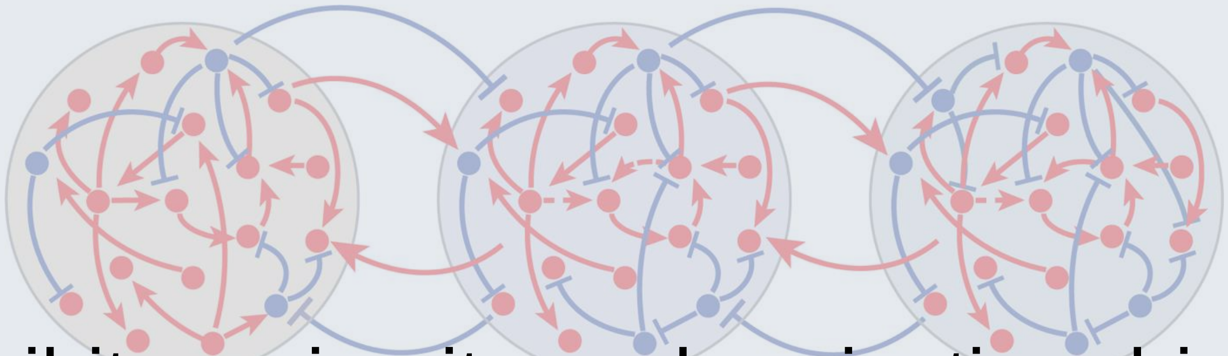

Inhibitory circuit synchronization drives working memory computation

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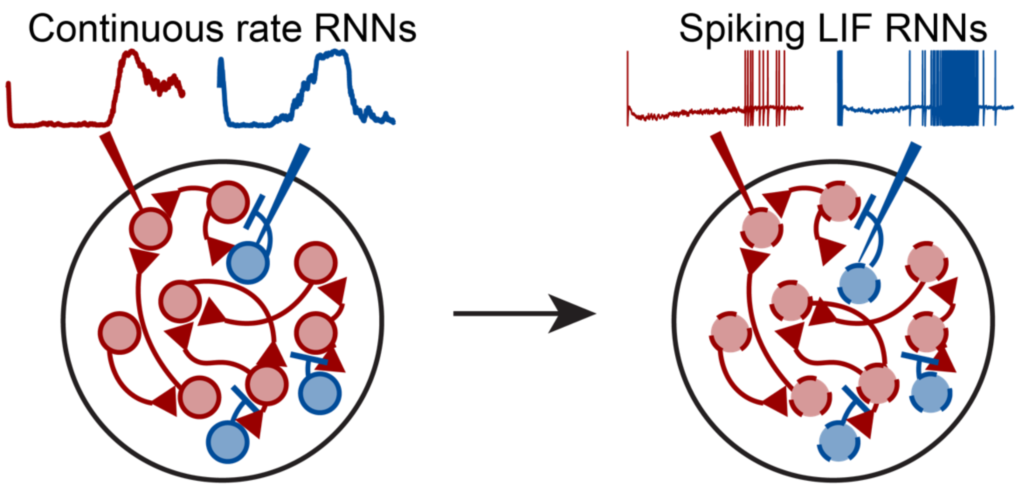
Abstract

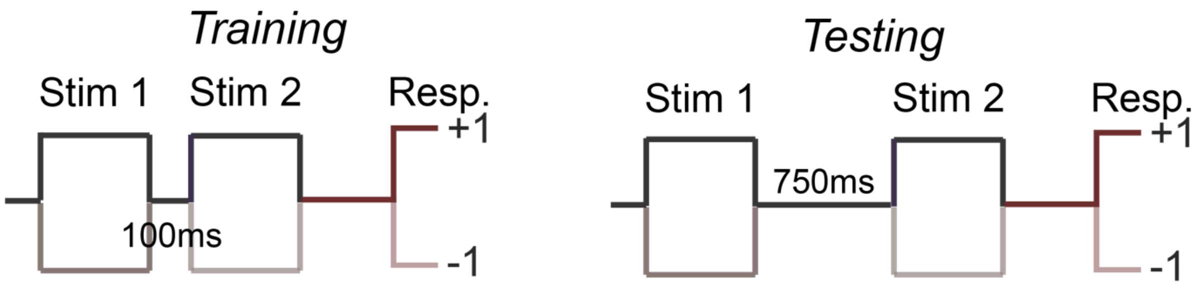
Recent advances in human intracranial recordings have significantly deepened our understanding of complex cognitive functions like working memory (WM) at the circuit level. While single-neuron analyses, primarily within the medial temporal lobes, have elucidated how individual neurons contribute to memory computation, the role of local field potential (LFP) dynamics in complementing single-unit activity during WM tasks remains poorly understood. To address this, we developed biologically plausible spiking recurrent neural networks (RNNs) trained on a delayed match-to-sample (DMS) task which involves neural coding and persistent representation of sequential stimuli. In these spiking models, we computed LFP-like signals via post-synaptic input currents. Our results reveal that inhibitory power spectra vary significantly across frequency bands based on WM performance. Furthermore, disinhibitory circuits (inhibitory-to-inhibitory; I→I connections) are essential for generating neural synchrony in high gamma frequencies that are critical for WM maintenance. Inhibitory synchronization emerged as a key mechanism in maintaining memory representation, suggesting potentially universal computational principles of inhibition in memory. These findings advance our understanding in computational and systems neuroscience by providing a theoretical framework that integrates gamma oscillations and inhibitory signaling in cognitive function. Finally, we are currently in the process of validating these predictions using intracranial recordings from human participants performing DMS tasks, which will offer deeper insights into the circuit dynamics underlying working memory computation in humans and further bridge the gap between computational and biological neural networks.

Recurrent neural network (RNN) models & delayed match-to-sample (DMS) task

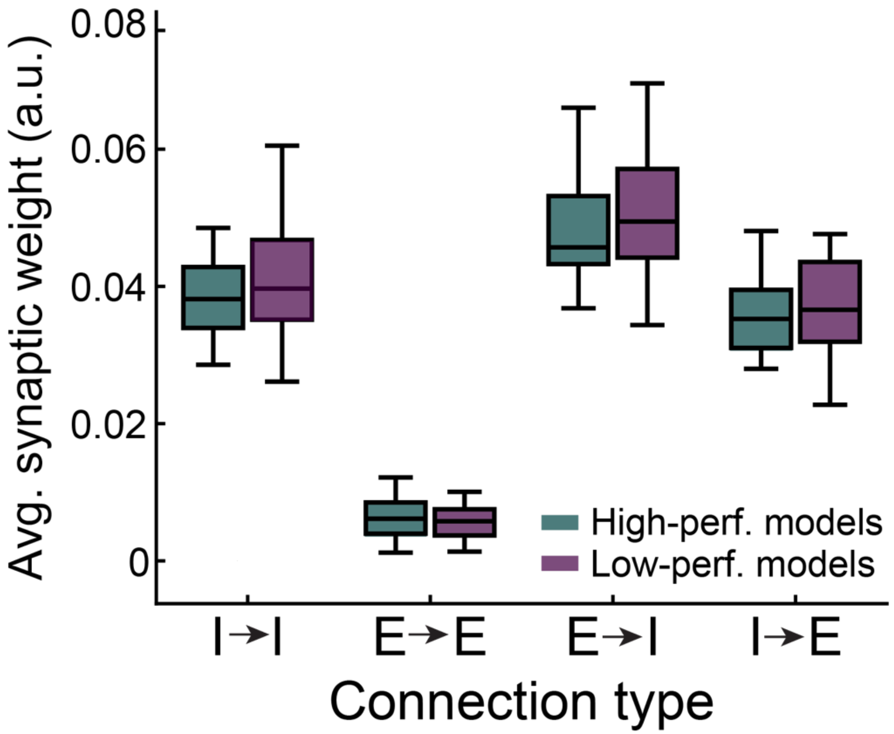


Rate and leaky integrate-and-fire (LIF) models contain 200 units with 80% excitatory (red) and 20% inhibitory (blue). Outputs include firing rates and spikes respectively.

Kim et al, PNAS, 2019

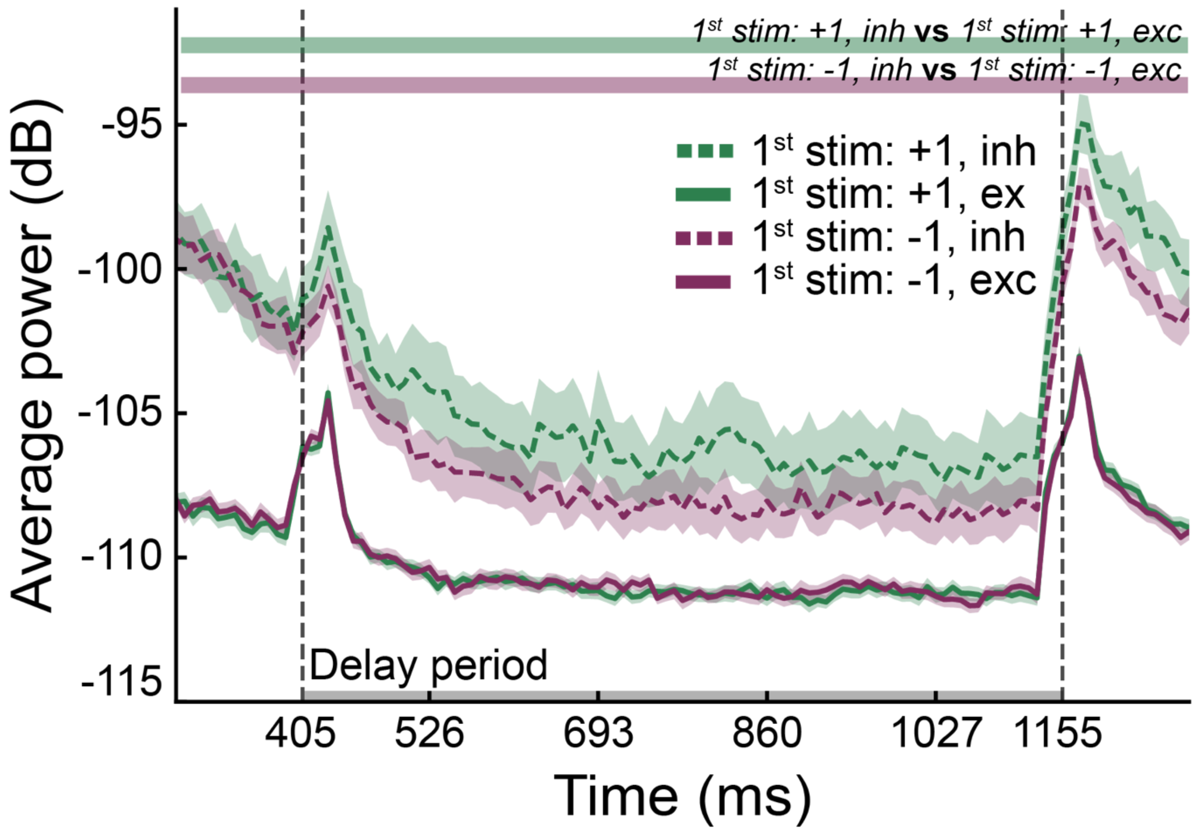


The DMS task paradigm requires memory of stimulus 1 across a delay period, after which stimulus 2 is shown and a response of +1 (same stimuli) or -1 (different stimuli) is generated.

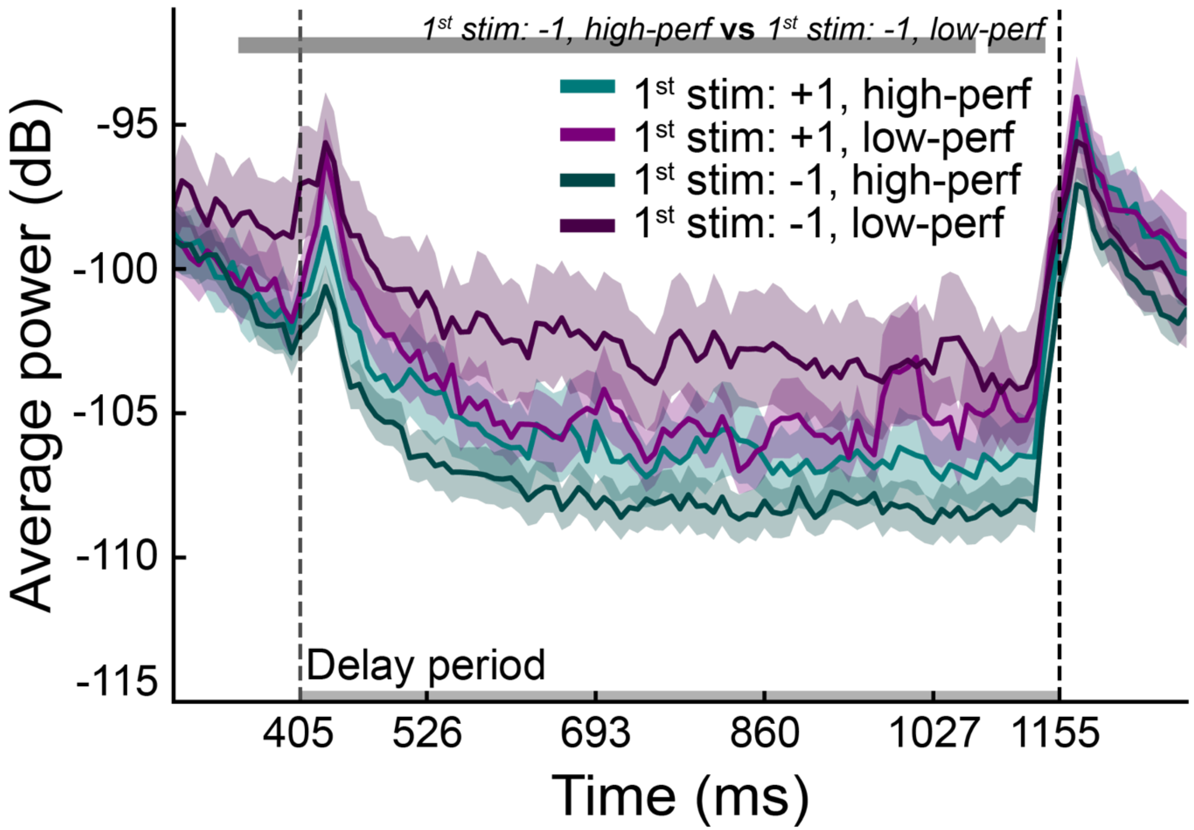


No differences in average synaptic weights between high-performing (n=41) and low-performing (n=26) models ($p>0.05$, Wilcoxon rank-sum test).

High gamma inhibitory signals contribute to working memory

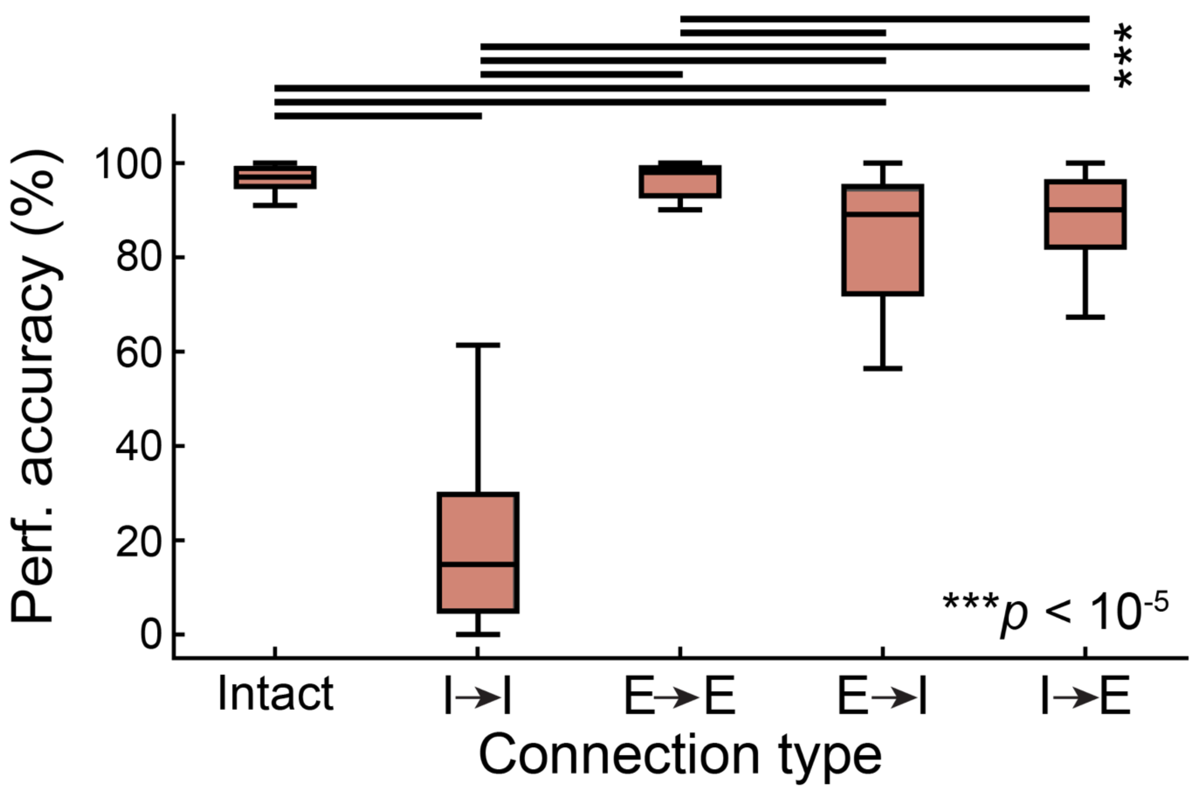


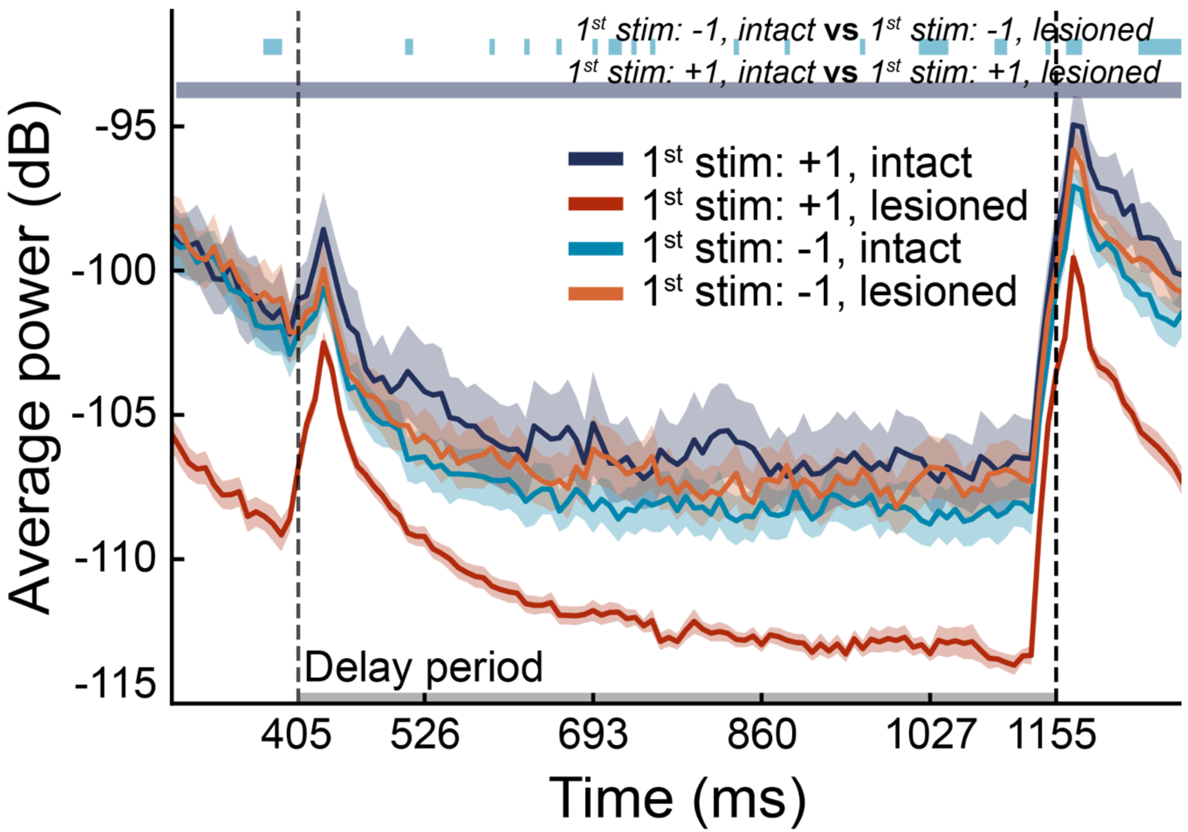
Inhibitory power in the high gamma band is different from excitatory power ($p<0.05$, bootstrapped n=1000 repetitions)



Inhibitory high gamma power is different between high-performing and low-performing models during the delay period ($p<0.05$, bootstrapped n=1000 repetitions)

Inhibitory-to-inhibitory (I-I) connections are critical for high gamma power and working memory





Lesioning inhibitory-to-inhibitory (I-I) connections results in decreased working memory performance ($p<0.00001$ by Wilcoxon rank-sum test)

Lesioning I-I connections results in decreased inhibitory high gamma power ($p<0.05$, bootstrapped $n=1000$ repetitions)

Conclusions

- We can train a spiking LIF model to perform a working memory task and perform spectral analyses on the post-synaptic input current to gain insights on population-level dynamics
- Inhibitory-to-inhibitory connections are critical for generating high gamma power during working memory maintenance
- Next steps: Investigate whether LFP changes similar to those observed in our model also take place in human cortical areas via analysis of single neuron and LFP data from human intracranial recordings

References

Kim, R., Li, Y. & Sejnowski, T. J. Simple framework for constructing functional spiking recurrent neural networks. *Proceedings of the National Academy of Sciences* **116**, 22811–22820 (2019).

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