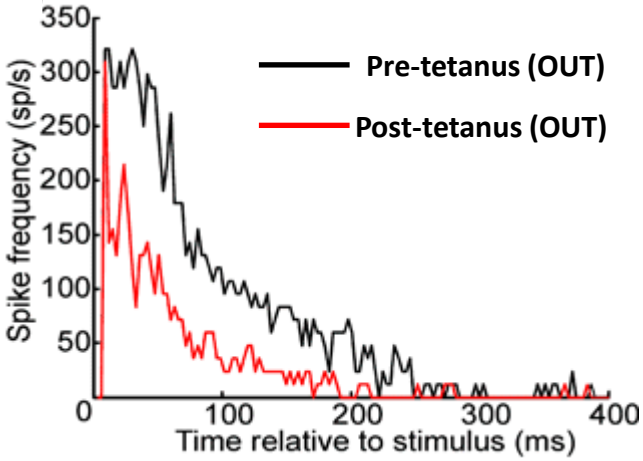
IN



ISO



OUT



Chiappalone et al., European_Journal_of_Neuroscience , 2008

GENERAL OBSERVATIONS:

Why is it important to study the stimulation effects on neuronal dynamics ?

What's its application in our life?

Video 5
https://www.youtube.com/watch?v=kWAVOhl9OFk

Video 6
https://www.youtube.com/watch?v=0F1Ey654LJk

Summary

1. Reverse engineering the brain.

2. Neuronal networks coupled to MEAs show great variability of activity patterns.

3. Engineering networks with different neuronal organization show complex and specific dynamics.

4. Strong interplay between connectivity and networks dynamics.

5. Strong interplay between functional and structural connectivity

6. High-frequency electrical stimulation evokes synaptic plasticity

7. Possible application: Deep Brain Stimulation (DBS)