Cross-frequency coupling and information flow in a multiscale model of M1 microcircuits

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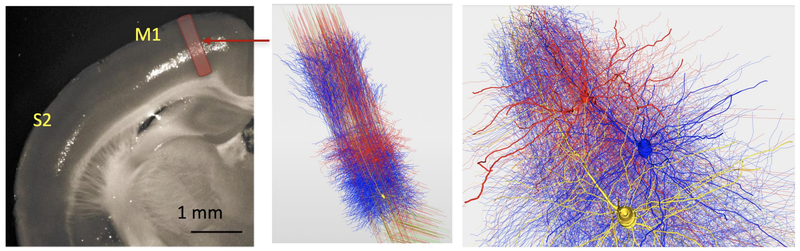
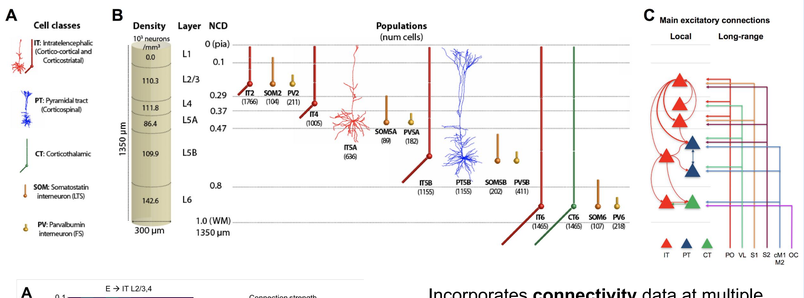
Multiscale model of M1 microcircuits

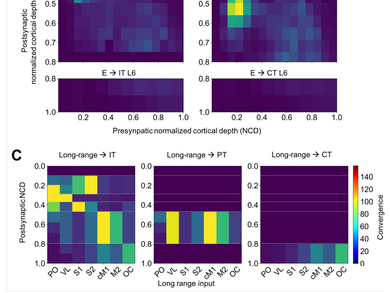
Modeled cylindrical volume of 300 μm (diameter) x 1350 μm (cortical depth) of mouse M1 with ~10k neurons (5 classes distributed in 15 populations) and ~30M synapses

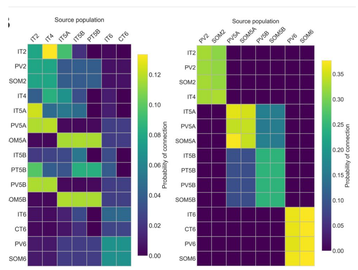


Cell morphology, physiology, laminar density and distribution based on experimental data.

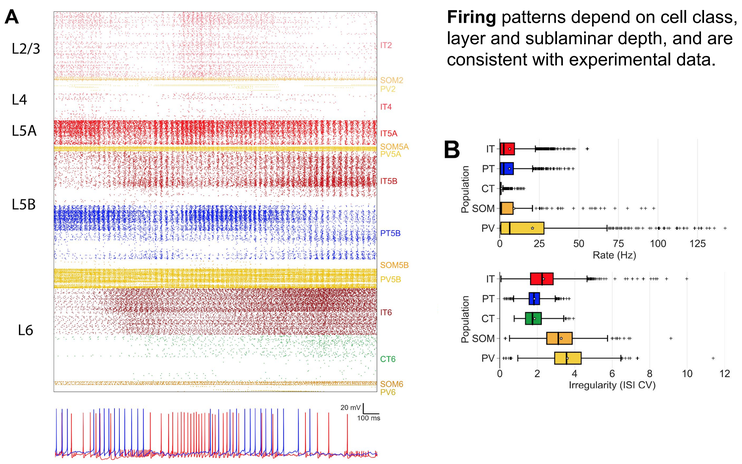


Incorporates **connectivity** data at multiple scales: long-range, local and dendritic, as a function of pre- and post-synaptic cell type and normalized cortical depth (NCD)

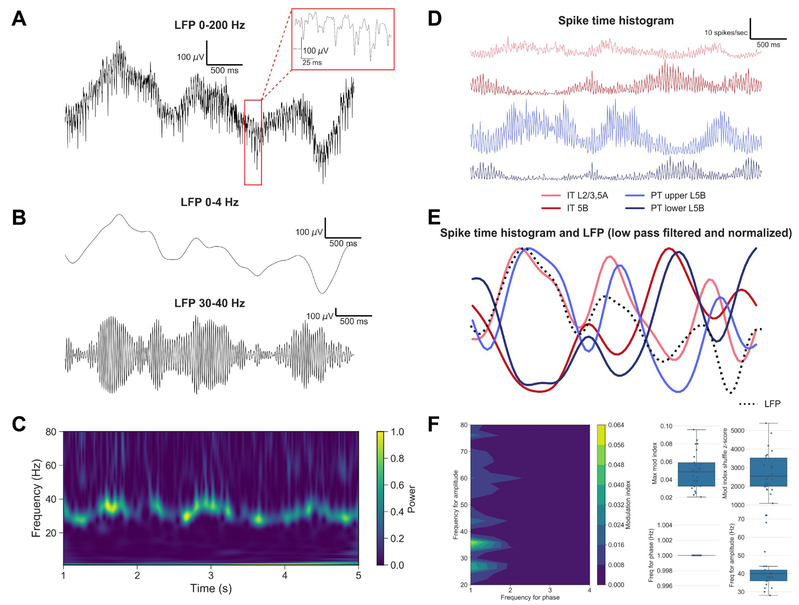




Firing patterns depend on cell class, layer and sublaminar depth, and are consistent with experimental data.



Cross-frequency coupling

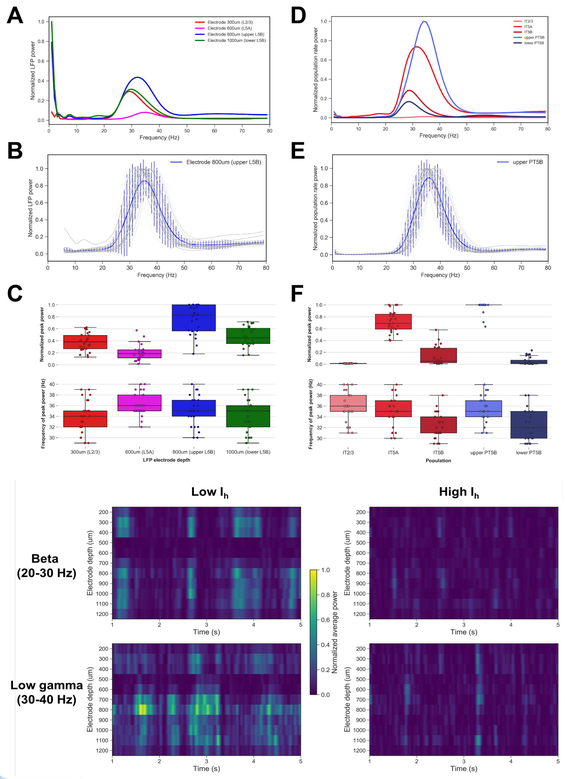


· Delta and beta/gamma oscillations **emerged** without rhythmic inputs.

· Delta phase was **coupled** to beta/gamma amplitude and frequency.

· Quantified via ***modulation index*** measure across N=25.

· Identified populations/subpopulations oscillating in **antiphase** (mediate frequency modulation)

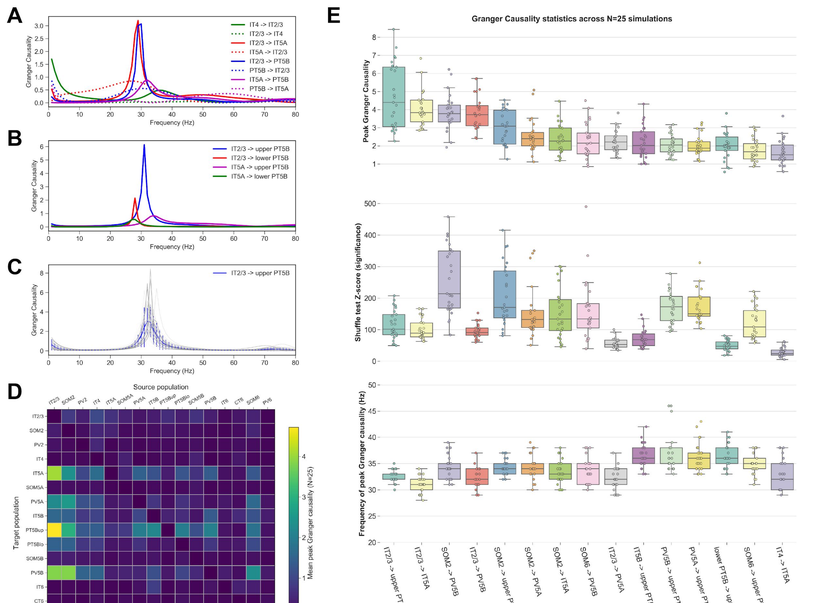


· **Peak frequencies** consistent across N=25 models with different randomizations.

· **Differences** in LFP vs spike time power spectra due to dendritic synaptic currents vs somatic spikes.

· High **Ih (HCN)** in L5B PT cells decreased beta and gamma power across all LFP electrodes (layers).

Information flow



· **Granger Causality** analysis confirmed strong IT → PT but not opposite; with peak in beta/gamma.

· **Functional connectivity** matrix revealed projections with stronger (IT2->PV5; SOM2->IT5,PT5,PV5 and PV5A->PT5B) and weaker (PV2->IT2,IT4; PV5B->SOM5B) effects than suggested by anatomy.

· Different information flow **peak frequencies** for superficial vs deep layers of origin.

Conclusions

· Developed biophysically detailed model of the M1 microcircuit integrating experimental data at multiple scales; can be used to explain observations, evaluate hypotheses, and make predictions.

· Spontaneous oscillations (delta and beta/gamma), phase-amplitude and phase-frequency coupling emerged without rhythmic inputs.

· Model allowed to investigate underlying mechanisms at the cell (e.g. ih modulation) and circuit level (e.g, populations oscillating in antiphase).

· Information flow (Granger causality) matrix revealed differences with structural connectivity, suggesting involvement of multi-synaptic inhibitory and disinhibitory pathways.

Publications

· Dura-Bernal S, Neymotin SA, Suter BA, Shepherd GMG, Lytton WW. (2019) **Multiscale dynamics and information flow in a data-driven model of the primary motor cortex microcircuit M1.** *bioRxiv 201707 (Under review in eLife)*

· Neymotin SA, Suter BA, Dura-Bernal S, Shepherd GMG, Migliore M, Lytton WW. (2017) **Optimizing computer models of corticospinal neurons to replicate in vitro dynamics.** J Neurophysiology; 117(1):148-162

· Dura-Bernal S, Suter B, Gleeson P, Cantarelli M, … , Neymotin SA, McDougal R, Hines M, Shepherd GMG, Lytton WW. (2019) **NetPyNE: a tool for data-driven multiscale modeling of brain circuits.** *eLife 2019;8:e44494* (www.netpyne.org)

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