Modeling Differences Between Schizophrenic and Control Responses to Auditory Click Stimuli Over a Range of Frequencies

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Introduction

- Patients with schizophrenia show **decreased preference for synchronization at 40 Hz** and **increased preference for 20 Hz** when presented with periodic auditory click stimuli
- Previous paper found **increasing IPSC decay time** replicated this at 20, 30, and 40 Hz
- We **extend results using a mean-field theory** over a range of frequencies and IPSC decay times, in addition to the few studied previously
- We **study the strength of excitatory and inhibitory connections** and how these could explain differences over more frequencies than previously considered

Methods

- **Theta (QIF) neuron model and the Ott-Antonsen ansatz**
- Differential equations for mean firing rate: r(t), mean membrane voltage: v(t), and mean synaptic input: s(t)
- Two populations of neurons (e is excitatory and i is inhibitory)
- **Models a large number of neurons with a small number of equations.**

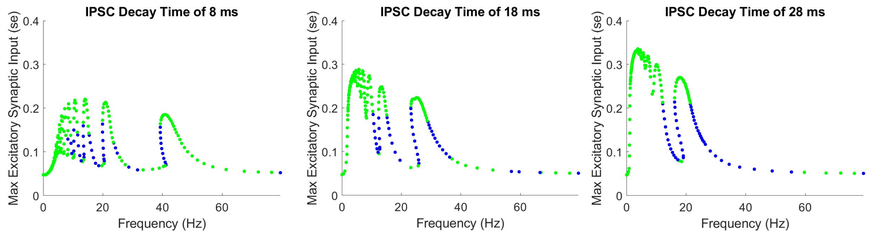
$$\frac{dr_e}{dt} = 2r_e v_e + \sigma$$
$$\frac{dv_e}{dt} = v_e^2 - r_e^2 + I_{drive}^e + I_f + g_{ee}s_e - g_{ie}s_i$$
$$\frac{ds_e}{dt} = \frac{1}{\tau_e}\left(-s_e + \frac{r_e}{\pi}\right)$$
$$\frac{dr_i}{dt} = 2r_i v_i + \sigma$$
$$\frac{dv_i}{dt} = v_i^2 - r_i^2 + I_{drive}^i + I_f + g_{ei}s_e - g_{ii}s_i$$
$$\frac{ds_i}{dt} = \frac{1}{\tau_i}\left(-s_i + \frac{r_i}{\pi}\right)$$

$$I_f = amp * e^{-\beta(1-\cos(\omega t))}$$

The **default parameter values** were

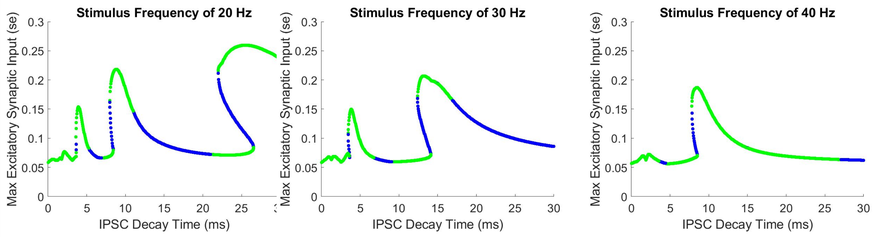
$$I_{drive}^e = 0.4,\ I_{drive}^i = 0,\ \sigma = 0.1$$
$$g_{ee} = 5.2,\ g_{ie} = 6.0,\ g_{ei} = 8.0,\ g_{ii} = 2.0$$
$$\tau_e = 2,\ \tau_{i,ctrl} = 8,\ \tau_{i,SZ} = 28$$
$$\beta = 50,\ amp = 0.3$$

As IPSC decay time increases, the high frequency peak in synchronization shifts from 40 Hz to 20 Hz, matching (some) experimental results



- Green is stable oscillations at the driving frequency, blue is period doubling bifurcations (non-regular oscillations) that match clinical results at 20 and 40 Hz
- Suggests bifurcations could also occur clinically at other frequencies
- Significant increase at 20 Hz found in some studies, not universally replicated
- Suggested to only occur in some patients -- could be a marker for extended IPSC decay time

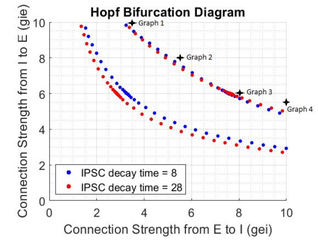
As stimulus frequency increases, peaks in synchronization tend towards lower IPSC decay times, matching expectations

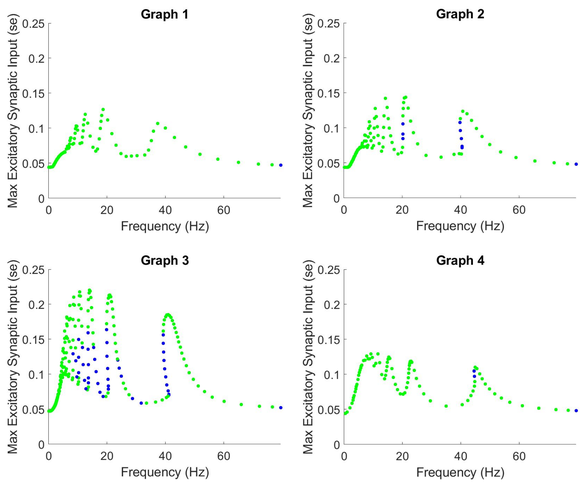


- Green is stable oscillations, blue is both period doubling and saddle node bifurcations
- Saddle node occurs at 20 Hz for large IPSC decay times
- Period doubling consistent with previous results
- Saddle node bifurcation could also explain discrepancies at 20 Hz

As connection strength changes, synchronization is decreased across all frequencies, suggesting need to consider additional factors

- Middle region has connection strengths where oscillations occur regardless of external stimuli
- Take points just outside this region, so external stimuli pushes the system to oscillations
- IPSC decay time has little effect on this region, used control value (8 ms)





- Green is stable oscillations, blue is period doubling bifurcations
- Synchronization is uniformly decreased over frequencies but experiments indicate non-uniform changes

Conclusions and Future Directions

- Using slightly modified model, previous results were replicated and extended over a range of parameters, revealing bifurcations and other interesting behaviors
- Variant of schizophrenia may include extended IPSC decay time that directly contributes to increased 20 Hz response
- Comparison to experimental results suggest additional factors
- Changes to the connection strength between excitatory and inhibitory populations could explain decreased response over an entire range of frequencies
- Future work could model other differences in observed responses (e.g. non-uniform decreases)

Acknowledgements

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