Mechanisms of top-down attentional control in thalamic reticular circuits and effects of inhibitory dysfunction

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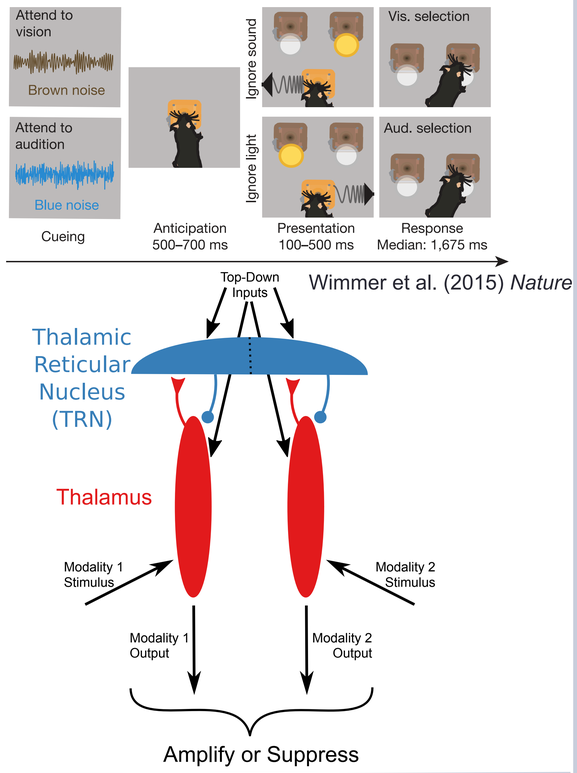
Introduction

Attention is a critical cognitive process, allowing us to filter unwanted stimuli and focus on signals important to the current task. Thalamus is a key area for attention and is implicated in neuropsychiatric disorders such as Schizophrenia. There has been a growing body of studies recorded thalamus during behavioral tasks, in combination with pharmacology or optogenetics. A thalamic models in the in-vivo regime that could summarize empirical data and provide predictions is in dire need.

Here, we built a thalamic circuit model in an in-vivo awake state. Well constrained by empirical data, the model exhibits attention effects found across studies. We also identified disorder-related perturbations which have altered thalamic circuit dynamics consistent to disease-related states.

Attention and top-down control across thalamic modalities



References: Halassa et al. (2011) *Nat Neurosci*; Wimmer et al. (2015) *Nature*; Halassa & Acsády (2016) *Trends Neurosci*; Nakajima et al. (2019) *Neuron*; Aizenberg et al (2019) *Cell Reports*

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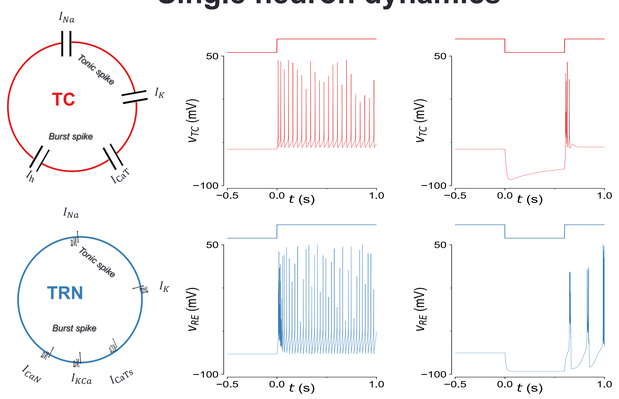
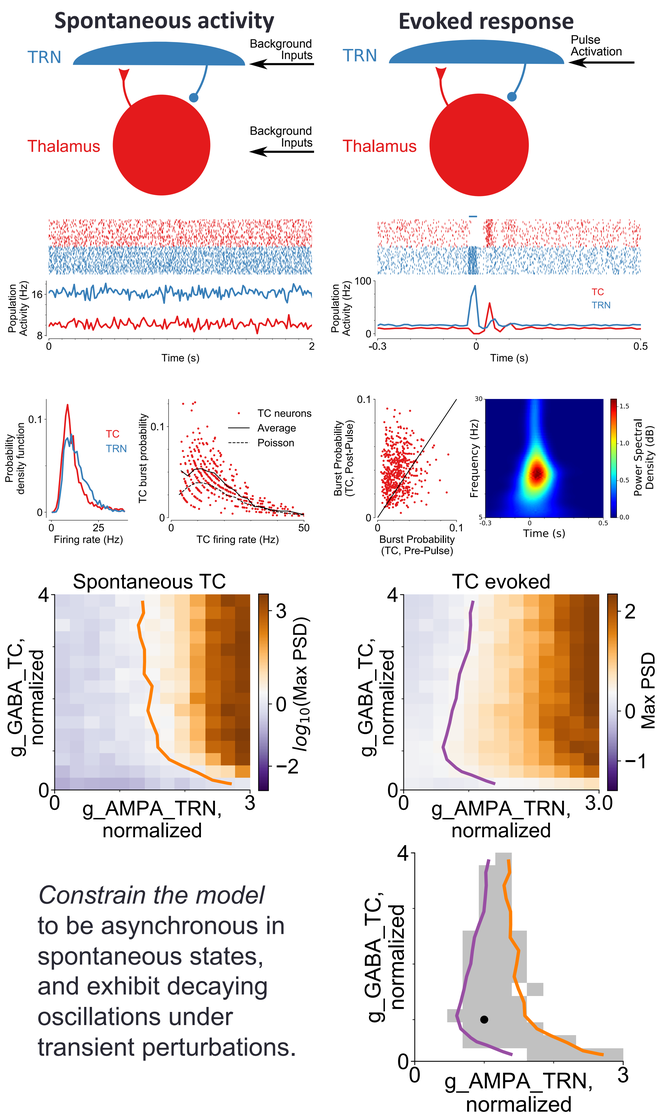
Single neuron dynamics

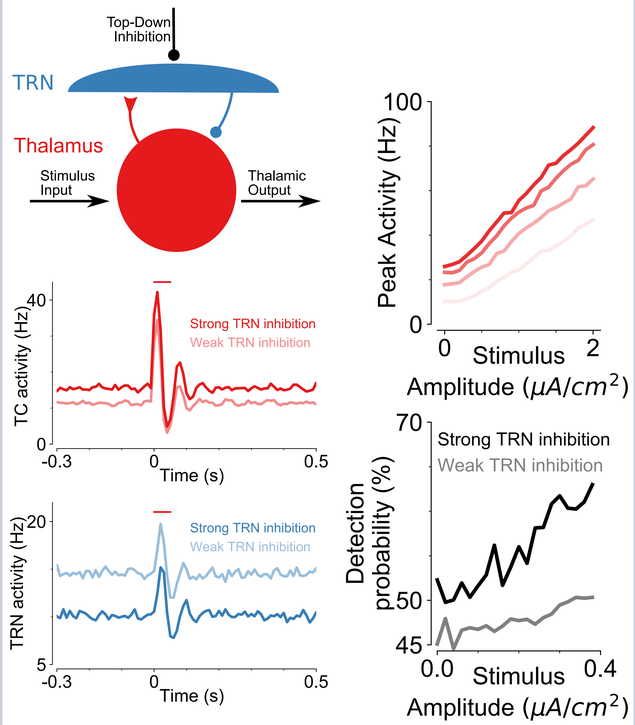


A circuit model in the *in vivo* regime



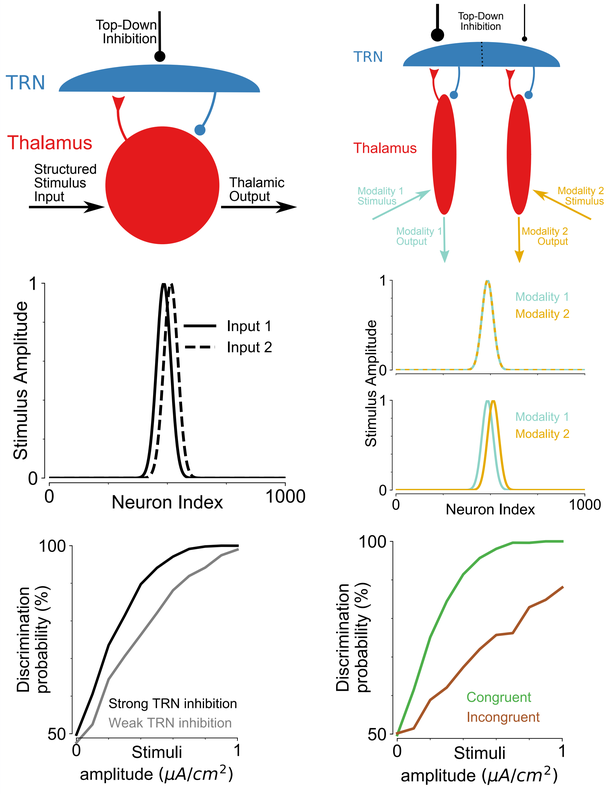
Constrain the model to be asynchronous in spontaneous states, and exhibit decaying oscillations under transient perturbations.

Attentional modulation across modalities

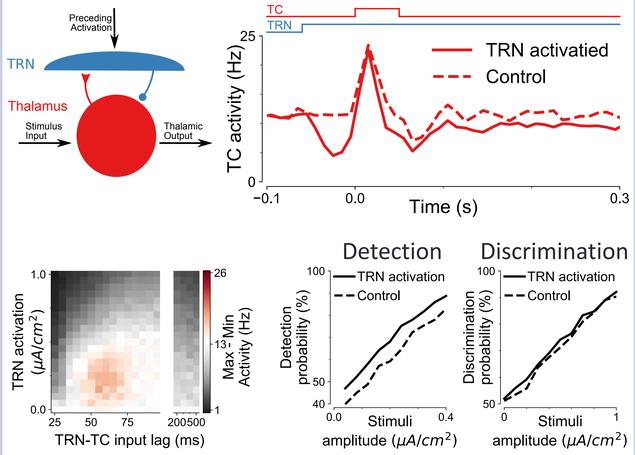


Top-down TRN inhibition disinhibits thalamus, modulating its response gain.

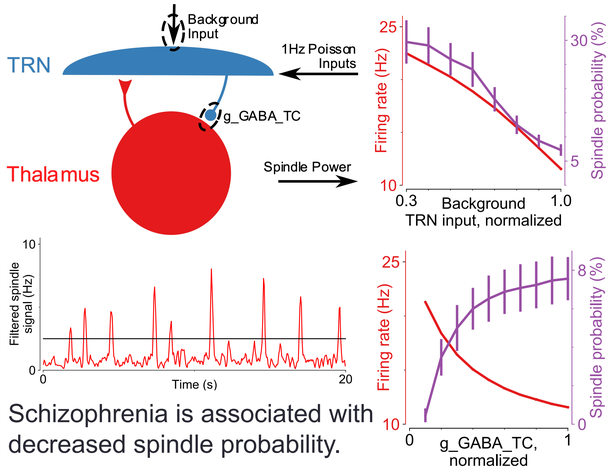
Attention effects on discrimination



Attention effects via transient TRN activation



Dissociable predictions from inhibitory dysfunction



Schizophrenia is associated with decreased spindle probability.

Conclusion

- *In vivo* regime thalamic reticular circuit model
- Attention effects mediated by top-down modulation
- Distinct pathways for inhibitory dysfunction differentially alter circuit dynamics

Future Directions

- Inhibitory dysfunction of attention modulation
- Other disease-related mechanisms of dysfunction
- Distributed thalamocortical interactions