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Modelling sleep EEG in children with epilepsy

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Introduction/Objectives

- The Electroencephalogram (EEG) provides a noninvasive measure of large scale brain activity
- Non-rapid eye movement (NREM) sleep is dominated by slow (delta) wave activity (0.6Hz - 4.5 Hz)
- Previous studies have provided evidence for differences in slow wave activity in children with epilepsy versus healthy controls[1]
- However, it is unclear what the underlying mechanisms driving these differences are and how they relate to the excitability of the epileptic brain

Slow wave activity in patients and controls

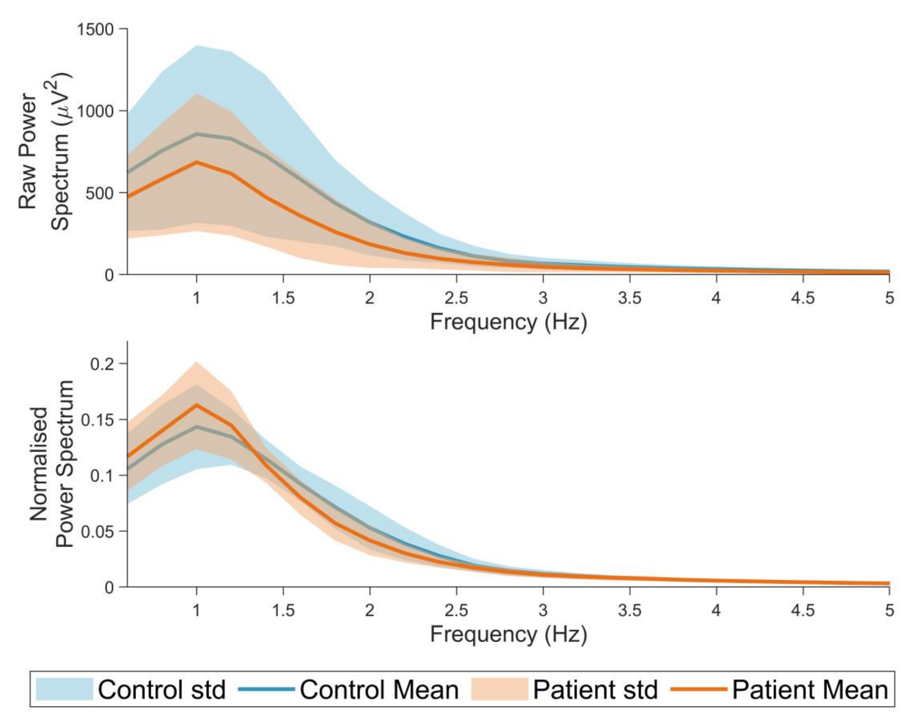

Figure 1: Power spectrum in patients with epilepsy and controls. There are subtle differences in the delta power between each cohort.

Methods

- Neural mass models (NMMs) can be used to simulate brain dynamics on the same scale as EEG recordings[2]

NMM structure

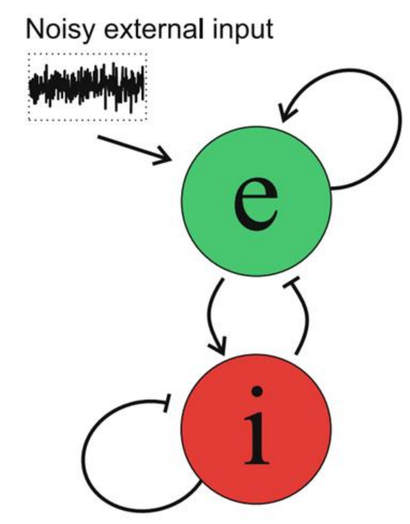

Figure 2: Structure of the NMM model used in this work. Neurones are grouped into excitatory and inhibitory populations.

$$I_k = g_k(V_n - E_k)S_{n_1 n_2}$$

- The conductance based model contains 22 parameters and adjusting these affects the dynamics

Horizontal visibility graph (HVG)

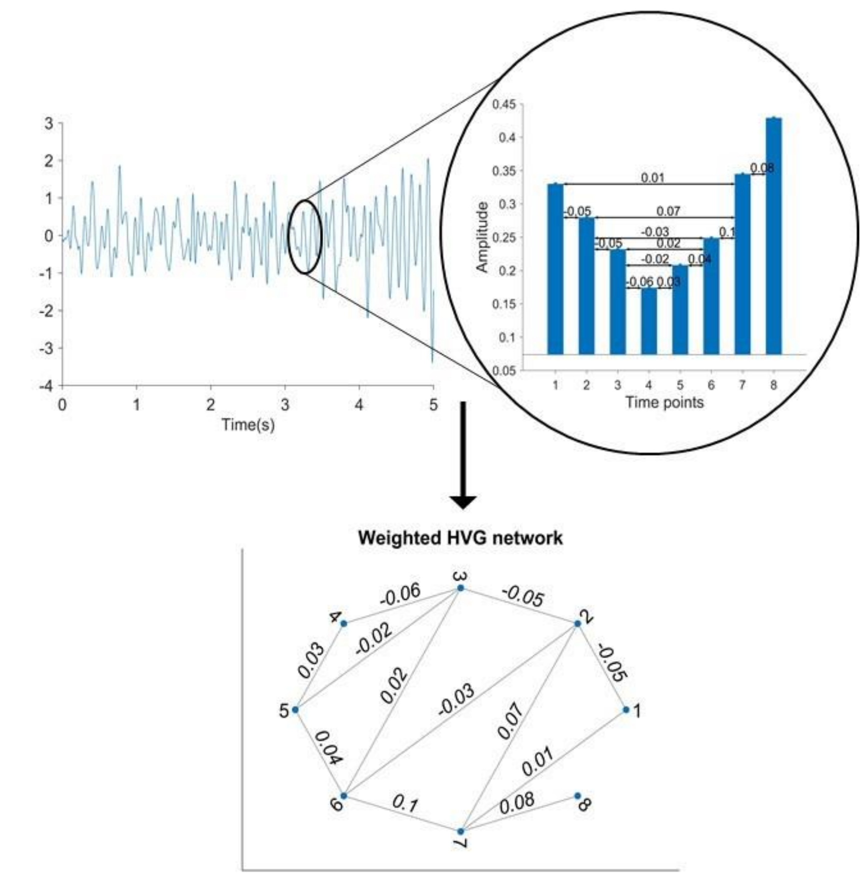

Figure 3: Horizontal visibility graph converts a time series into a graph network. The sum of the node degree of this network is used as an objective in the optimization.

- We then apply a **multi-objective genetic algorithm** to find the areas in parameter space where the model recreates these properties of the data

Results

- The model can accurately recreate both the power spectrum and the HVG node degree distribution across data subjects
- We repeat this optimization process many independent times and record the parameters that can explain the EEG data
- We find that the resulting Nernst potential of the leak and AMPA channels are significantly different between the controls and patients
- This corresponds to an increased AMPA current and stronger excitatory synapse in patients, counterbalanced by a reduced leak current to maintain homeostasis

Model fits to data

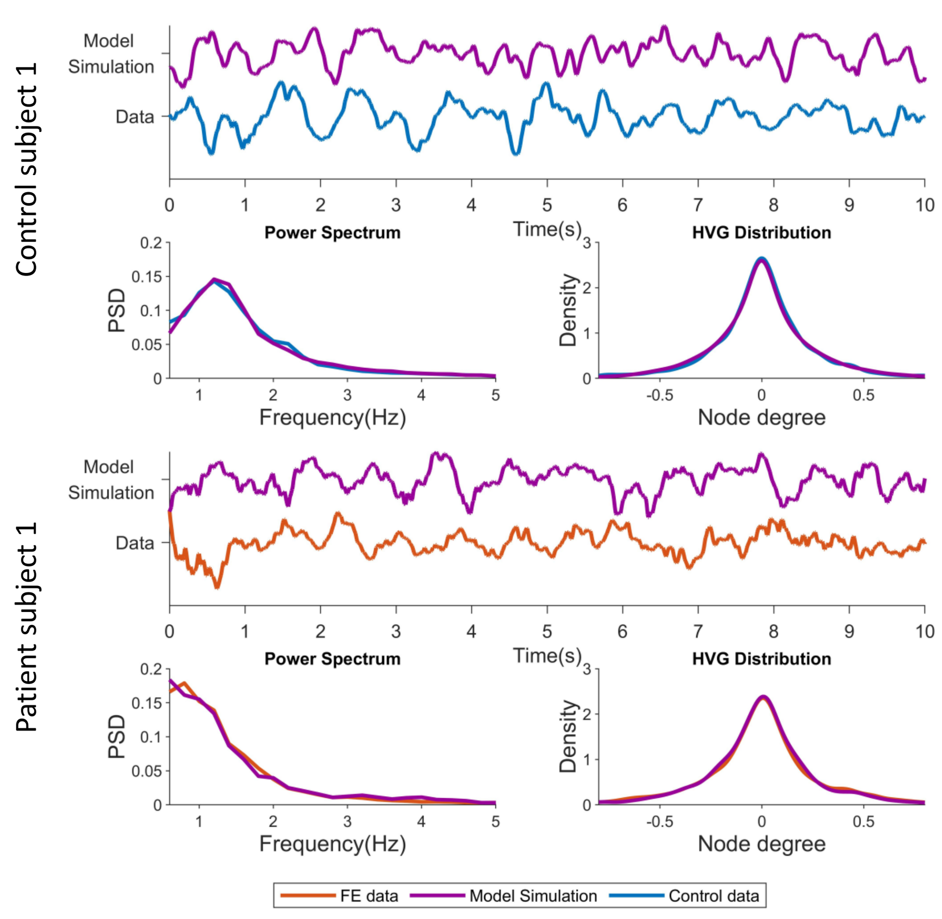

Figure 4: Example model fits to (a) control and (b) patient subjects. The model is capable of accurately recreating the rhythms during NREM sleep.

Parameter locations from model fits to patients and controls

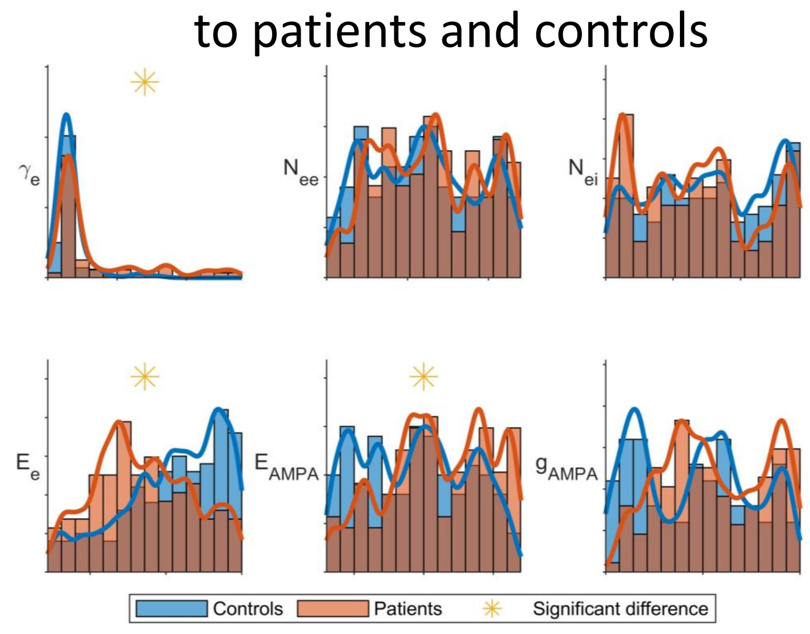

Figure 5: Optimal parameter locations from optimizing to the control and patient data (for a subset of the parameters). Significant differences are given by a Rank sum test with Bonferroni correction.

Currents from model fits to patients and controls

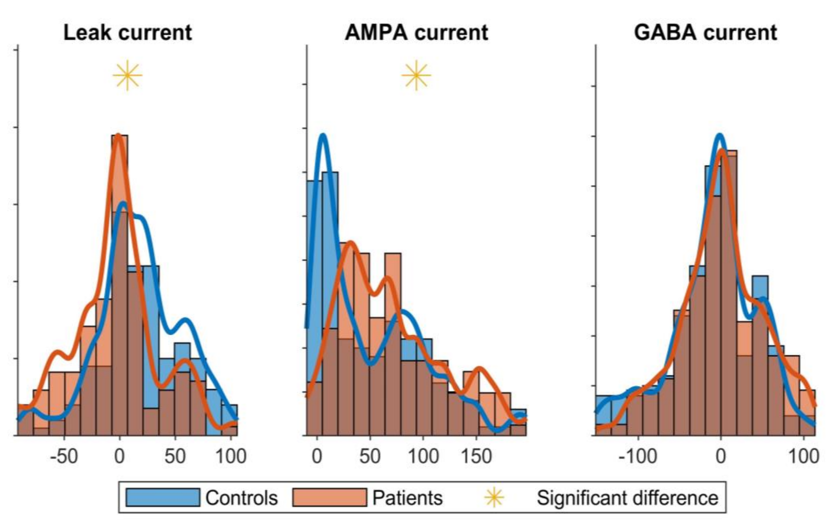

Figure 6: Projection on the resulting currents of the leak, AMPA and GABA channels from optimizing to the control and patient data.

Discussion/Conclusion

- We propose more sophisticated optimization methods, such as the one applied herein, are required to better understand the mechanisms generating EEG data
- We find that global multi-objective optimization can find regions in parameter space that accurately describe NREM sleep data in people with epilepsy and controls
- The model explains the differences observed in the data by changes to the excitatory synapses
- The model now provides a platform to test and apply treatments/perturbations in silico
- We can also use the model to explore how these differences in parameters may support increased propensity for seizures

References

1. Maria H Eriksson, Torsten Baldeweg, Ronit Pressler, Stewart G Boyd, Reto Huber, J Helen Cross, Bigna K Bölsterli, Samantha YS Chan medRxiv 2020.11.05.20226514; doi: https://doi.org/10.1101/2020.11.05.20226514
2. PrWeigenand A, Schellenberger Costa M, Ngo HVV, Claussen JC, Martinetz T (2014) Characterization of K-Complexes and Slow Wave Activity in a Neural Mass Model. PLOS Computational Biology 10(11): e1003923; doi: https://doi.org/10.1371/journal.pcbi.1003923