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Data-driven model of endogenous and exogenous electric fields modulation of cerebral cortex activity

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Introduction: Constraining neuroscience I

- Neuroscience is the scientific study of the nervous system. It is a multidisciplinary science (biology, medicine, mathematics, computer science, etc.)
- The nervous system is complex and non-homogeneous. CNS (brain and spinal cord) and PNS (somatic, autonomic and enteric subsystems)
- This thesis studies the cerebral cortex from a biophysical level

Introduction: Constraining neuroscience II

- In deep sleep the brain shows a pattern of slow oscillations [1]
- Endogenous (and exogenous) electric fields modulate the cerebral cortex activity [2]
- This thesis is titled: Data-driven model of endogenous and exogenous electric fields modulation of cerebral cortex activity

[1] G. T. Neske, “The slow oscillation in cortical and thalamic networks: Mechanisms and functions,” Frontiers in Neural Circuits, vol. 9
[2] B. Rebollo, B. Telenczuk, A. Navarro-Guzman, A. Destexhe, and M. V. Sanchez-Vives, “Modulation of intercolumnar synchronization by endogenous electric fields in cerebral cortex,” Science Advances, vol. 7, no. 10, 2021.

Workplan: What is the goal?

– Create a model for the slow oscillations activity in the brain cortex under external rotated electric fields

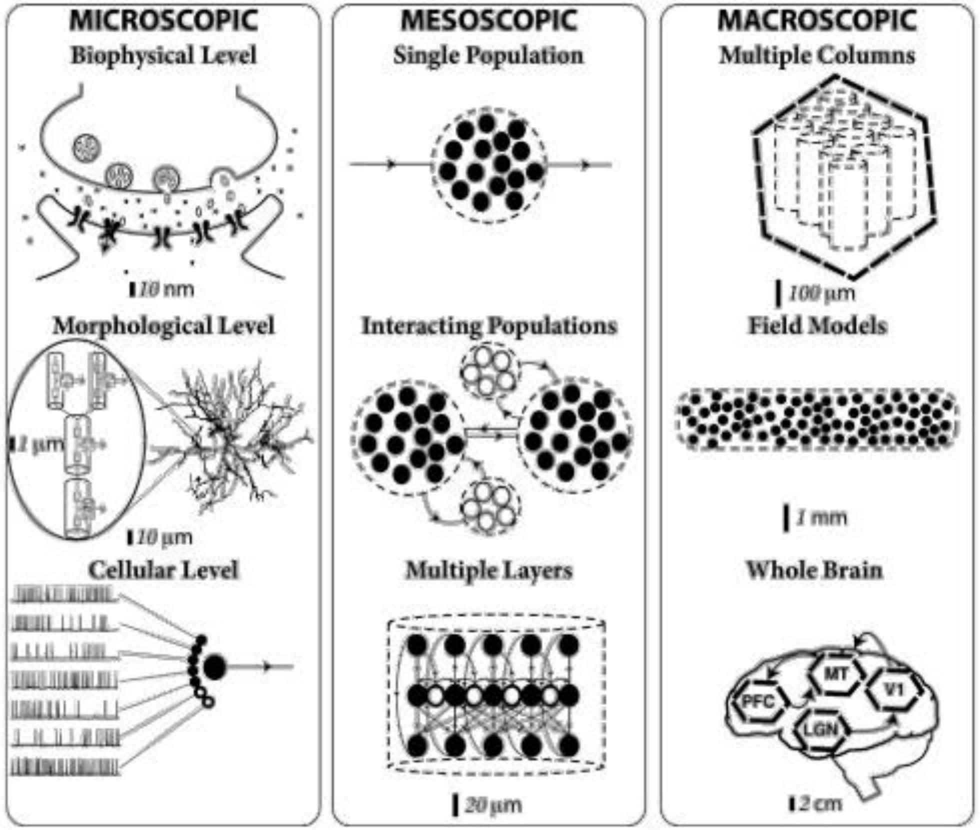
<u>The plan</u>

1. Understand, implement and analyze the model [1]
2. Obtain data and fit the model to the data

[1] B. Rebollo, B. Telenczuk, A. Navarro-Guzman, A. Destexhe, and M. V. Sanchez-Vives, “Modulation of intercolumnar synchronization by endogenous electric fields in cerebral cortex,” Science Advances, vol. 7, no. 10, 2021.

Modelling I: Introduction

– *Microscopic vs macroscopic.*



Modelling II: An argument for mean fields

– *Microscopic vs macroscopic. Why mean field models?*

– Ease of computation
– Mesoscopic signals (VSD, LFP)
– Design large-scale models of neural tissue [1]

[1] P. Sanz Leon, S. Knock, M. Woodman, L. Domide, J. Mersmann, A. McIntosh, and V. Jirsa, "The virtual brain: a simulator of primate brain network dynamics," Frontiers in Neuroinformatics, vol. 7, p. 10, 2013.

The model I: Dynamical equations

$$\tau_e \frac{v_e}{dt} = -v_e + n_e f_e(v_e + v_{ext}, v_i) + \sigma_e \eta_t$$

$$\tau_i \frac{v_i}{dt} = -v_i + n_i f_i(v_e + v_{ext}, v_i) + \sigma_i \eta_t$$

$$\tau_{adapt} \frac{dU_{adapt}}{dt} = -U_{adapt} + \beta_\tau v_{exc}$$

$$\langle g_{tot} \rangle = g_l + \langle g_e \rangle + \langle g_i \rangle = g_l + \sum_{s \in \{e,i\}} v_s B_s T_s$$

$$\mu_U = \frac{E_l g_l + E_e \langle g_e \rangle + E_i \langle g_i \rangle}{\langle g_{tot} \rangle} - U_{adapt}$$

$$\tau_{eff} = C / \langle g_{tot} \rangle$$

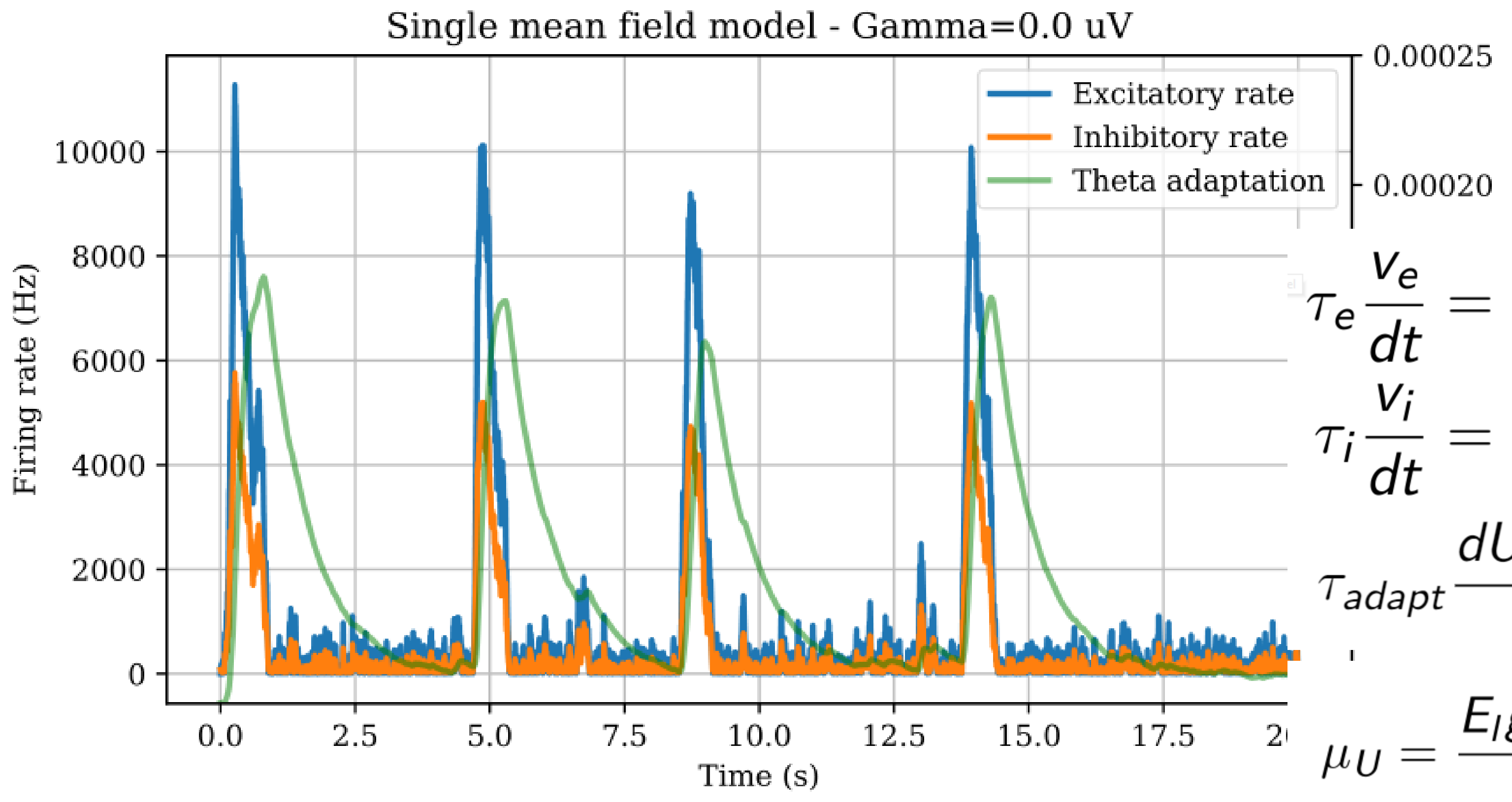
$$\sigma_U = \sum_{s \in \{e,i\}} v_s(\tau_{eff} + T_S) \left[\frac{(E_S - \mu_U) B_s T_s \tau_{eff}}{2C(\tau_{eff} + T_s)} \right]^2$$

$$f(v_e, v_i; \Theta) = \frac{1}{\tau_{eff}(v_e, v_i)} \mathrm{erfc} \left[\frac{\Theta - \mu_U(v_e, v_i)}{\sqrt{2\sigma_U}(v_e, v_i)} \right]$$

[1] B. Rebollo, B. Telenczuk, A. Navarro-Guzman, A. Destexhe, and M. V. Sanchez-Vives, “Modulation of intercolumnar synchronization by endogenous electric fields in cerebral cortex,” Science Advances, vol. 7, no. 10, 2021.

[2] A. Kuhn, A. Aertsen, and S. Rotter, “Neuronal integration of synaptic input in the fluctuation-drivenregime,”Journal of Neuroscience, vol. 24, no. 10, pp. 2345–2356, 2004.

The model II: Sample run



$$\tau_e \frac{v_e}{dt} = -v_e + n_e f_e(v_e + v_{ext}, v_i) + \sigma_e \eta_t$$

$$\tau_i \frac{v_i}{dt} = -v_i + n_i f_i(v_e + v_{ext}, v_i) + \sigma_i \eta_t$$

$$\tau_{adapt} \frac{dU_{adapt}}{dt} = -U_{adapt} + \beta_\tau v_{exc}$$

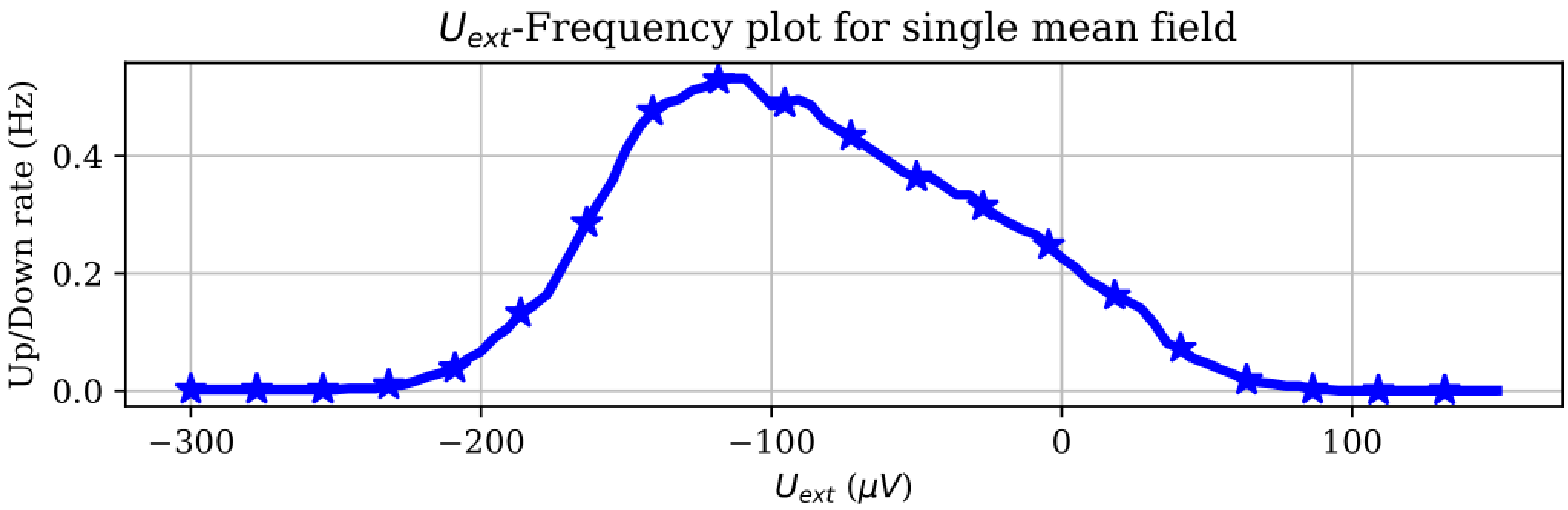
$$\mu_U = \frac{E_l g_l + E_e \langle g_e \rangle + E_i \langle g_i \rangle}{\langle g_{tot} \rangle} - U_{adapt}$$

[1] G. T. Neske, “The slow oscillation in cortical and thalamic networks: Mechanisms and functions,” Frontiers in Neural Circuits, vol. 9

[2] B. Rebollo, B. Telenczuk, A. Navarro-Guzman, A. Destexhe, and M. V. Sanchez-Vives, “Modulation of intercolumnar synchronization by endogenous electric fields in cerebral cortex,” Science Advances, vol. 7, no. 10, 2021.

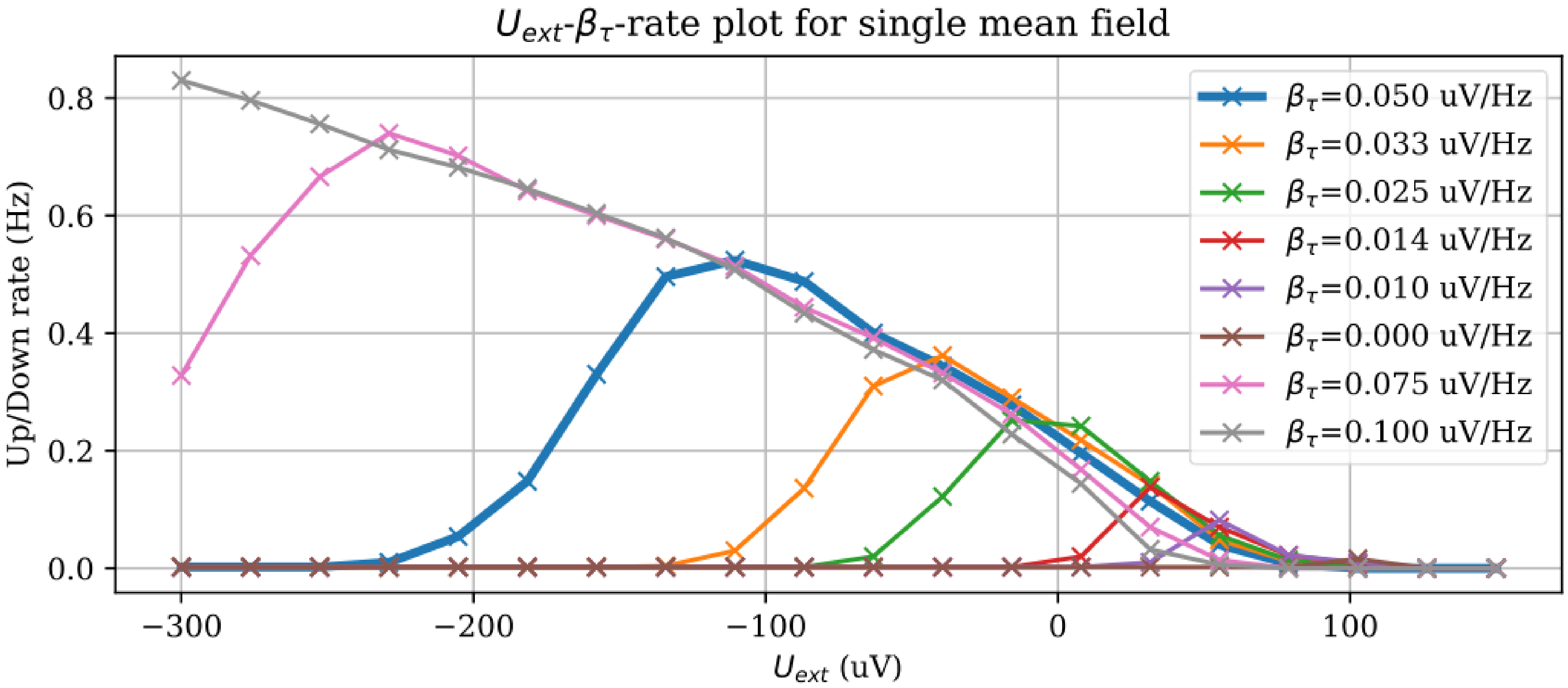
Model analysis: single population I

$$\mu_U = \frac{E_l g_l + E_e \langle g_e \rangle + E_i \langle g_i \rangle}{\langle g_{tot} \rangle} - \underline{U_{adapt}} + \underline{U_{\mathrm{external}}}$$

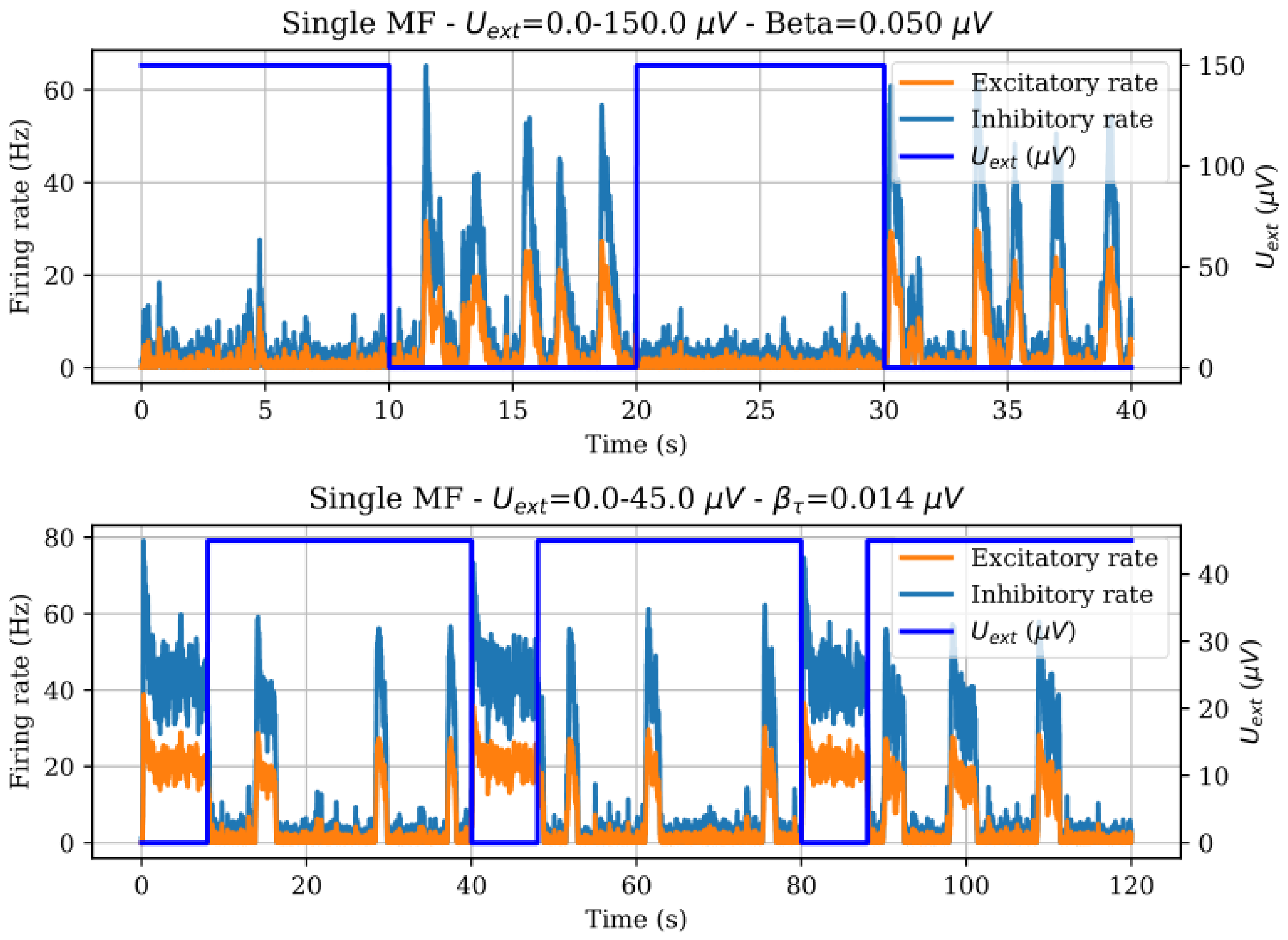


Model analysis: single population II

$$\mu_U = \frac{E_l g_l + E_e \langle g_e \rangle + E_i \langle g_i \rangle}{\langle g_{tot} \rangle} - U_{adapt} + U_{external} \qquad \tau_{adapt} \frac{dU_{adapt}}{dt} = -U_{adapt} + \beta_\tau v_{exc}$$

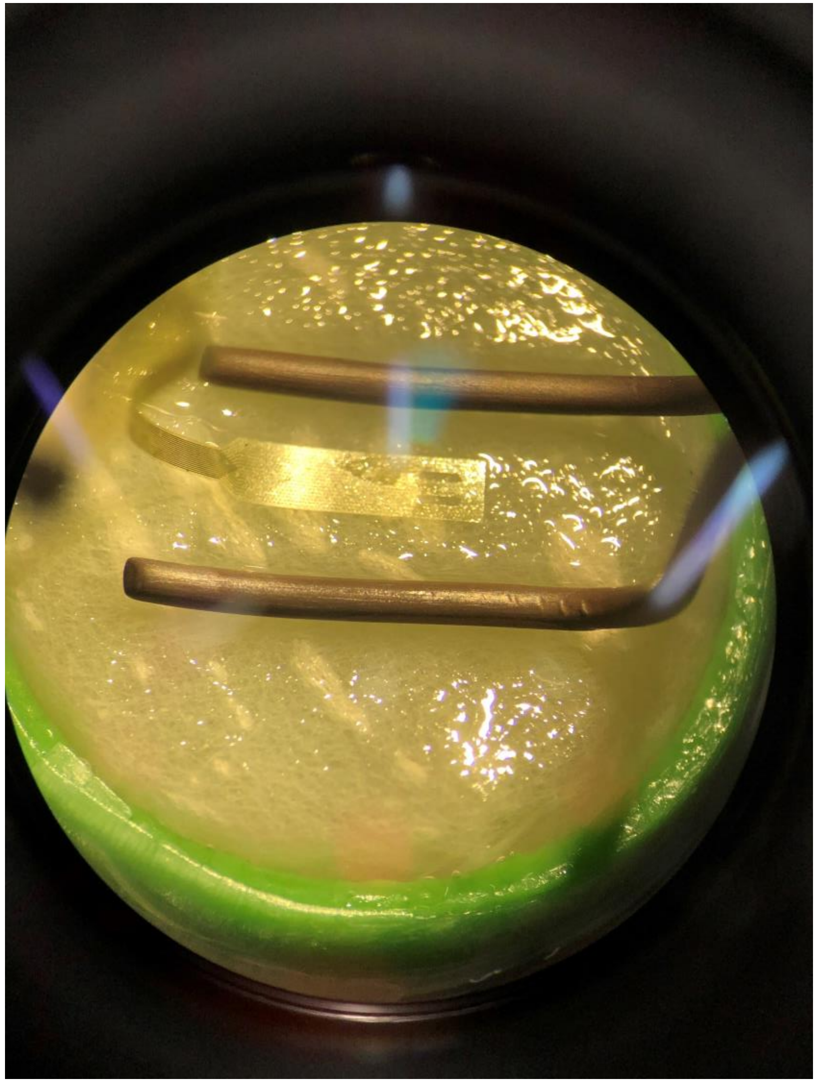


Model analysis: single population III



Data analysis I: What do we have?

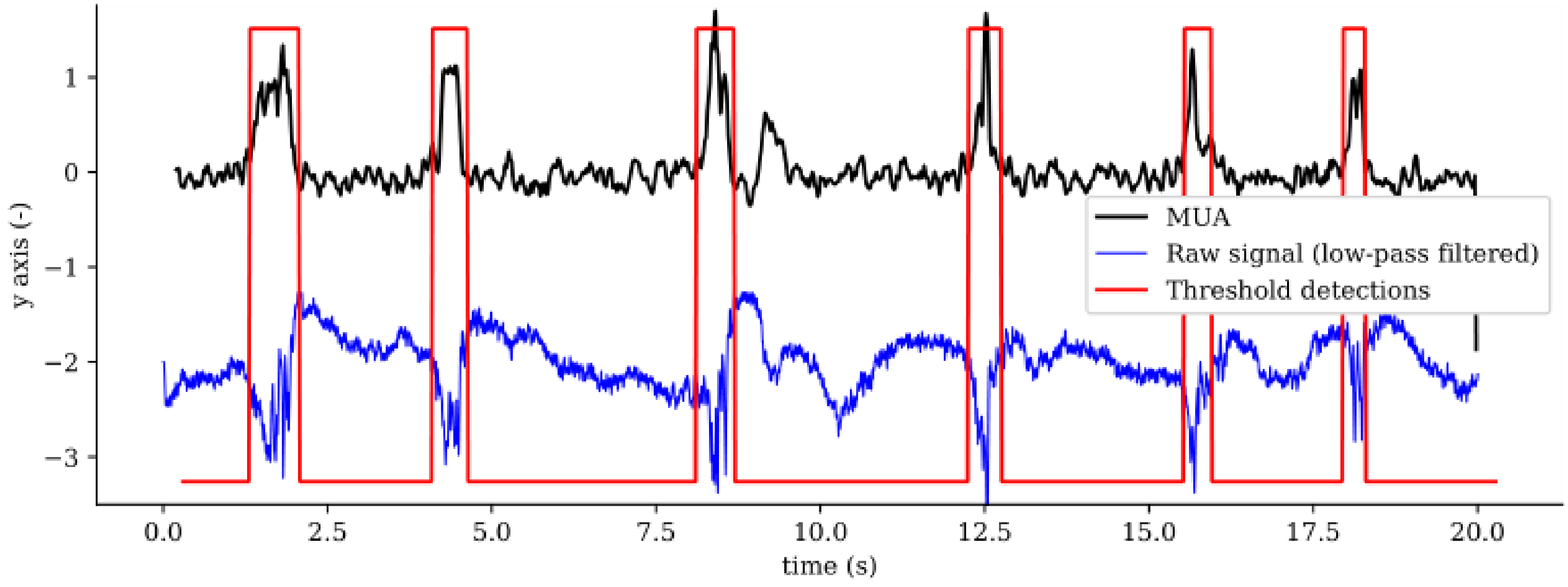
- Ferret cortical slices prepared in a chemical preparation
- Measurements using a micro electrode array (MEA) in a 16 channel grid configuration
- 3 different intensities (0, 3, -3) V/m and 3 different rotations (0, 45, 90) °



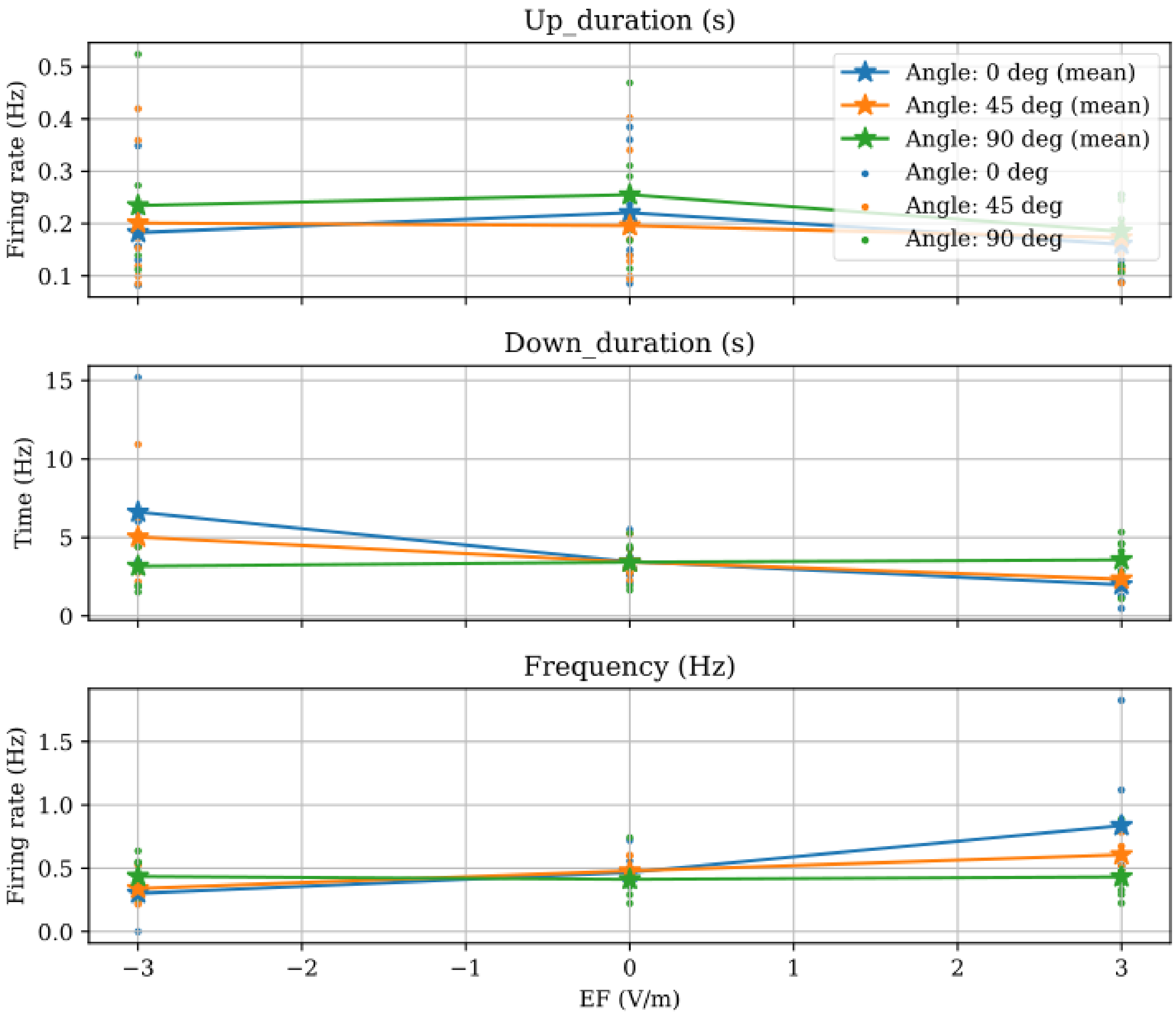
Data analysis II: Data processing

– We measure the Local Fiel Potential (V) and we want to compute the Up period, the Down period and the Frequency

– The metrics are computed over the original signal or the Multi Unit activity (section 7.1) using thresholds



Data :



Up_duration (s)
Firing rate (Hz)
0.5
0.4
0.3
0.2
0.1
Angle: 0 deg (mean)
Angle: 45 deg (mean)
Angle: 90 deg (mean)
Angle: 0 deg
Angle: 45 deg
Angle: 90 deg
Down_duration (s)
Time (Hz)
15
10
5
0
Frequency (Hz)
Firing rate (Hz)
1.5
1.0
0.5
0.0
−3
−2
−1
0
1
2
3
EF (V/m)

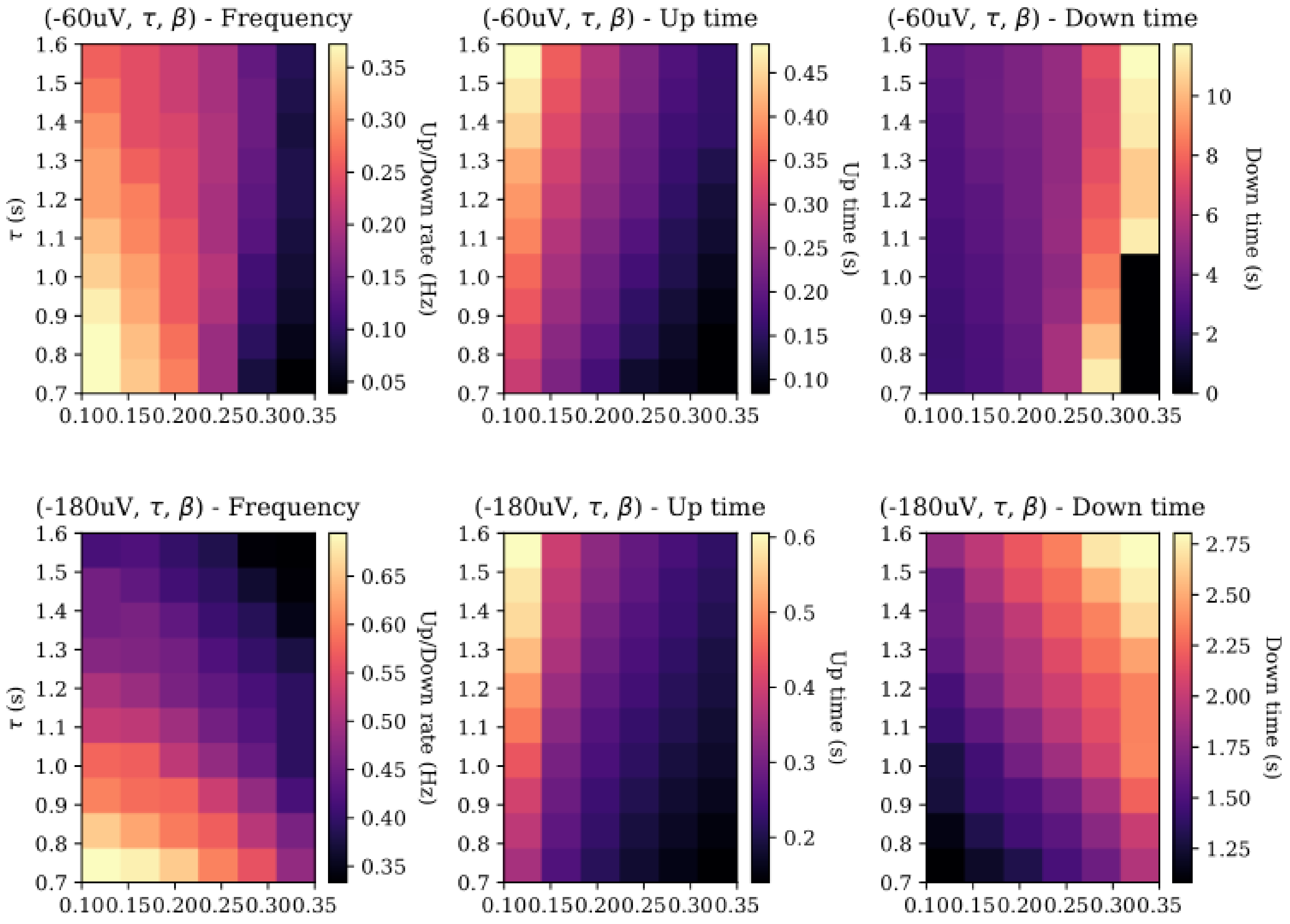
Fitting the model I: Hypothesis

– Hypothesis 1: Adaptation equation governs everything related to oscillations

$$\tau_{adapt} \frac{dU_{adapt}}{dt} = -U_{adapt} + \beta_T v_{exc}$$

$$\mu_U = \frac{E_l g_l + E_e \langle g_e \rangle + E_i \langle g_i \rangle}{\langle g_{tot} \rangle} - U_{adapt} + U_{\mathrm{external}}$$

– Hypothesis 2: A manual parameter search should be enough to fit the model


(-60uV, τ, β) - Frequency
(-60uV, τ, β) - Up time
(-60uV, τ, β) - Down time
(-180uV, τ, β) - Frequency
(-180uV, τ, β) - Up time
(-180uV, τ, β) - Down time
τ (s)
Up/Down rate (Hz)
Up time (s)
Down time (s)
0.100.150.200.250.300.35

x8

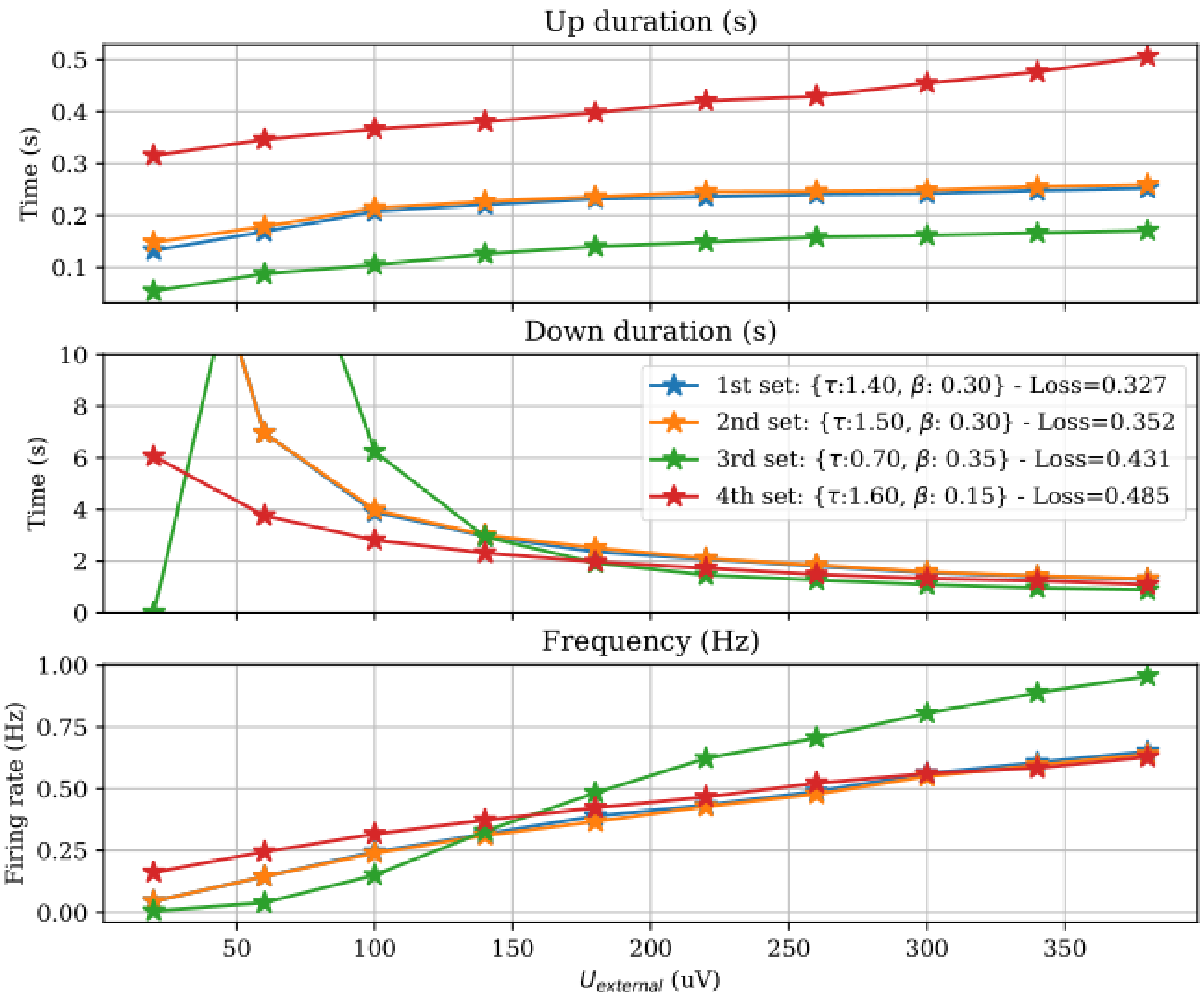
Fitting the model II: Algorithm

– Develop a parameter search algorithm that:
  – Optimizes over three objective variables (up, down, frequency)
  – Given three parameters
  – While one of the parameters is a search problem itself (U_ext)

– The final algorithm does:
  – Compute a custom wheighted squared loss for each parameter set

$$Loss_{\Omega}^{EF} = w_{freq}(freq_{\Omega} - freq_{measured})^2 + w_{down}(down_{\Omega} - down_{measured})^2 + w_{up}(up_{\Omega} - up_{measured})^2$$

  – Picks (only) smallest loss for each tau beta combination
  – Sorts parameters (tau, beta) according to smallest loss



Up duration (s)
Time (s)
Down duration (s)
Time (s)
1st set: {τ:1.40, β: 0.30} - Loss=0.327
2nd set: {τ:1.50, β: 0.30} - Loss=0.352
3rd set: {τ:0.70, β: 0.35} - Loss=0.431
4th set: {τ:1.60, β: 0.15} - Loss=0.485
Frequency (Hz)
Firing rate (Hz)
$U_{external}$ (uV)

Fitting the model III: X-axis

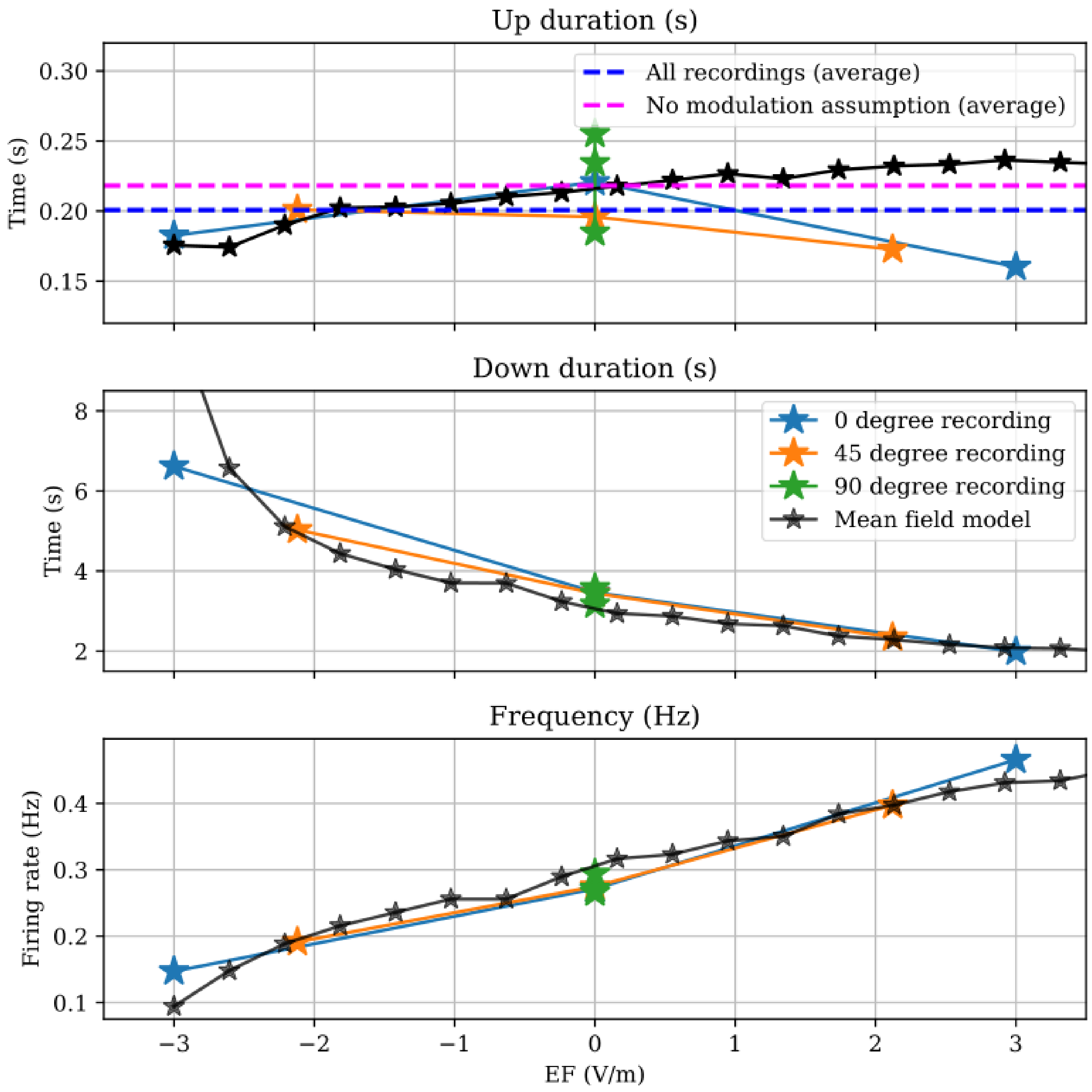
So far we have fitted the y-axis. Still missing the x-axis

– Scaling of the x-axis

$$U_{external} = \gamma_{external} * EF * \cos(angle).$$

– Shift of the x-axis

$$\theta_e^{new} = \theta_e^{old} + shift$$



Up duration (s)
All recordings (average)
No modulation assumption (average)
Time (s)
0.30
0.25
0.20
0.15
Down duration (s)
0 degree recording
45 degree recording
90 degree recording
Mean field model
Time (s)
8
6
4
2
Frequency (Hz)
Firing rate (Hz)
0.4
0.3
0.2
0.1
−3
−2
−1
0
1
2
3
EF (V/m)

Summary

– Studied and learnt about computational neuroscience

– Implemented the model and ran several simulations

– Wrote signal processing code for data analysis

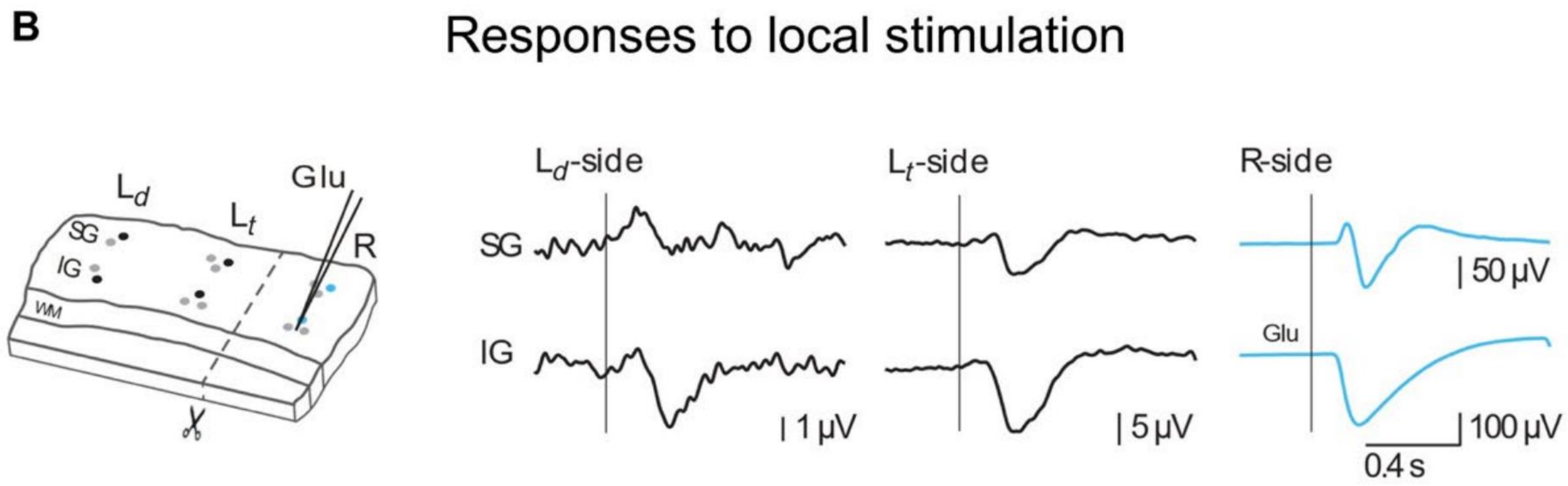
– Fitted model to the analyzed data

Thanks for your attention!

Biology: Rebollo et al. Publication [1]

- **Peak amplitude decreases with distance:**

L_t = 6.70±1.06 uV, L_d=3.54±0.82 uV



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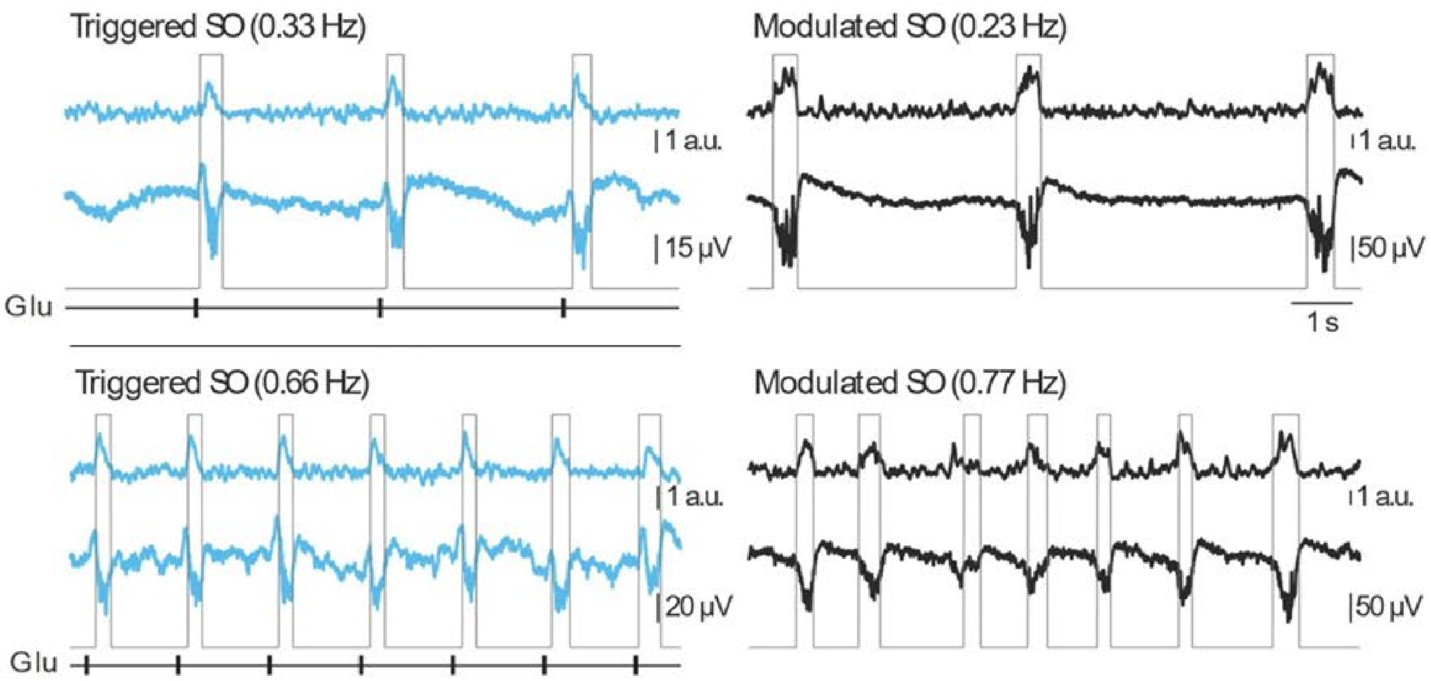
Biology: Rebollo et al. Publication [1]

- Endogenous fields affect synaptic activity



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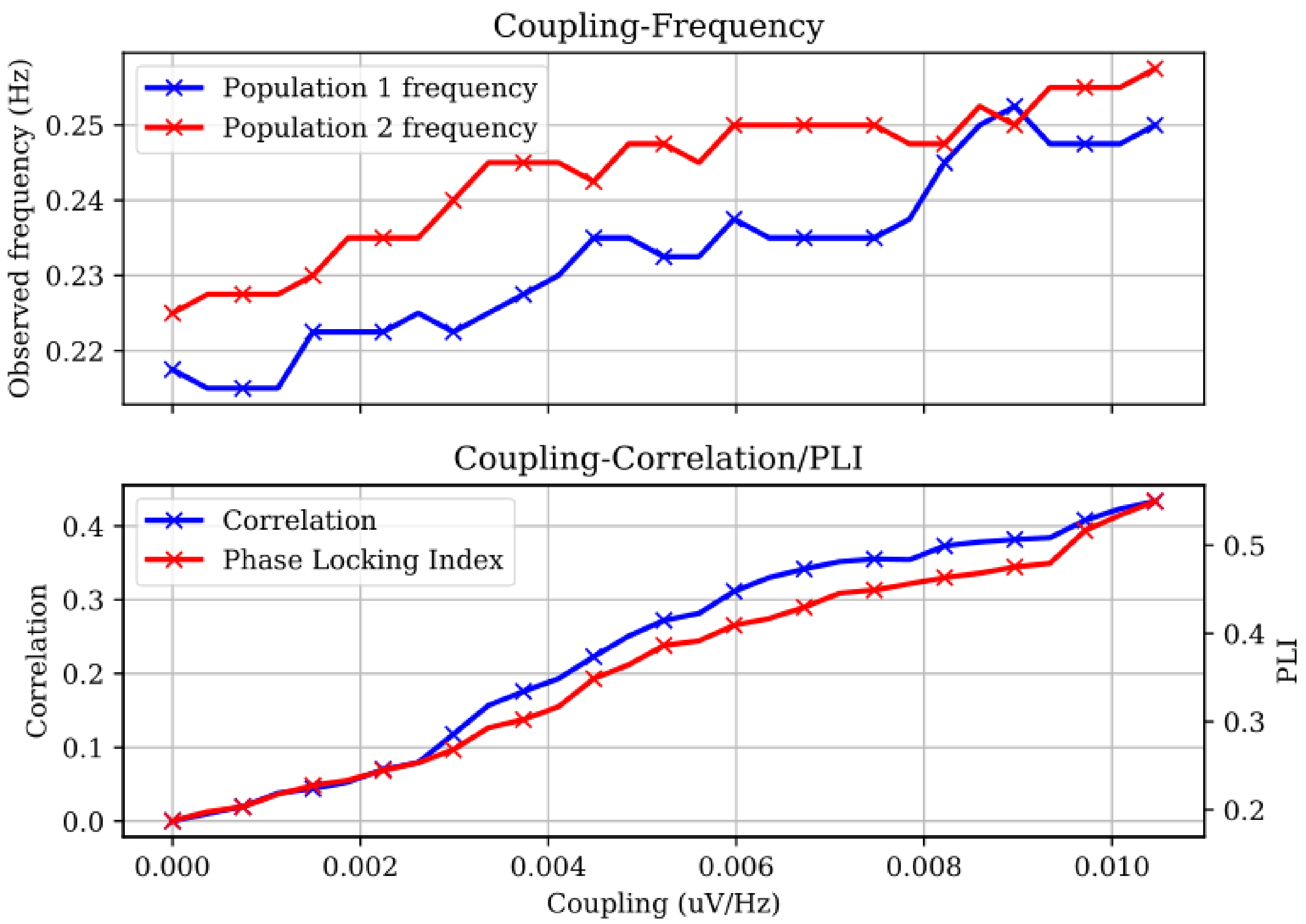
Model analysis: two populations I



Model analysis: two populations II