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► To cite this version:

Sarah Hamdi Cherif, Candice Roux, Valentine Bouet, Jean-Marie Billard, Jérémie Gaidamour, et al.. Investigating hippocampal synaptic plasticity in schizophrenia: A computational and experimental approach using MEA recordings. Bernstein Conference, Sep 2024, Frankfurt, Germany. 2024, 10.12751/nmcn.bc2024.244 . hal-04835241

HAL Id: hal-04835241

<https://hal.univ-lorraine.fr/hal-04835241v1>

Submitted on 13 Dec 2024

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Investigating hippocampal synaptic plasticity in Schizophrenia

computational and experimental approach using MEA recordings

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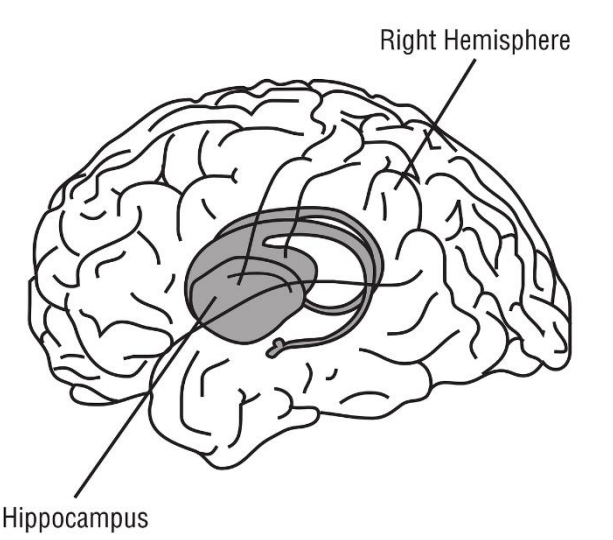
Schizophrenia

- Severe psychiatric disorder affecting about **1%** of the population
- Etiology remains unclear (genetic and environmental factors' association)
- Marked by significant variability in symptom expression among patients
- Poor management of **negative** and **cognitive symptoms** by current treatments

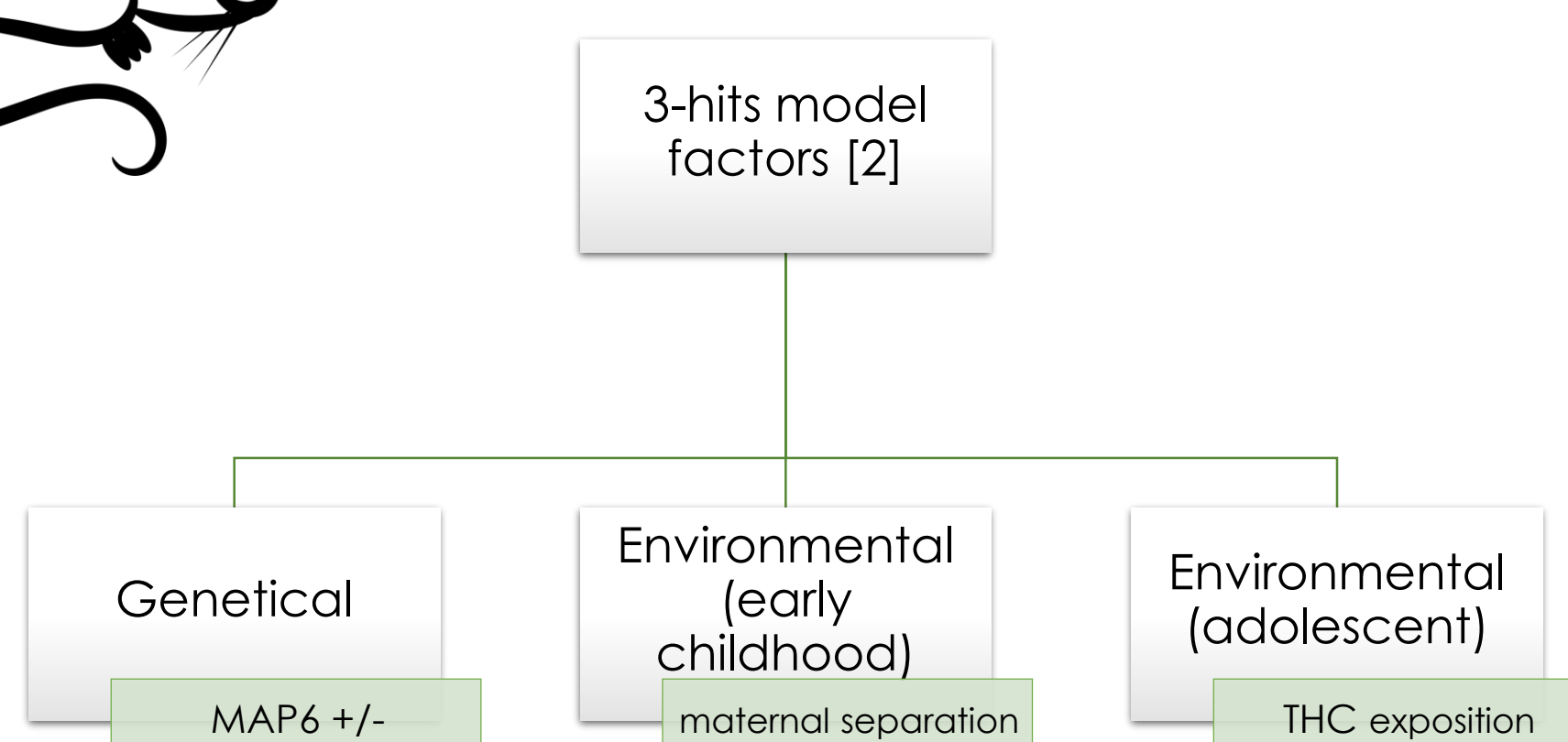
cognitive impairments

Hippocampus

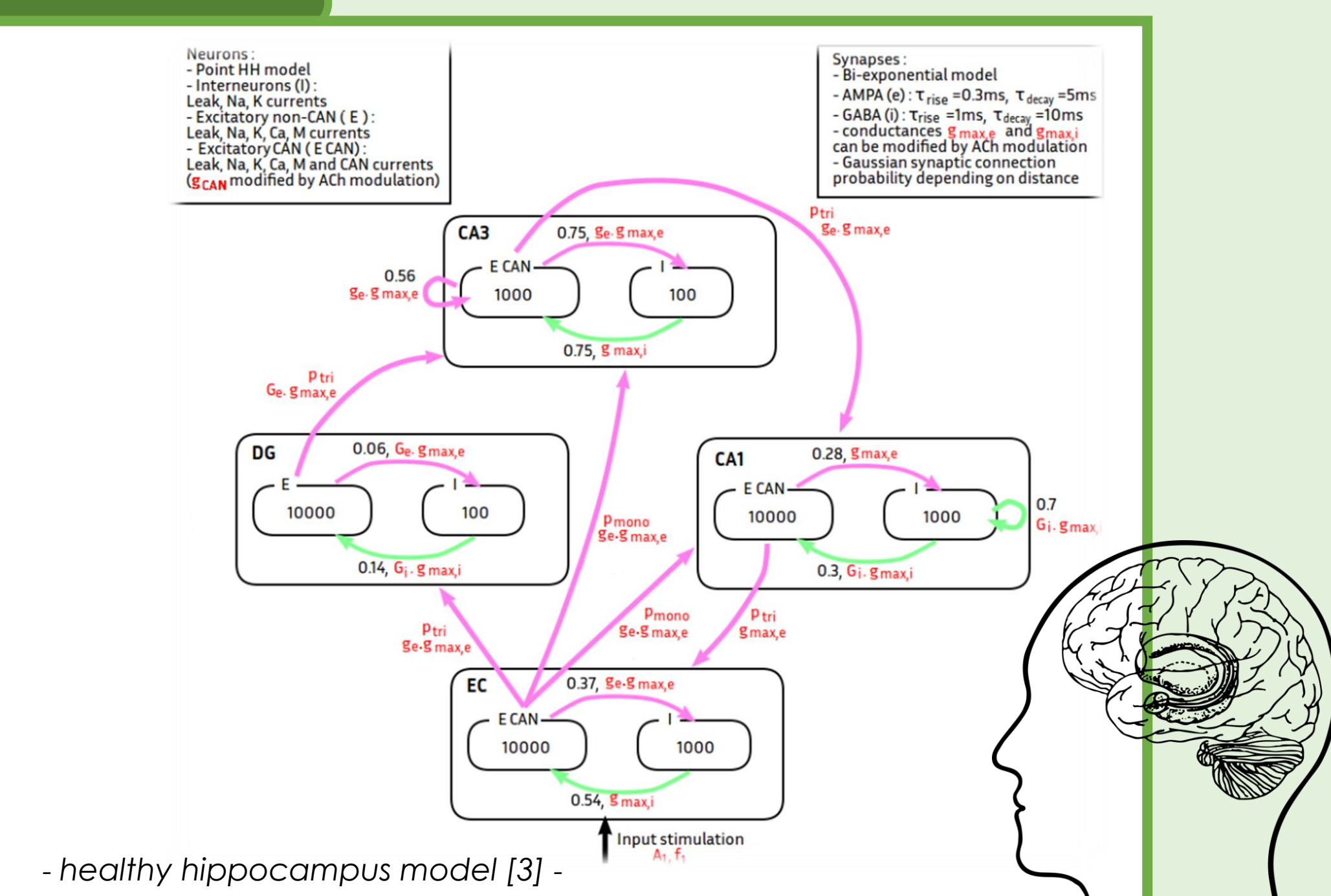
- Structural alteration [1]
- Functional alteration
- **Plasticity alteration [2]**
 - Loss in IN number (PV+, SST, CCK)
 - Synaptic pruning (4x more than normal)
 - **NMDA-related Long Term Potentiation (LTP)** alteration



From biological data to computational modelling

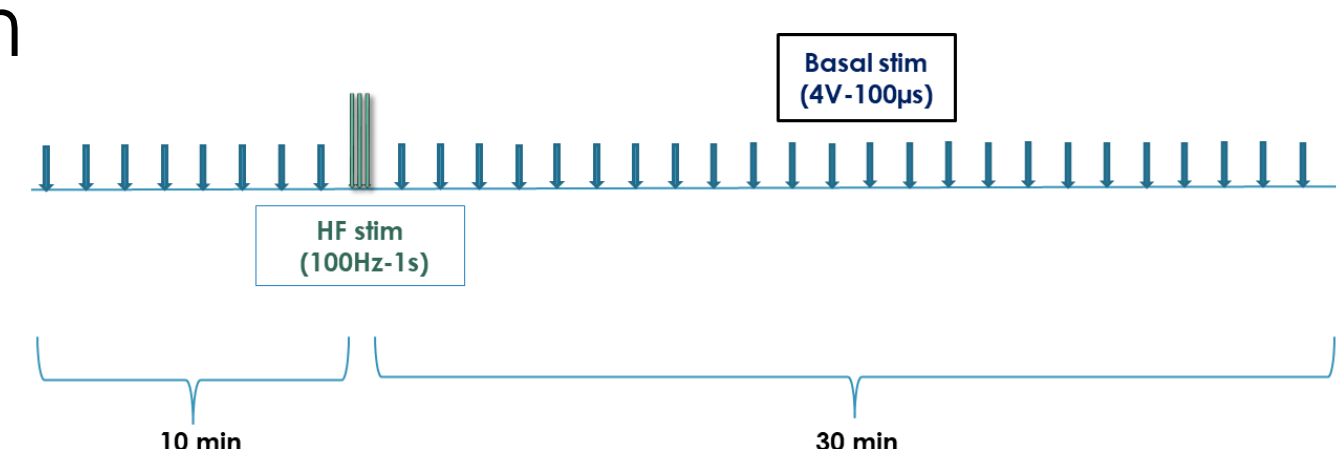
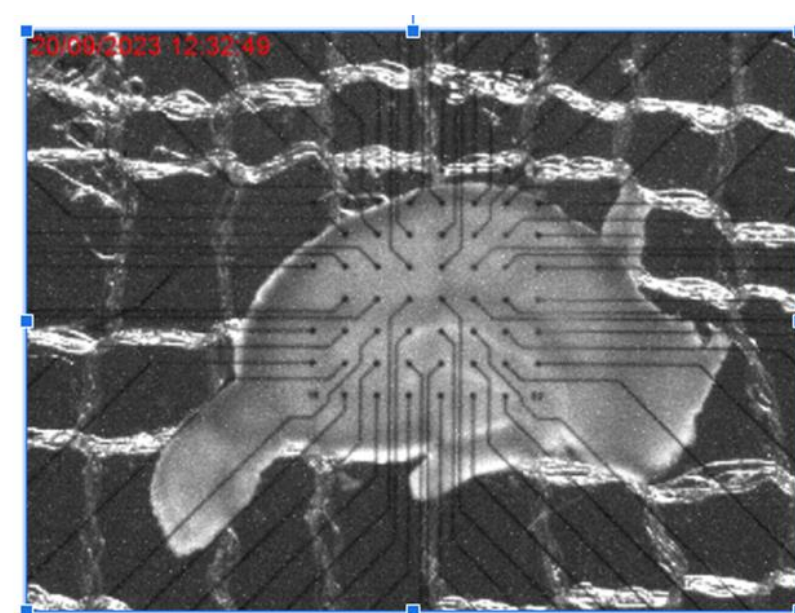


- Develop effective methods for processing and visualizing MEA data to isolate and characterize hippocampal synaptic plasticity.
- Optimize experimental protocol parameters to enhance the quality and relevance of the data obtained.
- **Long term** : Integrate the extracted data into a computational model [3] to simulate hypotheses in schizophrenia.



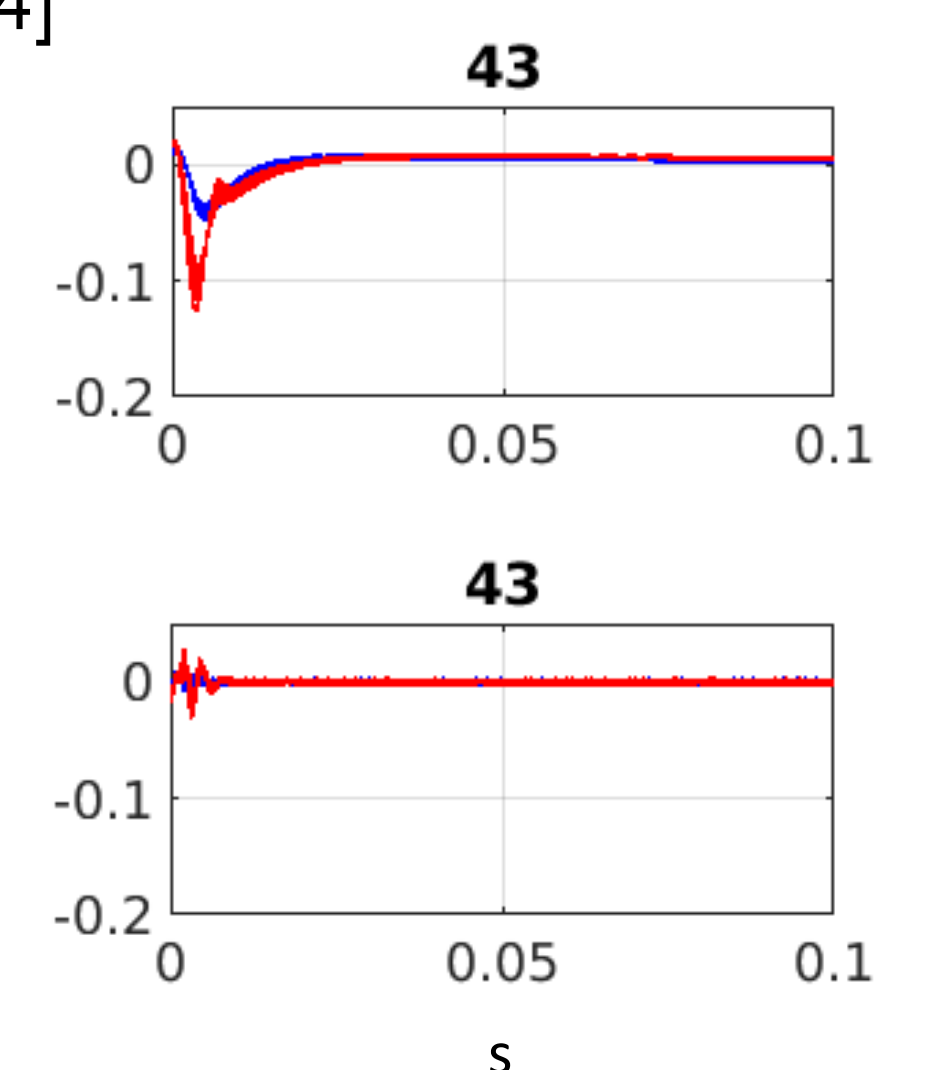
Material & Methods

- MEA200 composed of 60 electrodes
- High Frequency Protocol (HFS)
 - 10 min basal stim of the Schaffer collaterals
 - 1s high-frequency train (100Hz)
 - 20 min basal stim
- Induces an LTP



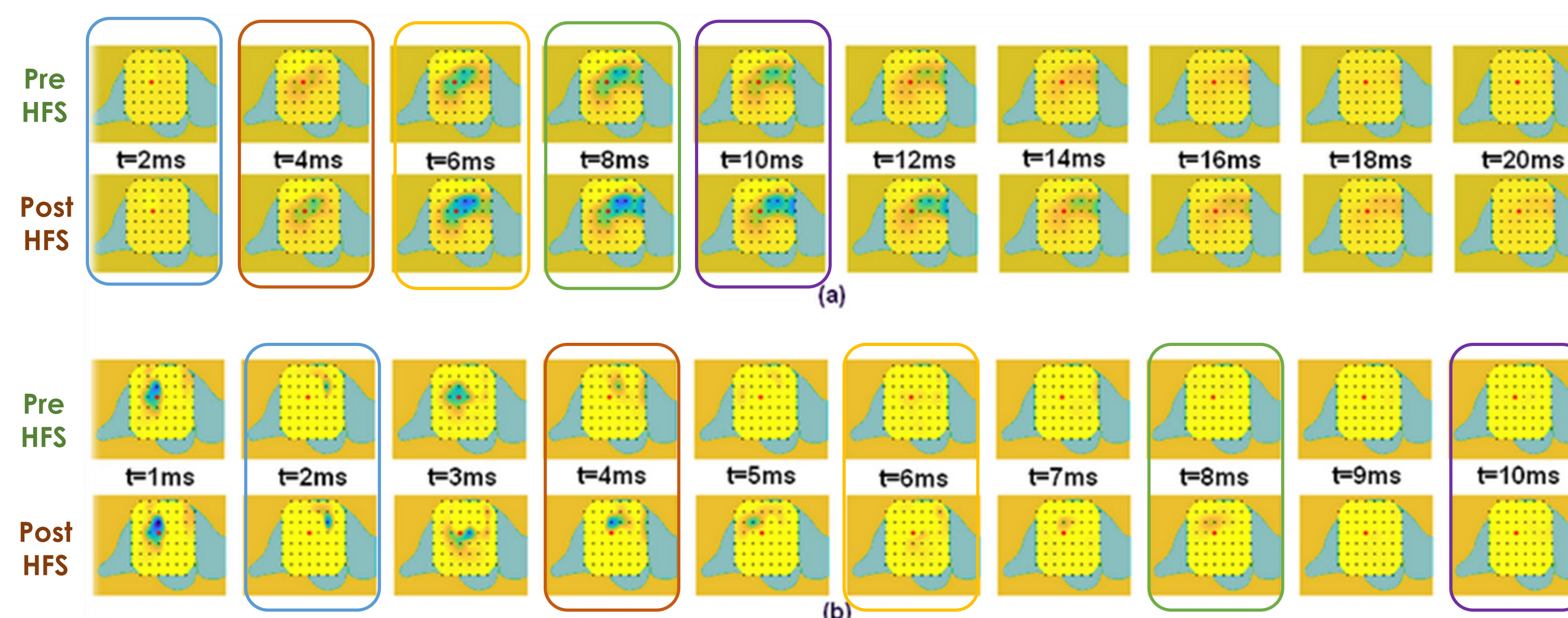
Data Processing

- Blanking/ reference canceling [4]
- Filtering
 - <80 Hz LFP (EPSP)
 - >300 Hz multi units
- Identifying basal stimulation
 - Before HFS (Blue)
 - After HFS (Red)
- Compute averages for each electrode



Results (wild type mice)

- There is a marked enhancement in synaptic activity post-HFS (**figure a**) in both intensity and duration, which could be correlated to a successful induction of LTP.
- The spatial evolution seems to follow the physiological path for synaptic transmission.



- The increase in spiking activity post-HFS (**figure b**) suggests that the neurons within the slice have become more responsive, likely due to enhanced synaptic efficacy caused by LTP or to the electric field's propagation.

Conclusion

- These preliminary results show a functional data processing pipeline and visualisation tool to continue our study.

Next steps

- Vary the experimentation (different protocols, stimulation zone and/or the stimulation characteristics)
- Validate the current results on more data
- Quantify plasticity and extract information that can be used in the computational model.
- Collect data from an SCZ animal model

[1]Howes O, et al. Glutamate and dopamine in schizophrenia: an update for the 21st century. J Psychopharmacol. 2015 Feb; 10.1177/0269881114563634

[2]Perceley S, et al. Functional Dysregulations in CA1 Hippocampal Networks of a 3-Hit Mouse Model of Schizophrenia. International Journal of Molecular Sciences. 2021; 22(5):2644. 10.3390/ijms22052644

[3]Aussel A, et al. "Design of Experiments and Sobol' sensitivity analysis of a hippocampus computational model," 2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), Mexico, 2021, pp. 6146-6150, 10.1109/EMBC46164.2021.9630725

[4]Ranta R, et al. Reference estimation in EEG recordings. Annu Int Conf IEEE Eng Med Biol Soc. 2010;2010:5371-4., 10.1109/IEMBS.2010.5626488

