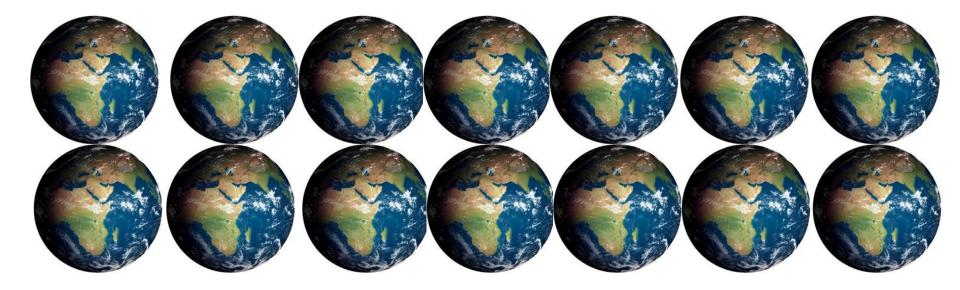
Spontaneous and evoked neuronal dynamics in cultured networks coupled to micro-electrode arrays

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Complexity of the brain

10¹¹ 100.000.000.000



Connections

10¹⁴ 100.000.000.000.000

(1000:10000 connections each cell)

Information flow



Reverse engineering the brain

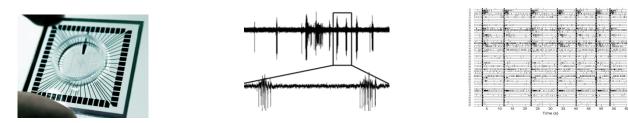
Why is it important to decode the neuronal information ?

Paralysed woman moves robot with her mind

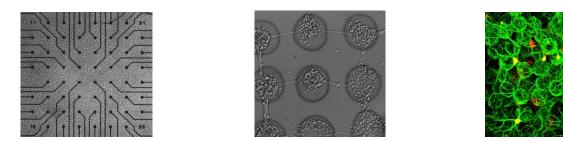
Video 1 https://www.youtube.com/watch?v=ogBX18maUiM

<u>Outline</u>

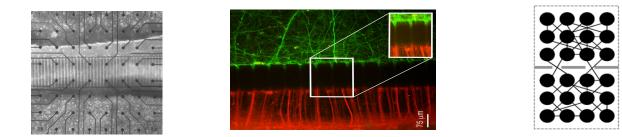
1. Neuronal networks coupled to Micro-electrode arrays (MEAs)



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

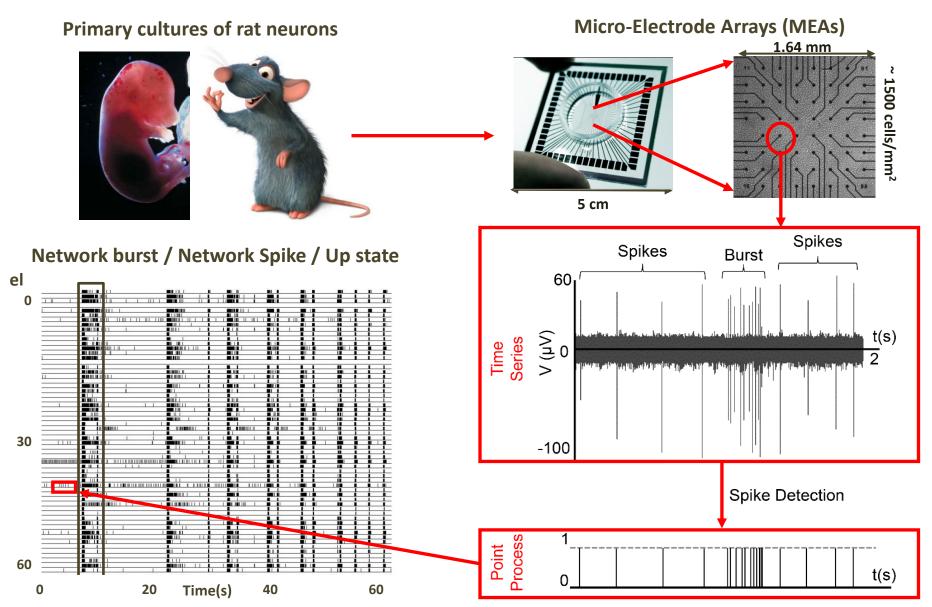


3. Interplay between connectivity and network dynamics



4. Electrical stimulation on MEA evokes network plasticity

Neuronal networks coupled to MEA



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

<u>Electrophysiological activity of neuronal networks coupled to</u> <u>micro-electrode array</u>

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Rat neurons grown on a computer chip

fly a simulated aircraft

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

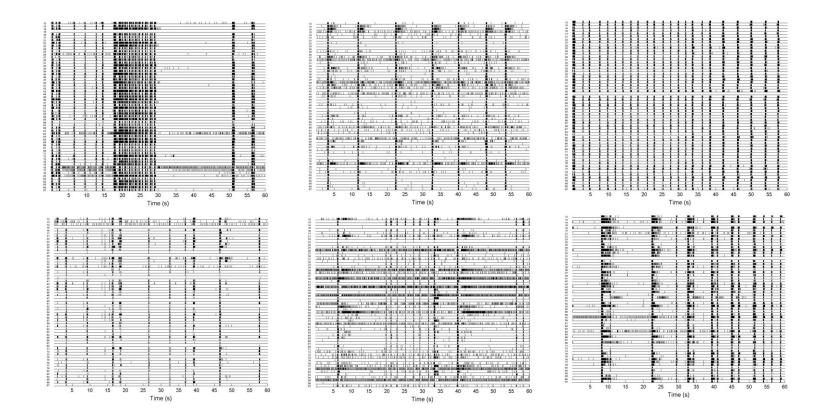
Robot controlled by neurons

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

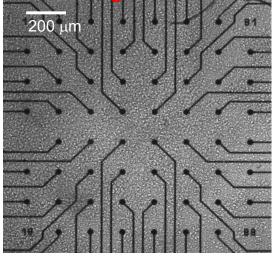


Scientific Question:

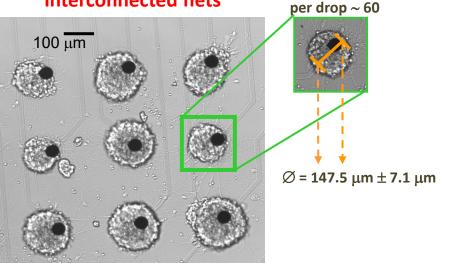
How neuronal connectivity shapes dynamics (and vice-versa)?

Homogeneous vs. Interconnected networks

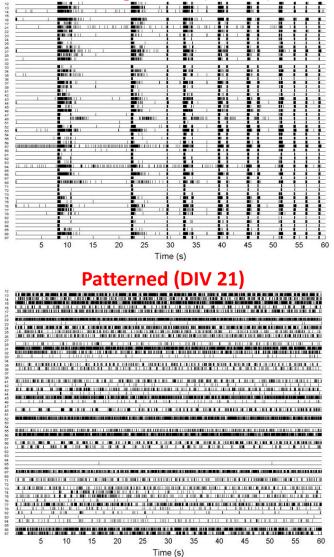




Interconnected nets



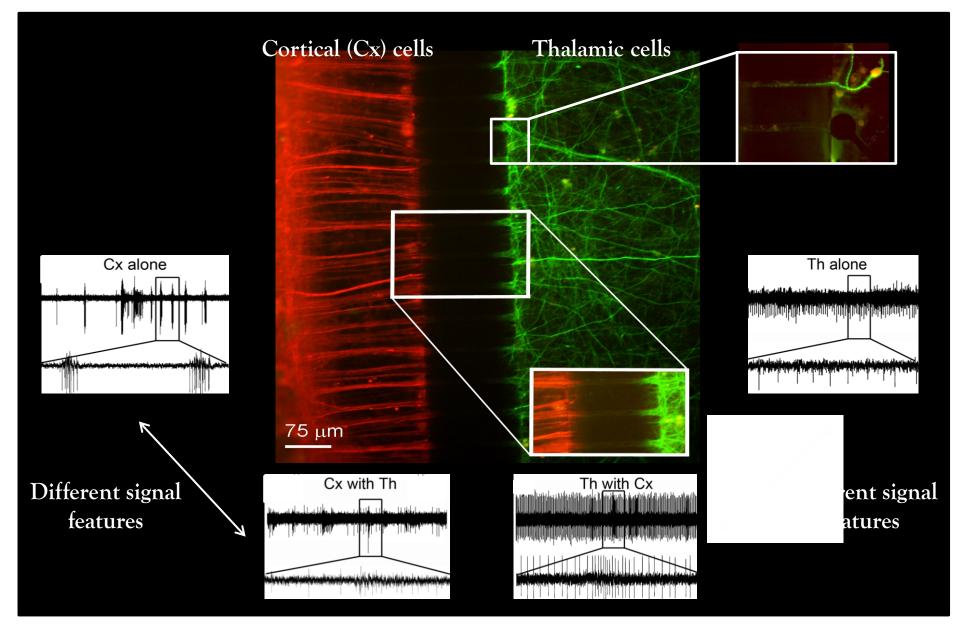




Macis E. et al., J. Neurosci. Meth., 2007 Massobrio & Martinoia, J. Neural Eng., 2008

Number of neurons

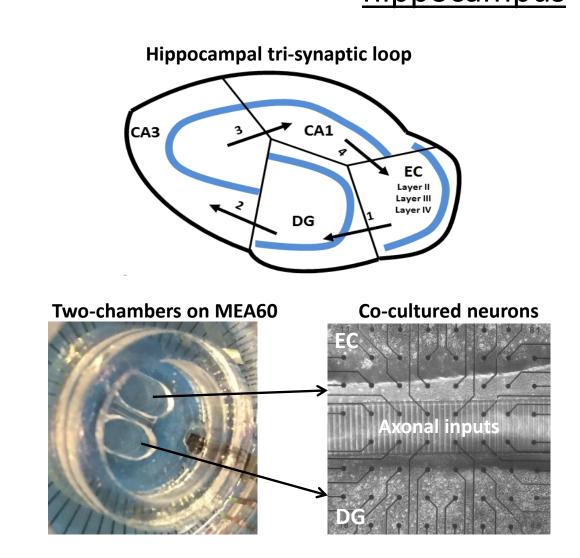
Homogeneous vs. Heterogeneous networks

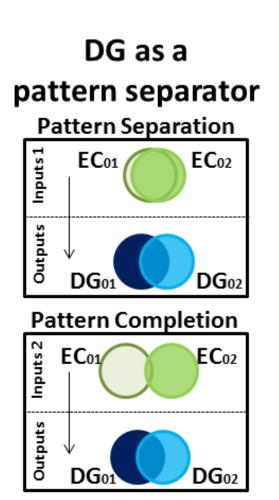


The history behind the b-27 media system

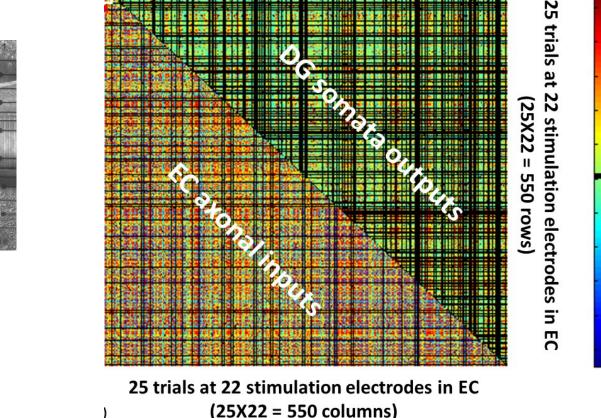
Video 3 <u>https://www.youtube.com/watch?v=xQBkyo0yuzM</u>

<u>Coding of memory in engineered heterogeneous and</u> <u>interconnected neuronal networks reconstructed from</u> hippocampus

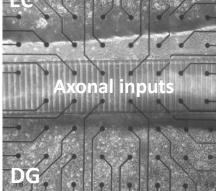




In vitro hippocampal networks ascribe functions for encoding episodic memories: Pattern Separation of EC axonal inputs transmitted via microtunnels into DG



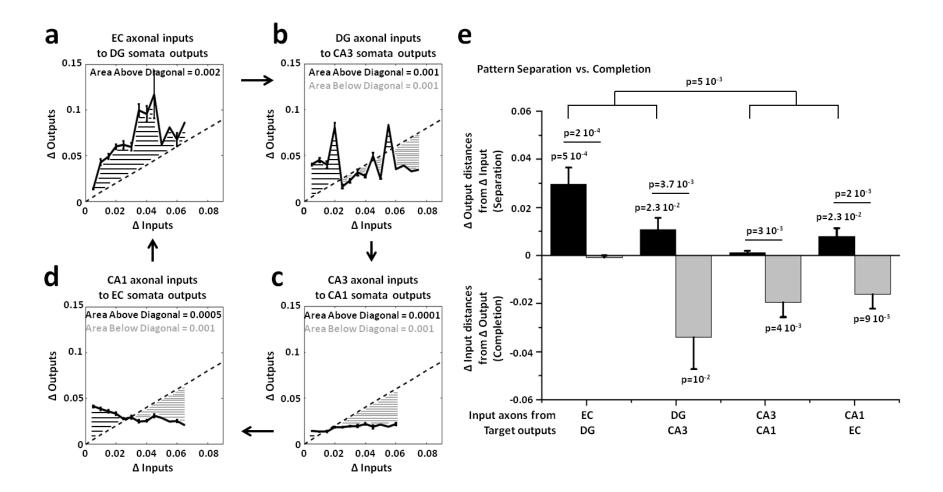
Co-cultured neurons



1

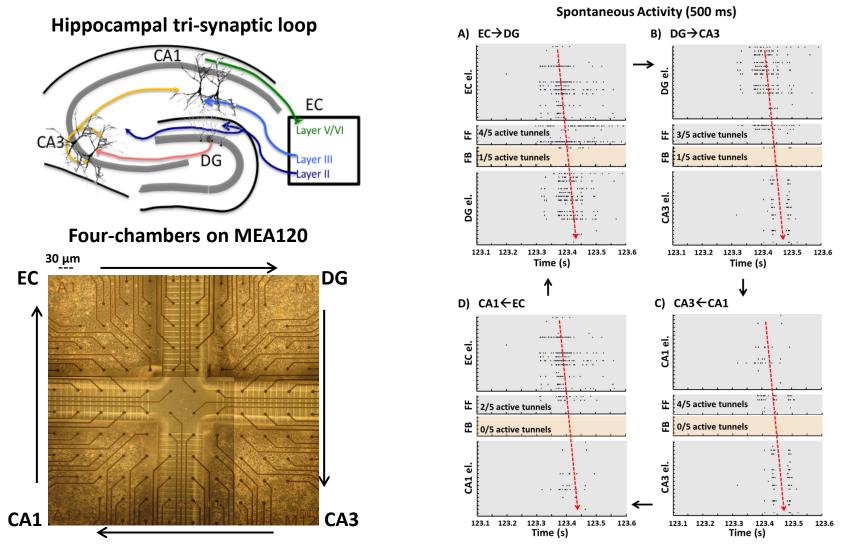
Pearson Correlation (r

Pattern Separation of EC axonal inputs and Pattern Completion in CA3

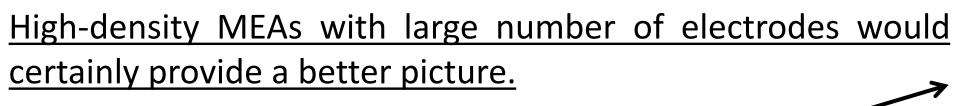


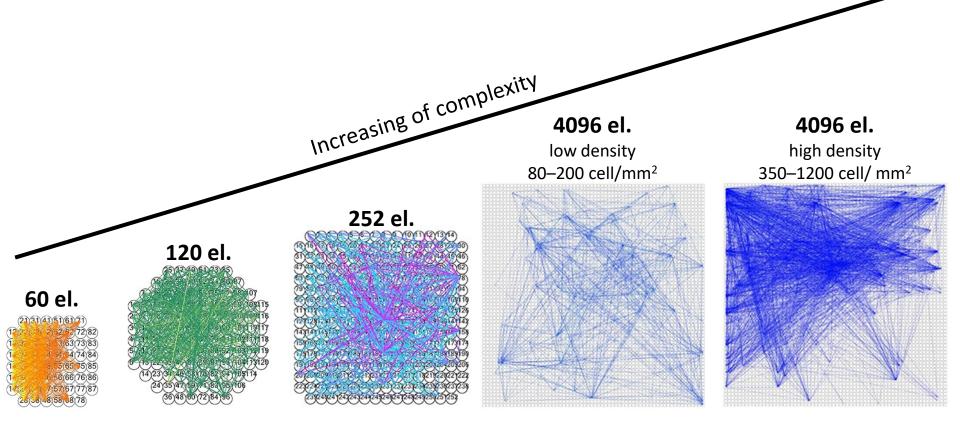
Axonal transmission between each pair of four stages

of the EC-DG-CA3-CA1 circuit



Poli D. et al., GNB 2018

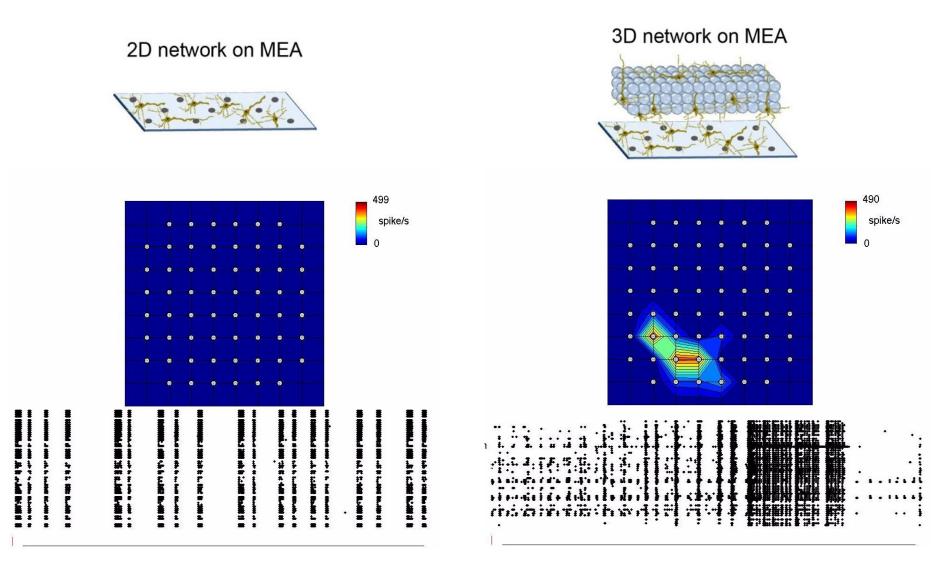




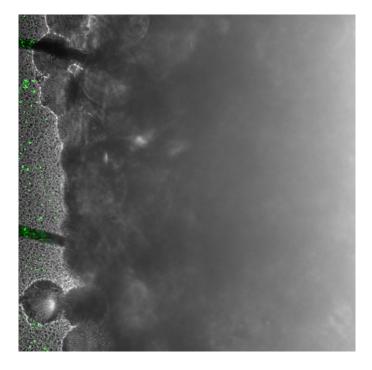
The high spatial resolution of high-density MEAs, would allow a more thorough investigation of the topological architectures of neuronal assemblies

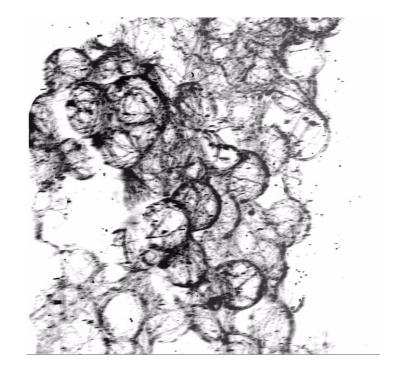
1 mm

2D vs. 3D neuronal assemblies (1)

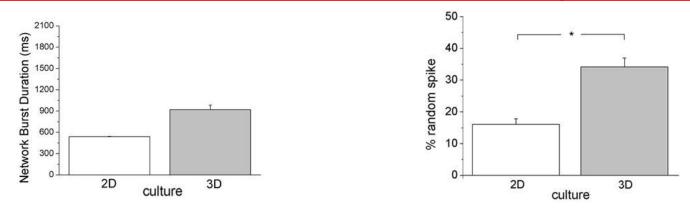


2D vs. 3D neuronal assemblies (2)



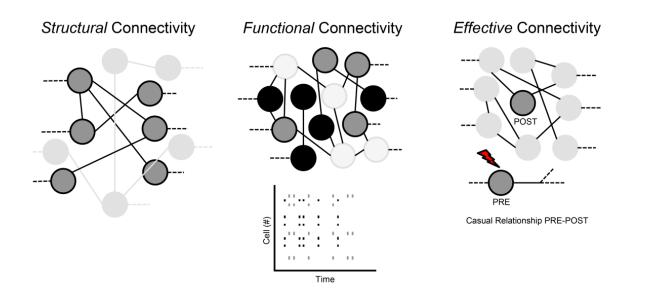


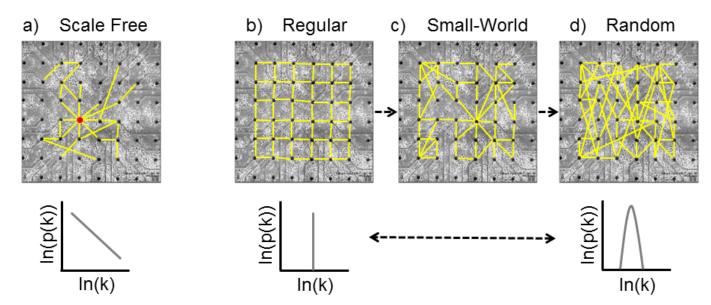
3D neuronal assemblies show network burst and random spikes: In vivo like!



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

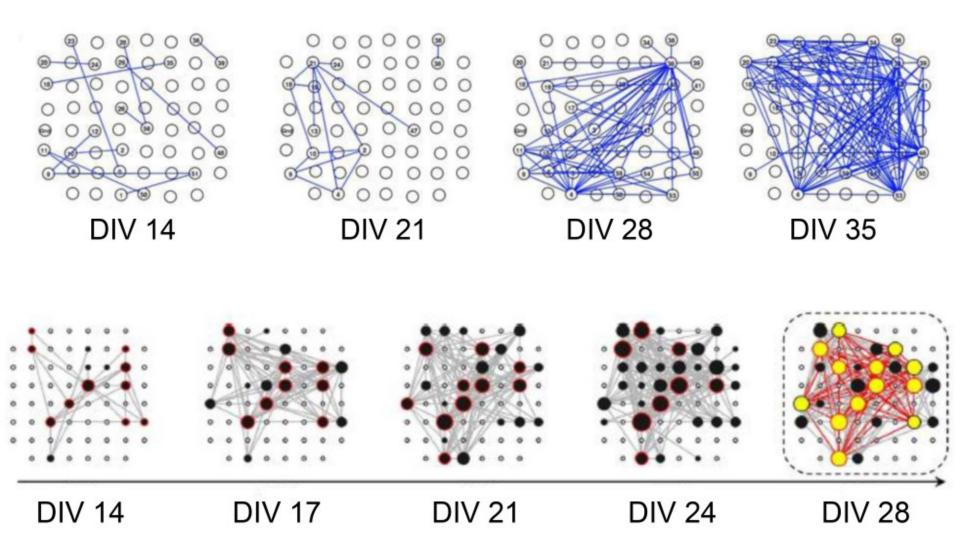
Interplay between connectivty and network dynamics





Poli et al., Frontiers in Neural Circuits, 2015

Topological network properties during development

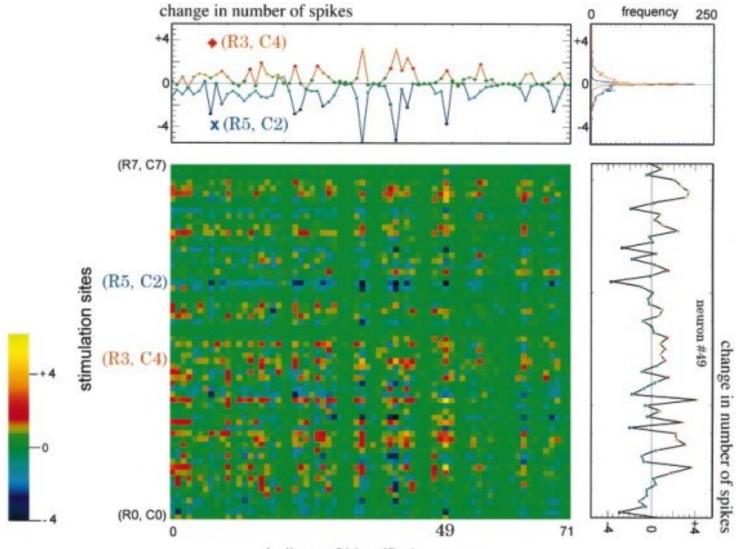


<u>Neuronal dynamics evoked by electrical stimulation for</u> <u>studying signal processing and network plasticity</u>

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

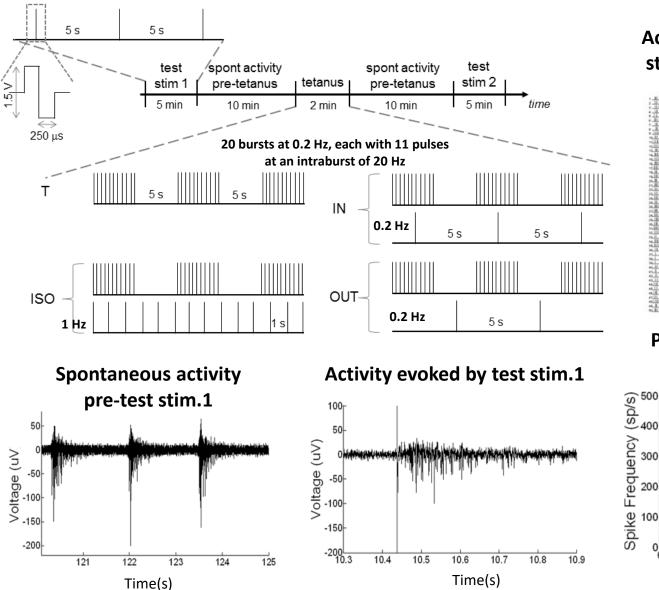
Video 4 <u>https://www.youtube.com/watch?v=eyfN6TPILts</u>

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



indices of identified neurons

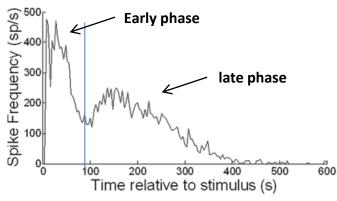
What about different protocols of tetanic stimulation?



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

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

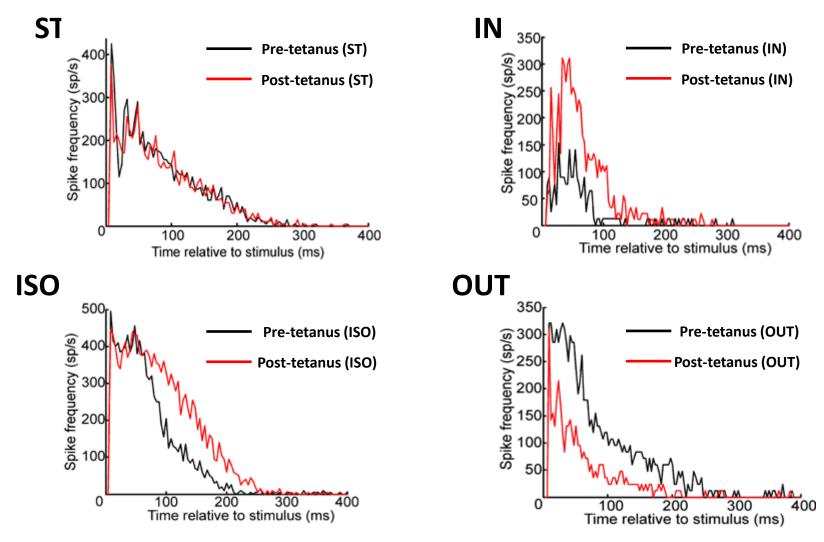


Poli and Massobrio, Physical Biology, 2018 Chiappalone et al., European_Journal_of_Neuroscience, 2008

Different protocols of tetanic stimulation evoke network plasticity

(depression or potentiation)

PSTHs from one channel example for each protocol



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

<u>Summary</u>

- 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)