Large-scale, high-resolution electrophysiological imaging with microelectronic multielectrode arrays

the BioCAM

Journal Club

Marie-Angela Wulf

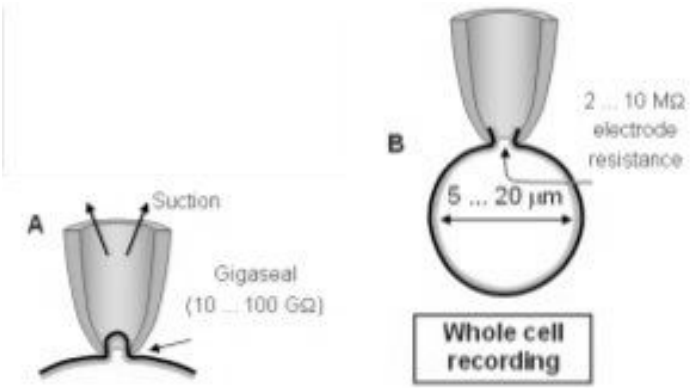
21.1.2014

Overview

electrophysiological recording techniques

intracellular

- Sharp electrodes
- Patch clamp
  - Cell attached
  - Whole cell
  - Inside-out
  - Outside-out



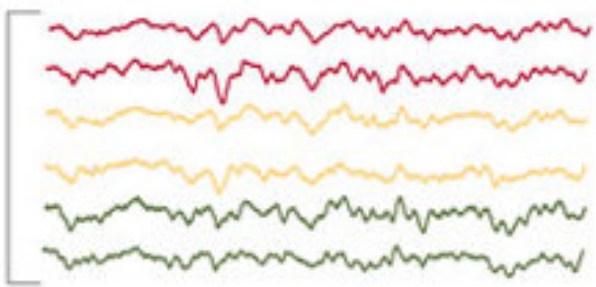
extracellular

- Single electrodes
- Multiple electrodes
  - Tetrodes
  - *Multi-electrode arrays (MEA)*
  - (EEG)

what do we measure extracellularly

- Voltage changes at electrode site
- Both: Local field potential and Spikes
- Spikes: fast frequency component. Reflects the AP of one or more neurons

- LFP: slow frequency component. Reflects simultaneous activity of dendrites of similar orientation and geometry



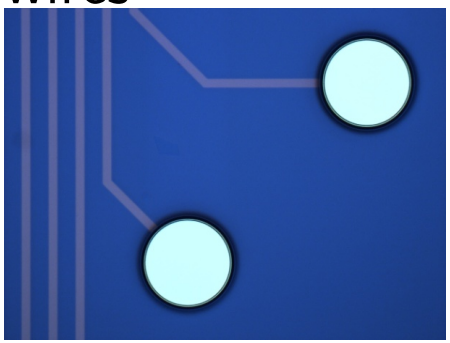
Things to consider for MEAs

- Passive vs. active electrodes
- Number, density and geometric arrangement of electrodes (spatial resolution)
- Sampling Rate (temporal resolution)
- Noise level (typical amplitude spikes: 100uV, LFP: up to mV)
- Power Consumption (Heating!)

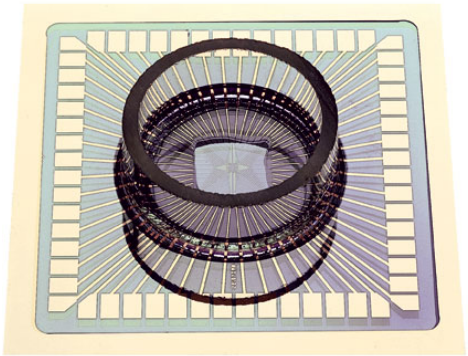
passive vs. active MEAs

conventional, passive MEA

each electrode individually wired: number of electrode = number of wires



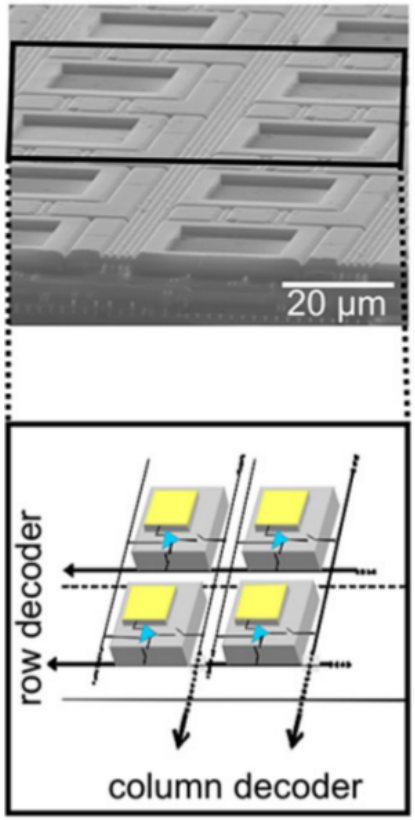
Examples



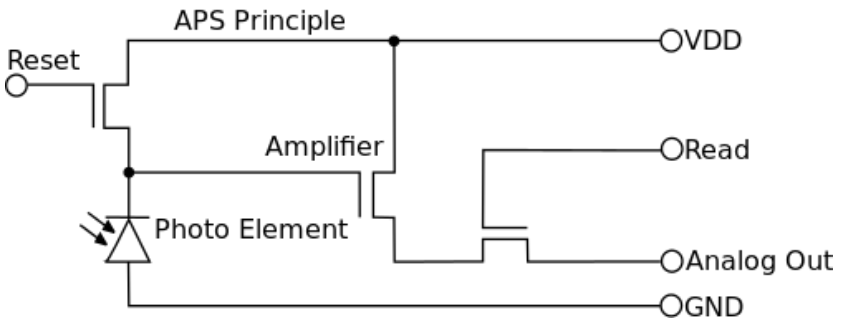
Multichannel-Systems

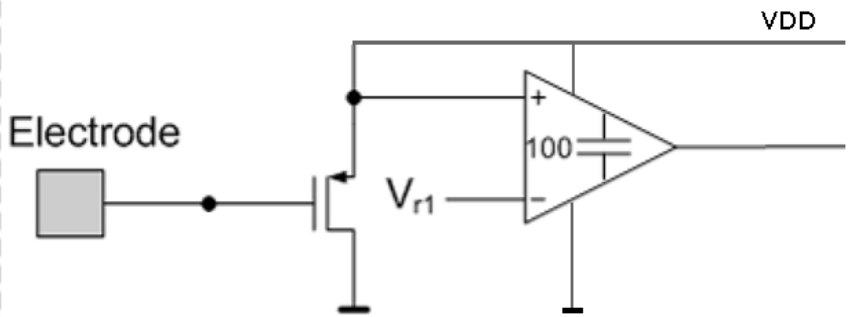
active MEA

amplifier under each electrode
multiplexing: 4096 electrodes on 16 output lines



the Active-Pixel-Sensor (APS)





Concept

represent the electrophysiological data as a time sequence of images
=> Spatial resolution ↑

Combine with high-speed camera technology
=> temporal resolution ↑

3 Articles

- Large-Scale, High-Resolution Data Acquisition System for Extracellular Recording of Electrophysiological Activity

  Kilian Imfeld*, *Member, IEEE*, Simon Neukom, Alessandro Maccione, Yannick Bornat, Sergio Martinoia, Pierre-André Farine, *Member, IEEE*, Milena Koudelka-Hep, and Luca Berdondini

  2008

- **Active pixel sensor array for high spatio-temporal resolution electrophysiological recordings from single cell to large scale neuronal networks†**

  Luca Berdondini,[*a] Kilian Imfeld,[b] Alessandro Maccione,[a] Mariateresa Tedesco,[c] Simon Neukom,[d] Milena Koudelka-Hep[b] and Sergio Martinoia[ac]

  2009

- frontiers in NEURAL CIRCUITS

  METHODS ARTICLE
  published: 14 November 2012
  doi: 10.3389/fncir.2012.00080

  Large-scale, high-resolution electrophysiological imaging of field potentials in brain slices with microelectronic multielectrode arrays

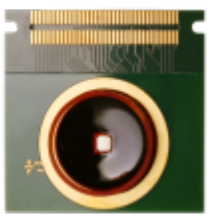
  *E. Ferrea[1], A. Maccione[1], L. Medrihan[1], T. Nieus[1], D. Ghezzi[1], P. Baldelli[1,2], F. Benfenati[1,2] and L. Berdondini[1]**

  [1] *Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Genoa, Italy*
  [2] *Department of Experimental Medicine, Università di Genova, Genoa, Italy*

  2012

the APS-MEA

- Active-pixel sensor multielectrode array (APS-MEA)
- 4096 electrodes simultanously
- 2.6x2.6mm^2 active area
- 567 pixels/mm^2
- Sampling rate: 7.8-125kHz (zoom)
- 21x21μm electrode size & 21μm inter-electrode distance



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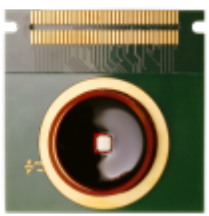

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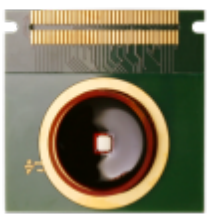

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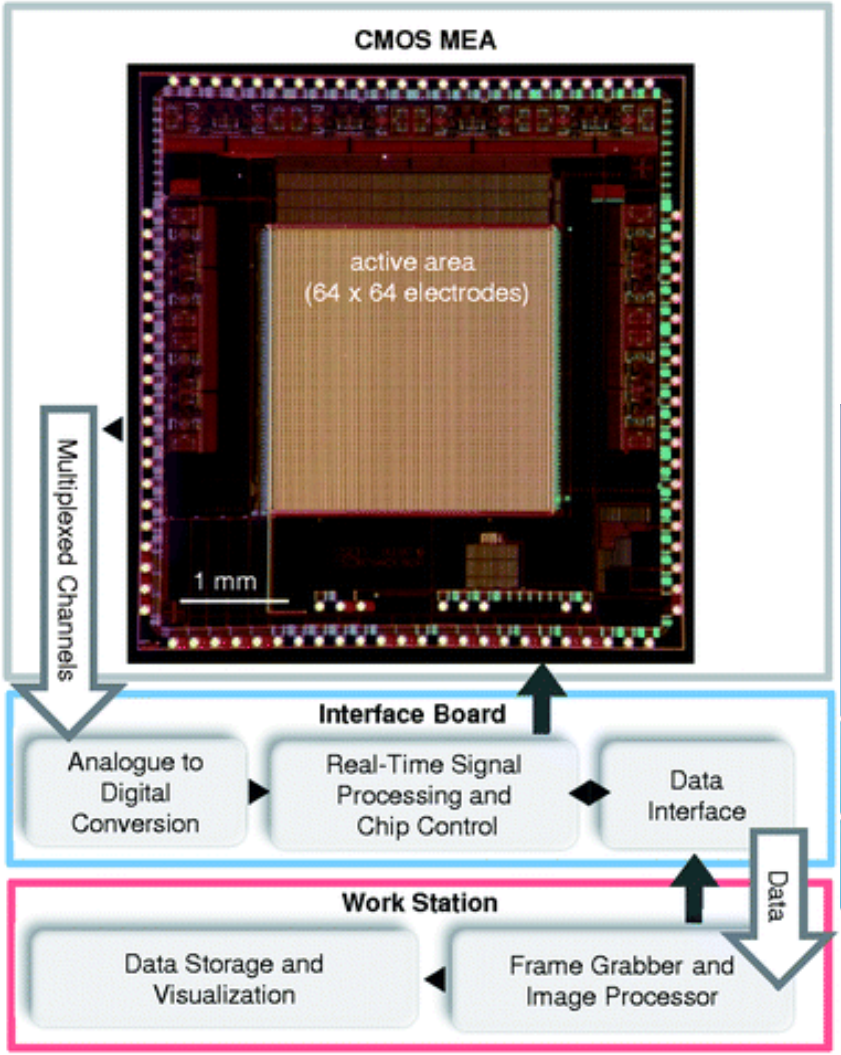
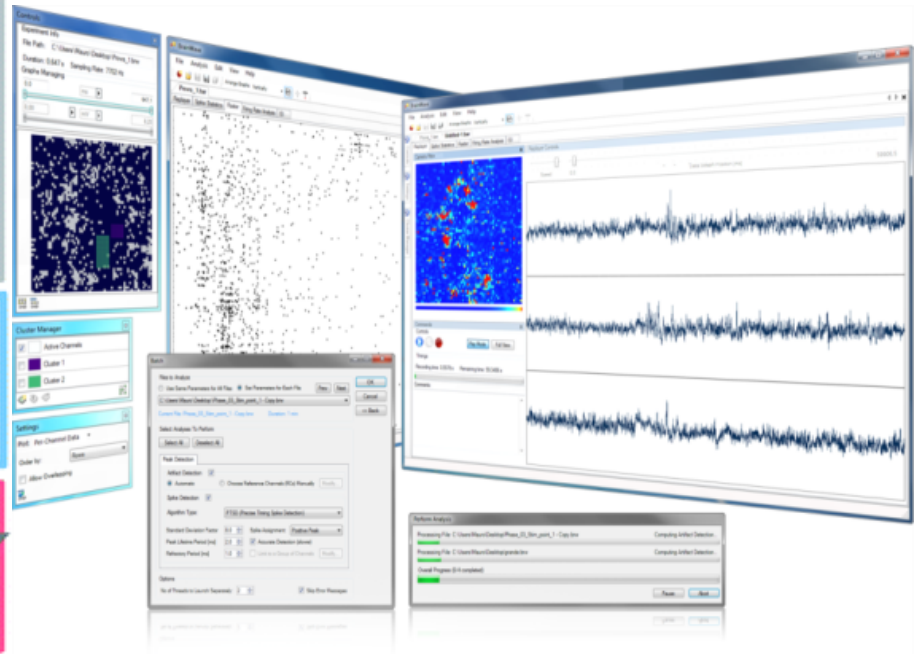

CMOS MEA
active area
(64 x 64 electrodes)
1 mm
Multiplexed Channels
Interface Board
Analogue to Digital Conversion
Real-Time Signal Processing and Chip Control
Data Interface
Work Station
Data Storage and Visualization
Frame Grabber and Image Processor
Data



Validation in hippocampal cell culture

Active pixel sensor array for high spatio-temporal resolution electrophysiological recordings from single cell to large scale neuronal networks†

Luca Berdondini,[*a] Kilian Imfeld,[b] Alessandro Maccione,[a] Mariateresa Tedesco,[c] Simon Neukom,[d] Milena Koudelka-Hep[b] and Sergio Martinoia[ac]

Lab on a Chip

Miniaturisation for chemistry, physics, biology, & bioengineering

www.rsc.org/loc

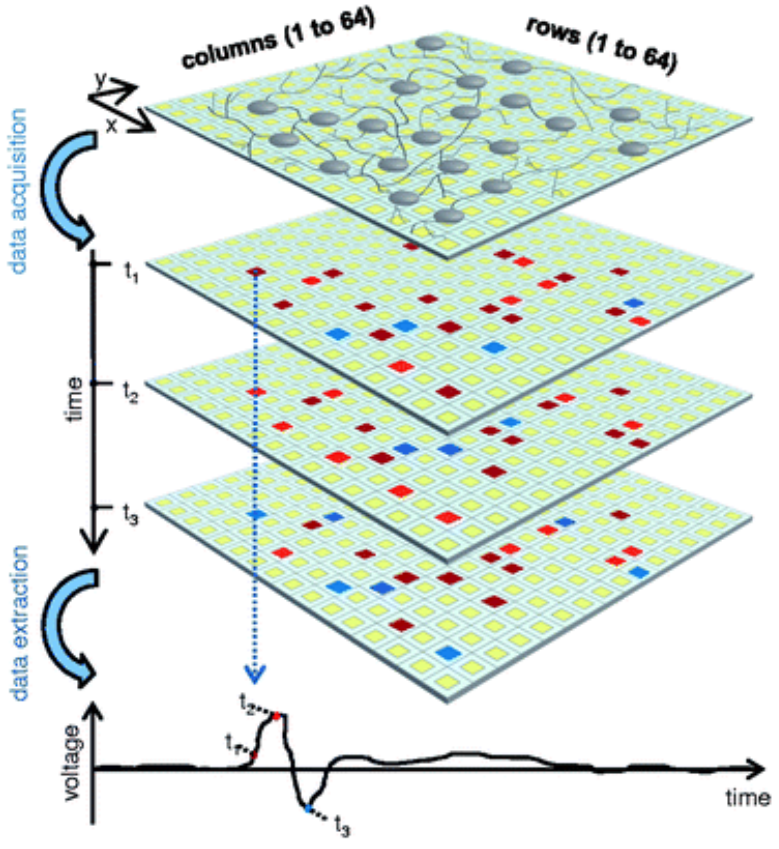
Volume 9 | Number 18 | 21 September 2009 | Pages 2613–2744

methods

recordings

- Dissociated hippocampal cell cultures grown on the Chip
- rat E18
- 150-1500cells/mm^2
- Recordings of spontanous activity from 2nd week
- 7.8kHz
- 2-10min

data processing

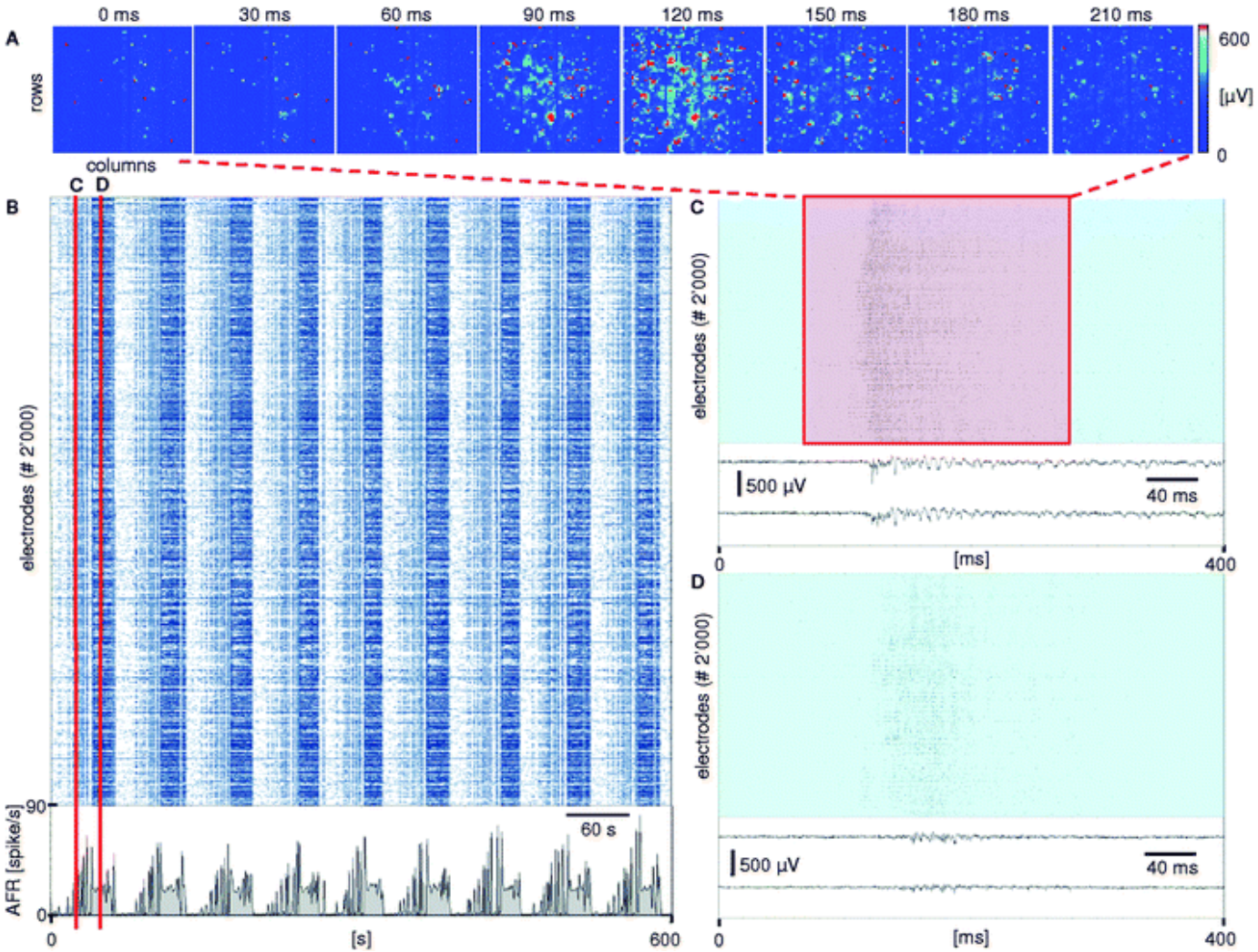


- spike and burst detection algorithm

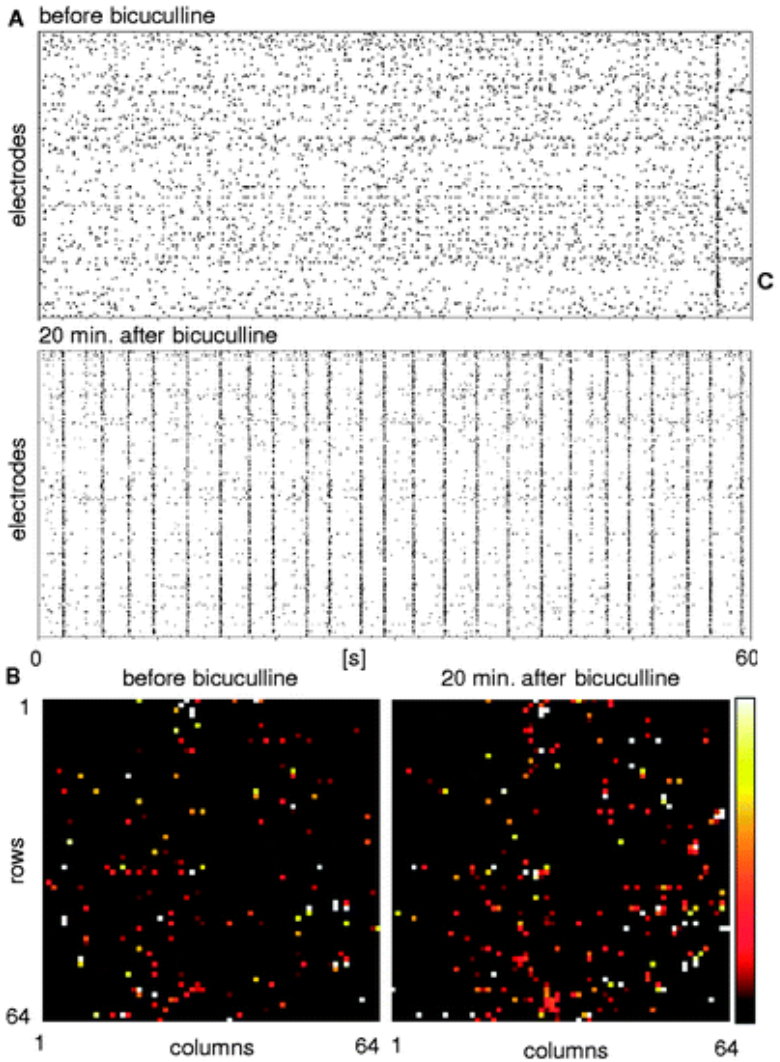
spontanous burst activity

Video: Supplement. Video 1 2009

spontanous activity analysis



stimulated activity



C

	before bicuculline	20 min. after bicuculline
No. Of Valid Channels	251	335
Global MFR [spike/sec]	0,48	0,67
Global Mean ISI [ms]	3754,9	3318,4
Global Bursts	17	29
Global Mean IBI [ms]	3587,9	2600,2
Global Mean Burst Duration [ms]	202,8	149,7
Global Mean IBS [spikes/burst]	5	6

network dynamics

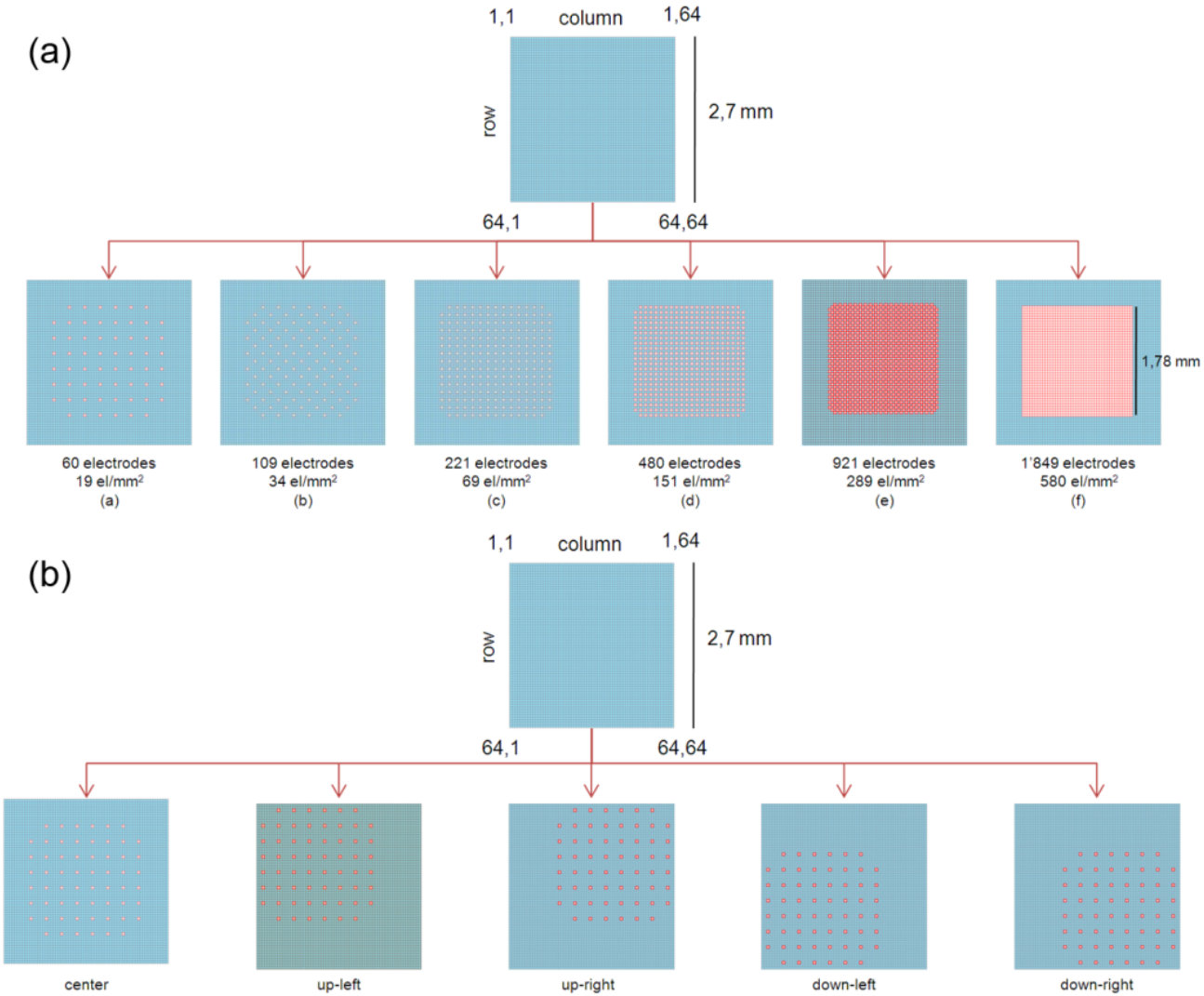
Video: Supplement. Video 2 & 3 2009

Trajectory analysis

Video: image 35.gif

Comparison to conventional MEA

image 10.gif



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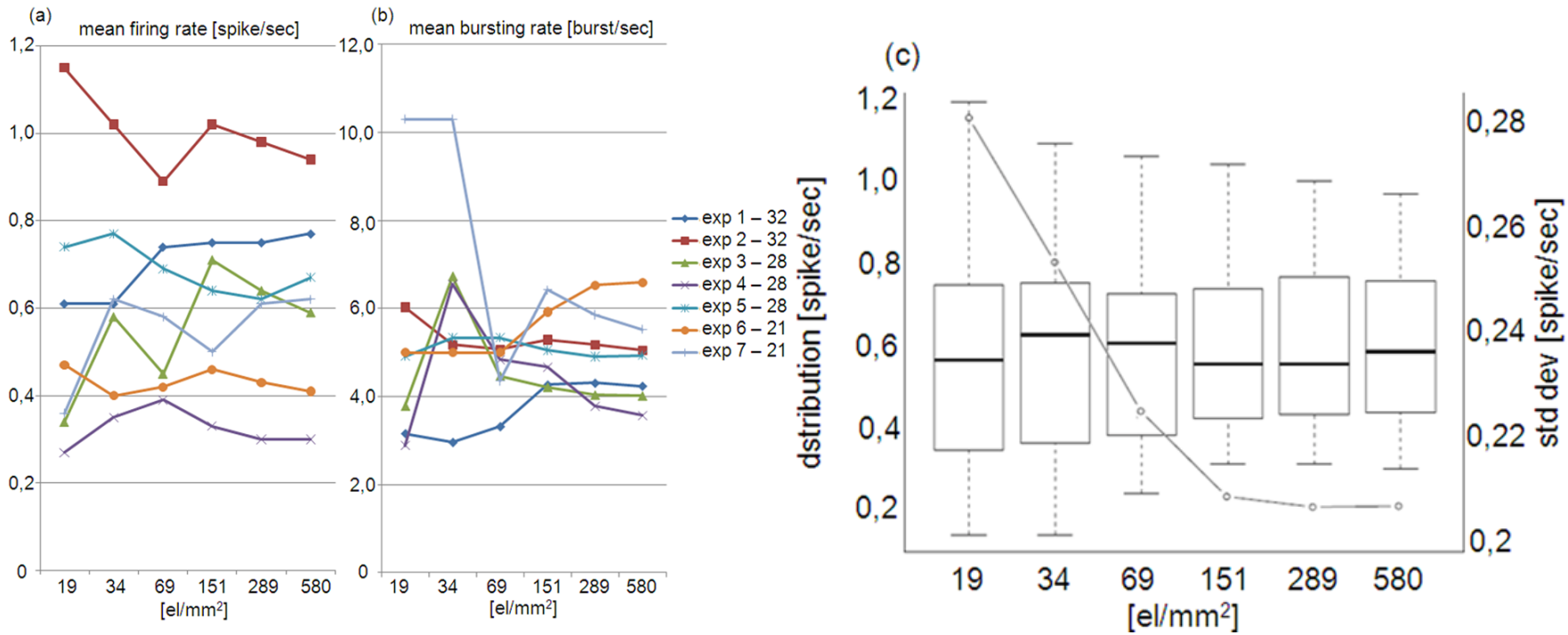

Source: Maccione et.al, Frontiers in Neuroengineering, 2010

Article 4 - Validation in acute slices

frontiers in
NEURAL CIRCUITS

METHODS ARTICLE
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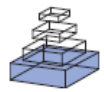

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recordings

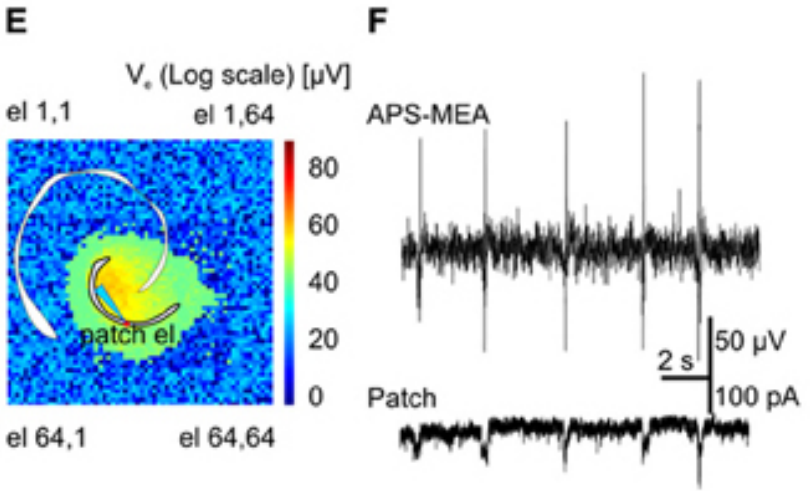
- Acute hippocampal slices
- Spontanous and evoked field excitatory postsynaptic potentials and spiking activity in the dentate gyrus (DG)
- 7.7kHz
- 20min recording
- Modulation with convulsant drugs (4-AP, THIP)

Spontanous activity

Video: Supplement. Video 1 2012

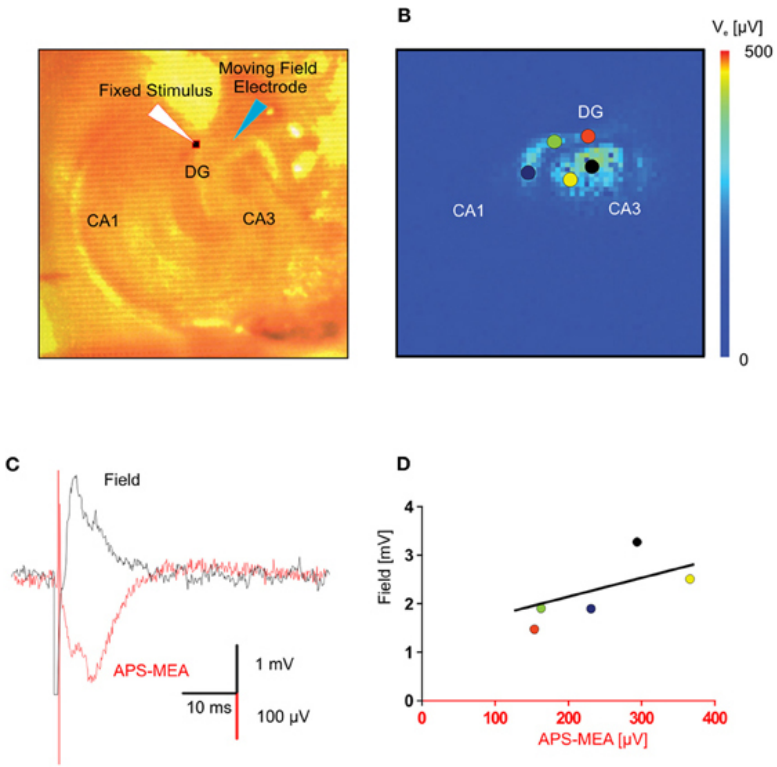
Comparison I - single intra- & extracellular electrode

Patch Clamp



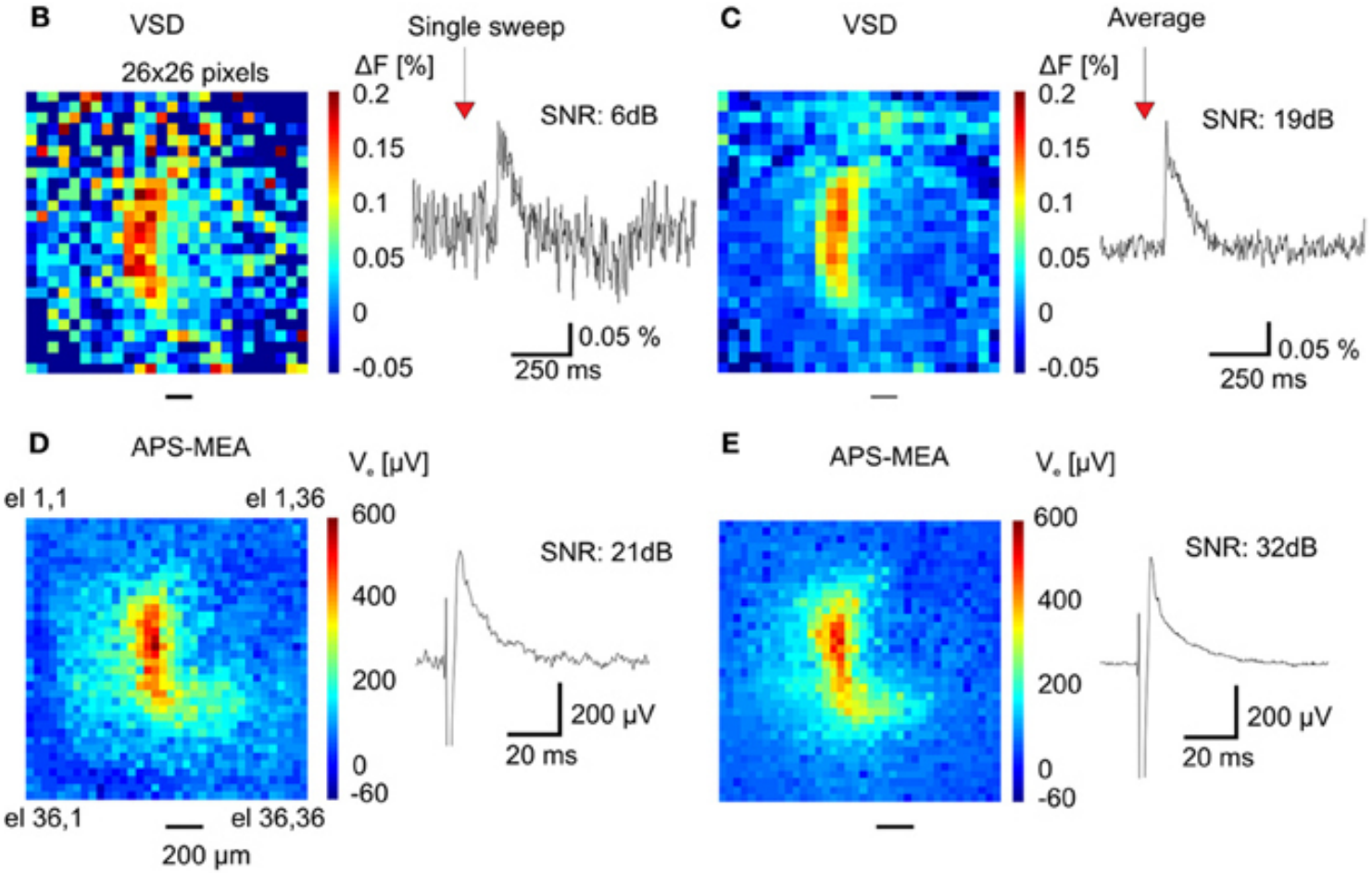
- patch-clamp and APS-MEA simultanously
- synchronization of slice with 4-AP

Single-electrode field recording



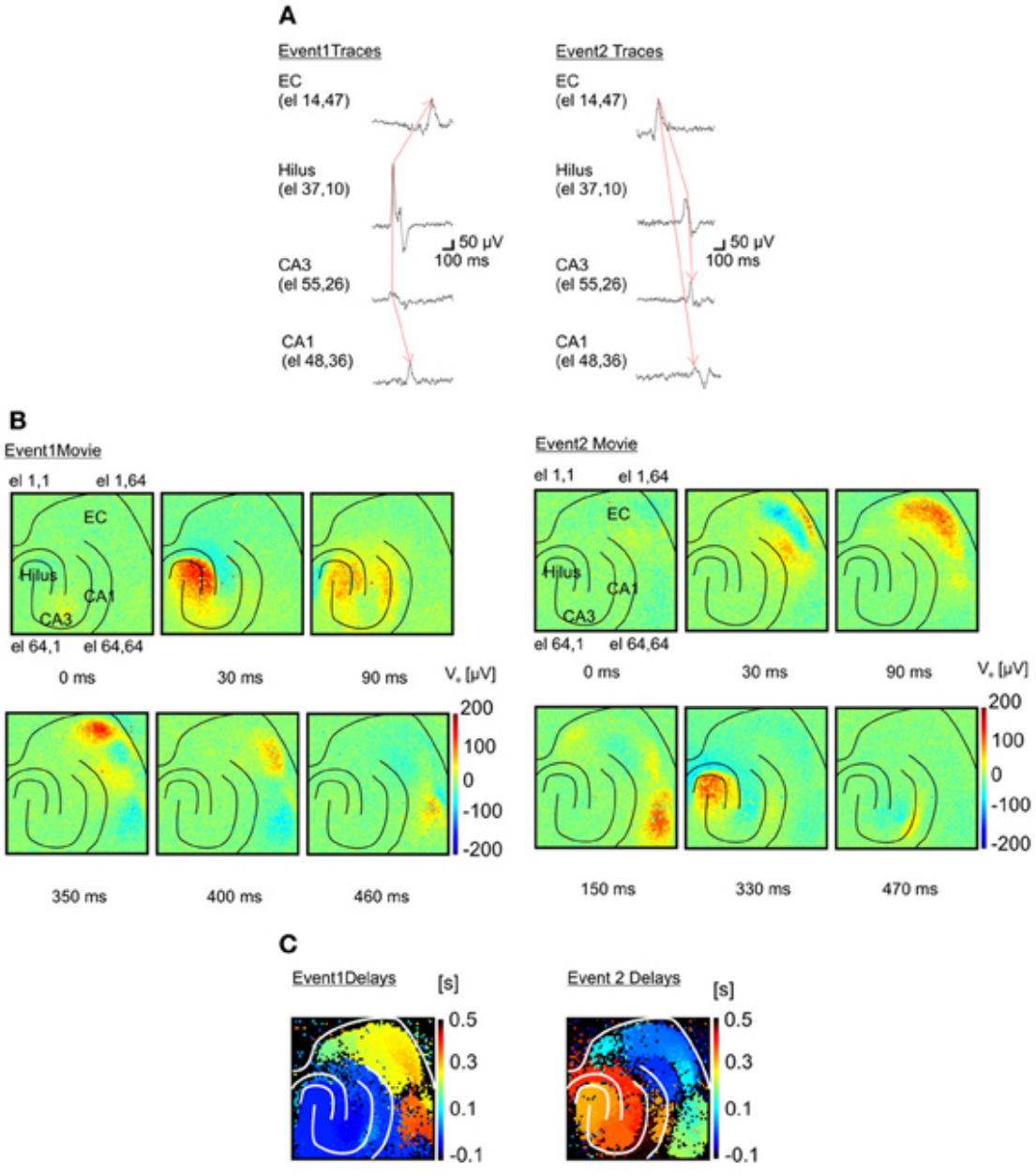
- electrical stimulation of perforant path
- recording from APS-MEA and moving conventional electrode

Comparison II - voltage-sensitive dyes

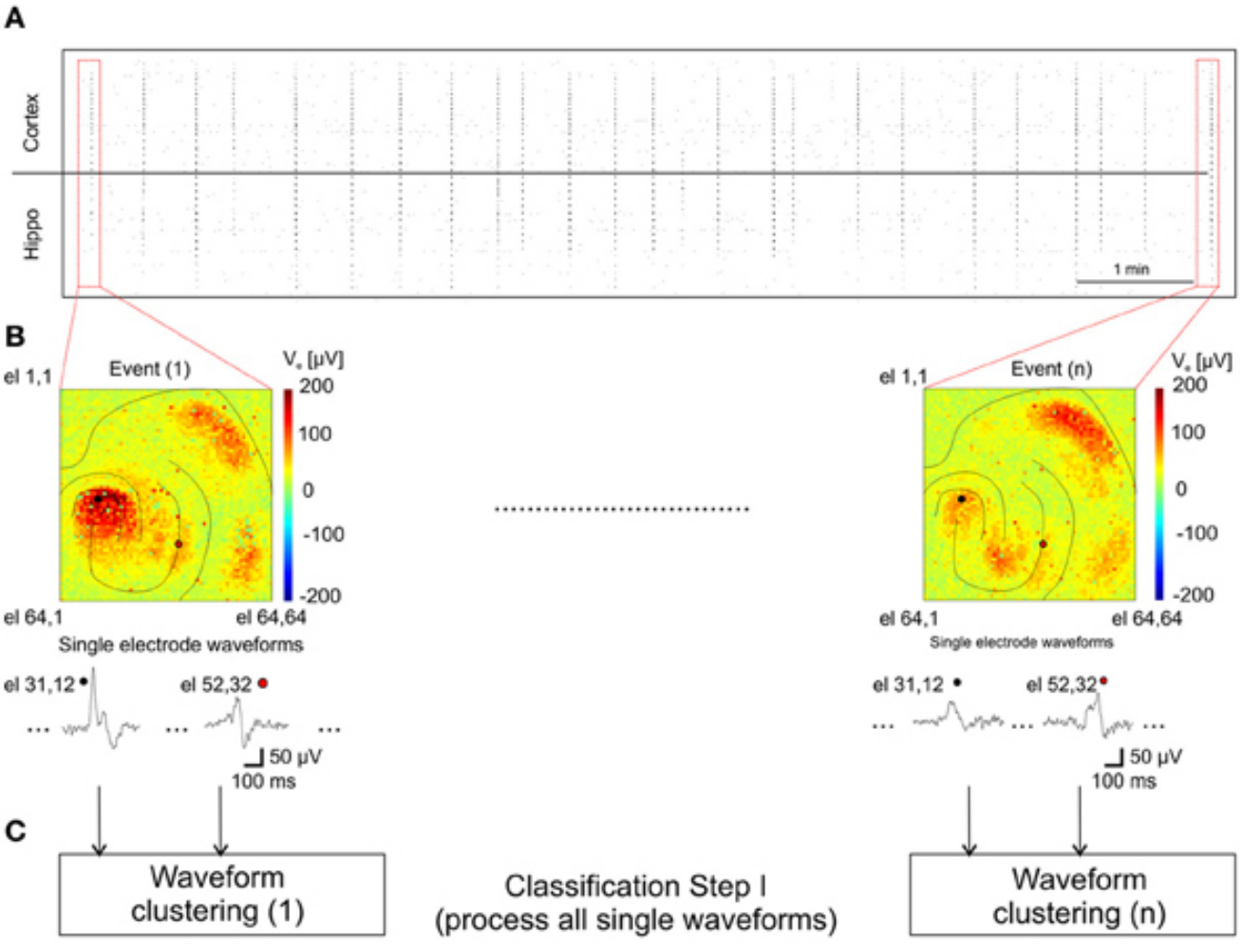


- dye: RH-795
- 80x80 pixel camera => image scaled
- sampling rate: 2 kHz

event propagation analysis



Classification algorithm of distinct events



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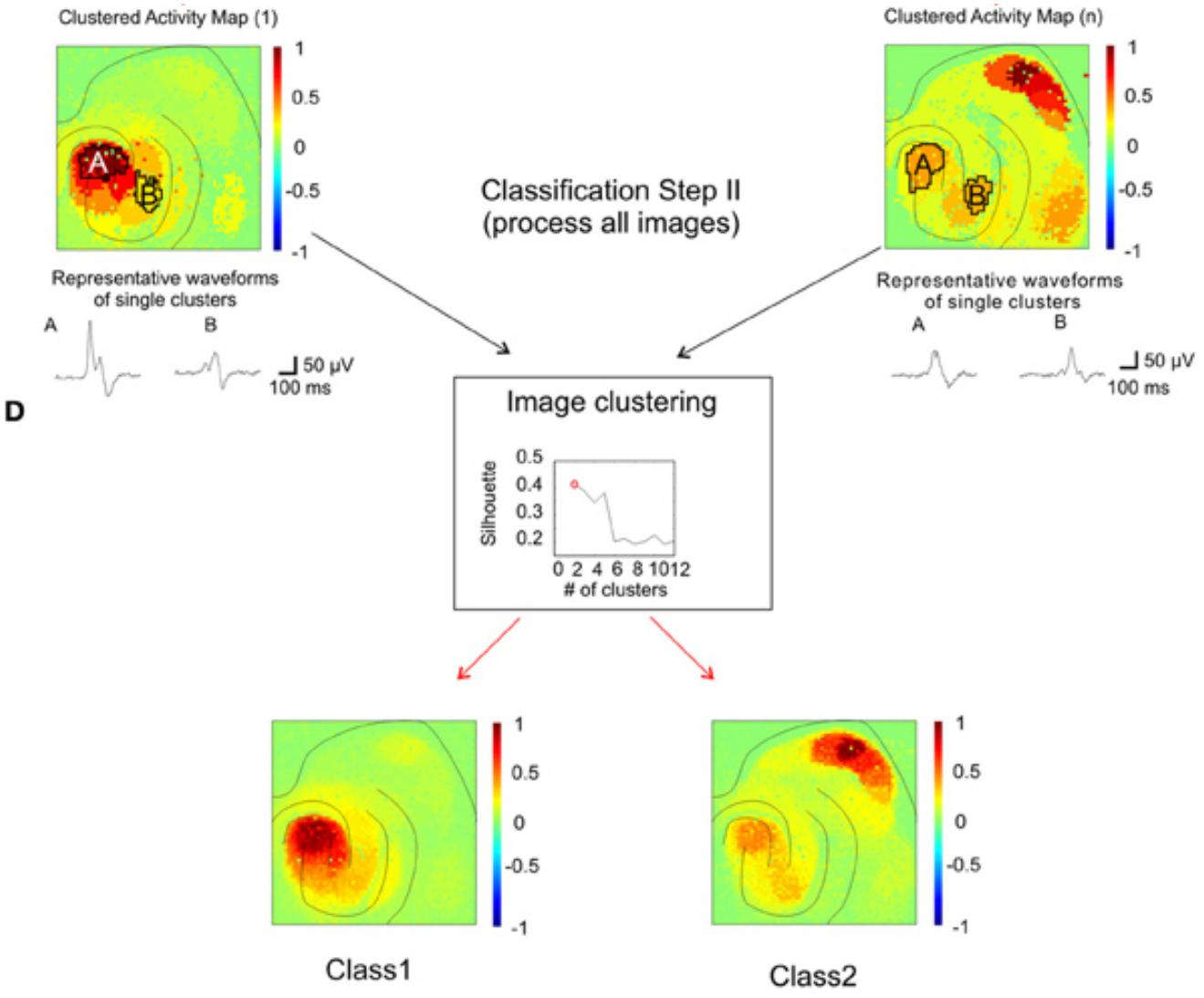
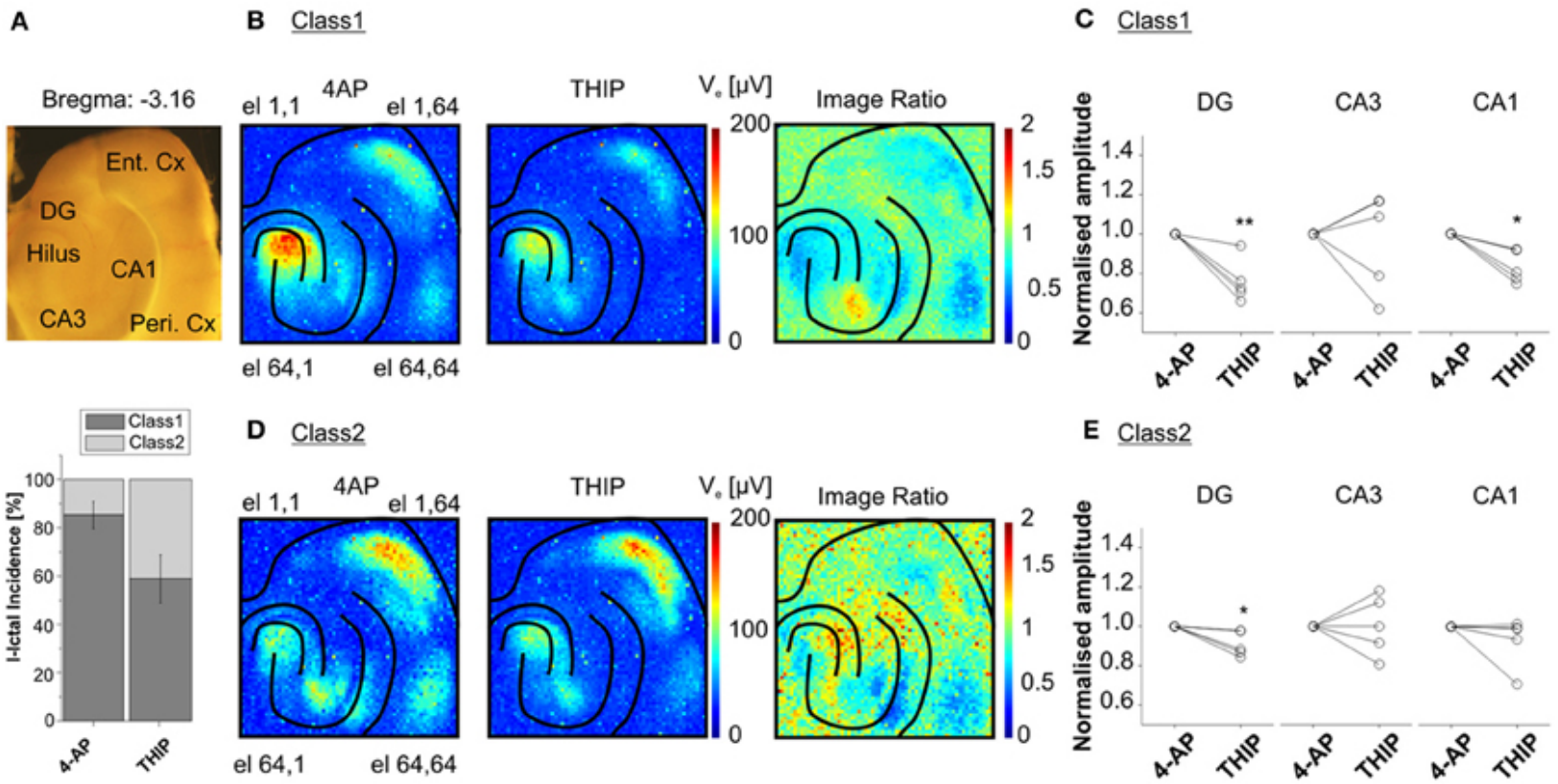
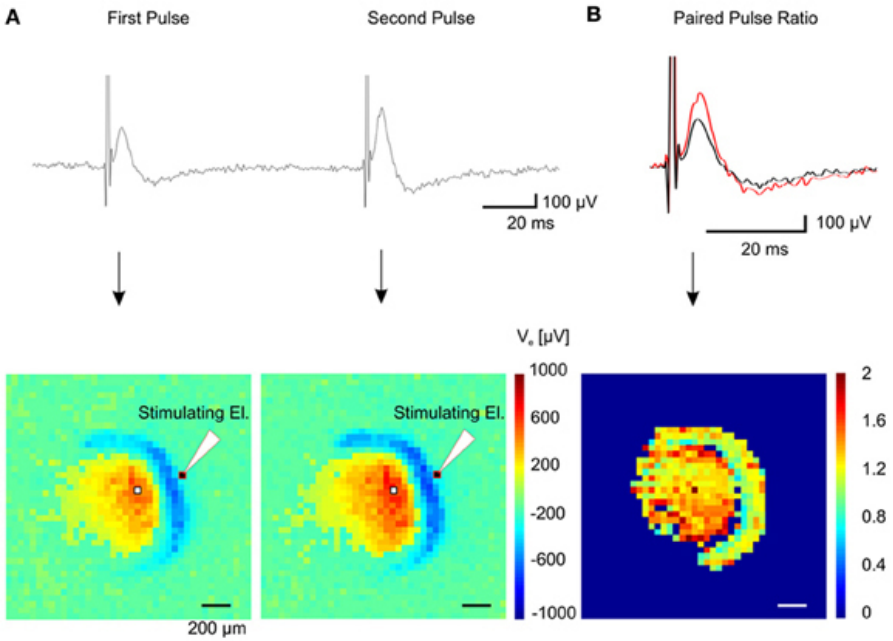


Changes of distinct Clusters among THIP treatment



Short-term plasticity analysis



Summary of (possible) Readouts

- Overall excitatory status
  - Firing and bursting rate
  - Inter-Spike and inter-burst interval
- Investigation of local field potentials
- Cluster analysis
- Trajectory analysis (including velocity)
- Investigation of Plasticity
- Connectivity analysis in cell cultures => Maccione et.al, Journal of Neuroscience Methods, 2012
- Investigation of cellular subtypes (Combination with Staining) => A. Maccione et al., SFN2011, 2011

Discussion

Advantages

- easy-to-use system
- reusable Chips
- good combination of high resolution with reasonable sampling frequence
- single-cell resolution in cell cultures
- fast acquisition of data
- free Software
- Detection of spikes and LFPs

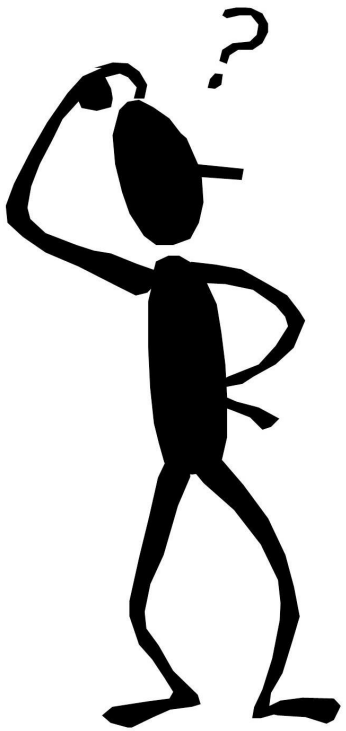
Drawbacks

- Origin of signal not clear in slices
- cumbersome data analysis
- generates huge amounts of data (about 60MB/s => ~36GB/ 10min)
- requires high-performance computers for certain types of analysis

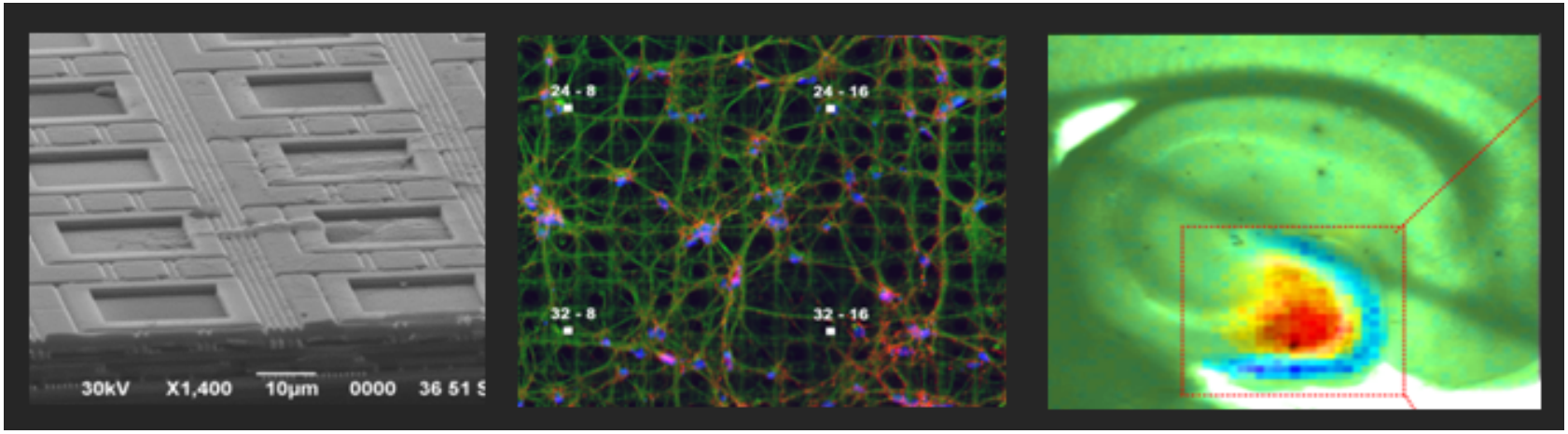
Conclusion

- useful for all experiments using extracellular recordings
- useful for an overview of activity and the analysis of network dynamics and connectivity
- useful for studying the effect of drugs on the network dynamics
- ideal for combination with recordings on intracellular level (Patch Clamp and VSDs)

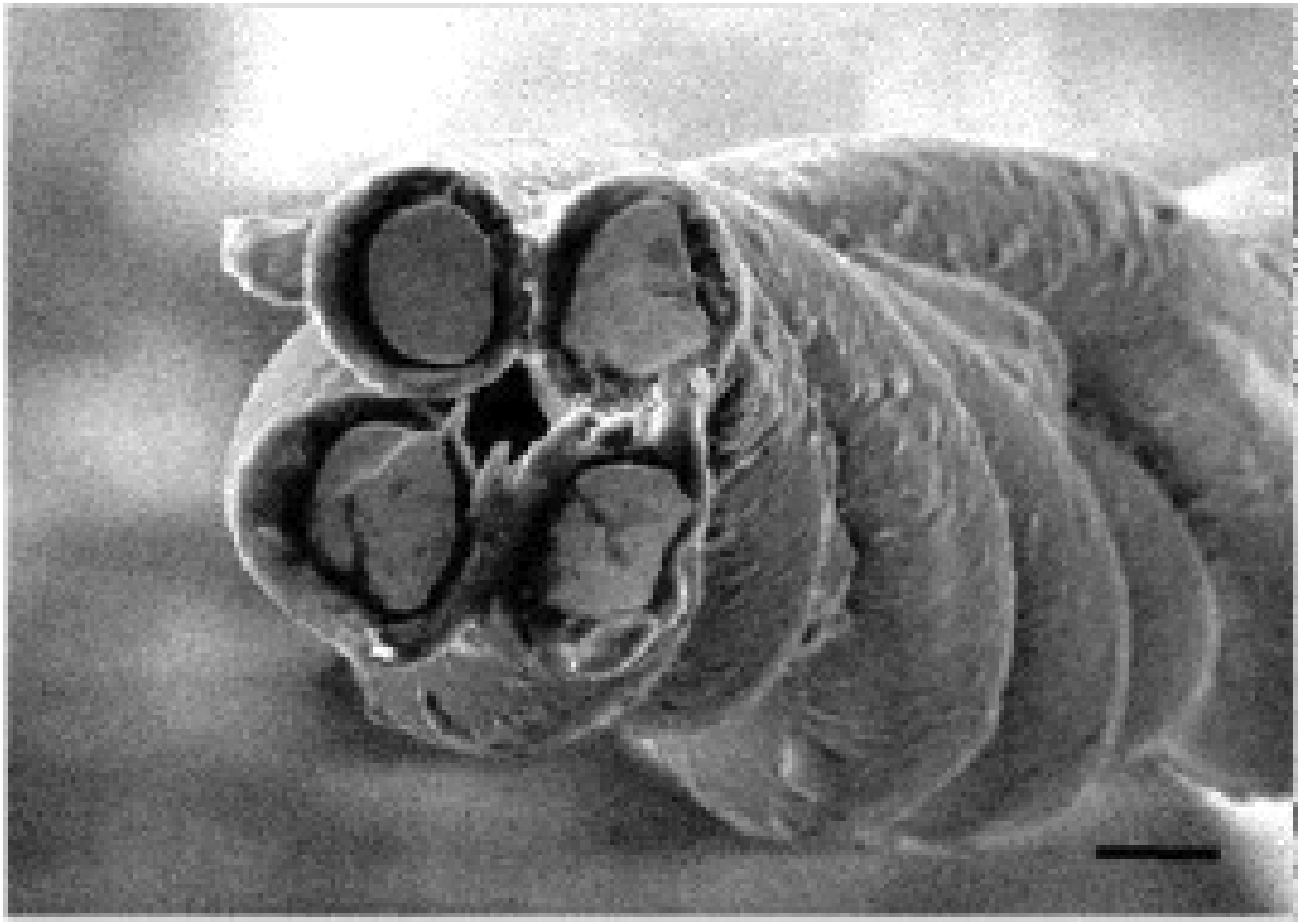
Questions?



Thank you!



Tetrode



Silhouette coefficient

Calculates whether an object is clustered correctly or not by using the distance to the other objects of n clusters