A Mechanistic Model Investigating iTBS Effects and TMS Data Trends in Individuals with Tourette's and Healthy Controls

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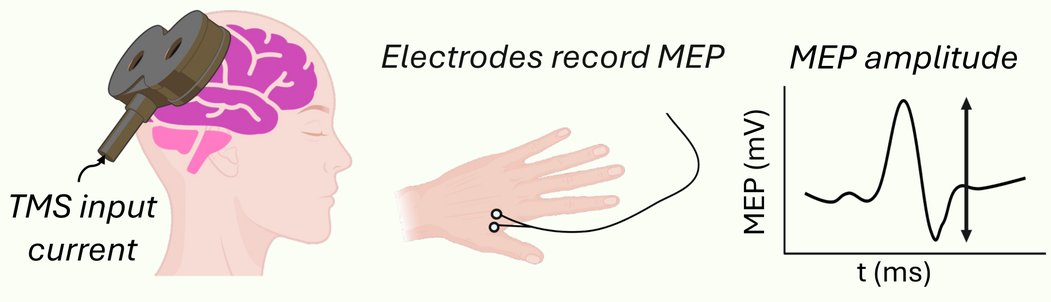
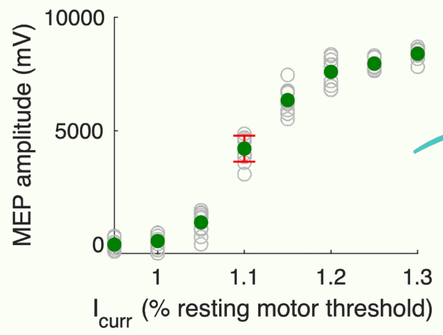
Overview

- **Tourette Syndrome (TS)** is a common neurological disorder (1 in 100 children in the UK) characterised by motor and vocal tics. The precise mechanisms underlying its symptoms are poorly understood.
- **Transcranial Magnetic Stimulation (TMS)** studies have shown differences between individuals with TS and healthy controls (HC) in trial-by-trial variability, indexed by the **coefficient of variation (CV)** of motor-evoked potentials (MEP) in response to stimulation.
- We developed a **mechanistic model** and fitted it to data, with changes in the fitting parameters before and after **intermittent theta-burst stimulation (iTBS)** and between patients and controls, providing potential **biomarkers** to differentiate between groups.

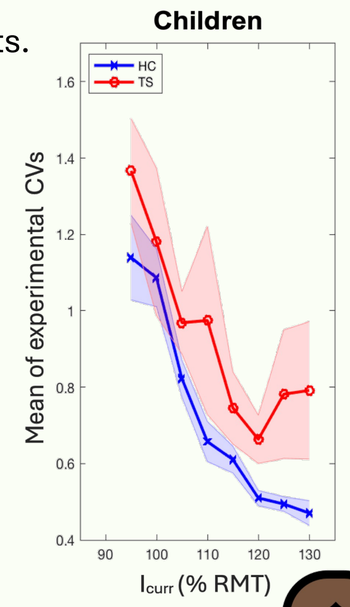
Experimental data

- **Motor-Evoked Potential** data obtained from 17 adults and 7 children with TS, and 18 healthy adults and 9 healthy children, by applying single pulse TMS to the motor cortex.
- MEP data before and after iTBS on motor cortex, for 10 healthy adults.





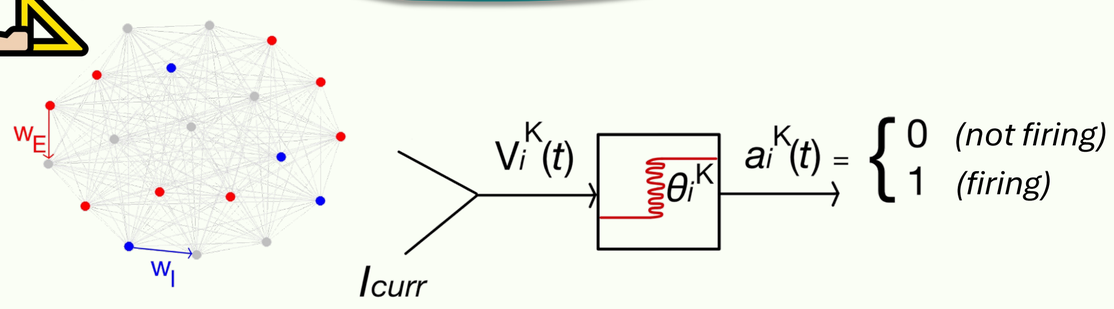
Coefficient of Variation = standard deviation / mean



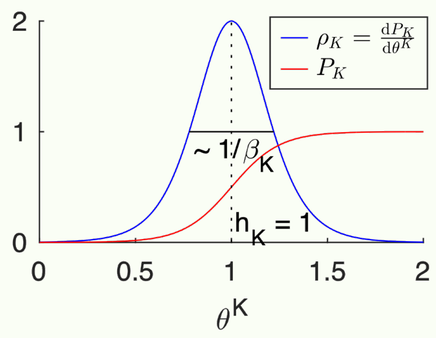
The coefficient of variation is higher in children with Tourette's than in healthy controls. In adults, the values do not differ!

We can build a biology-driven model that predicts these trends to help understand the possible neurophysiological differences that give rise to them!

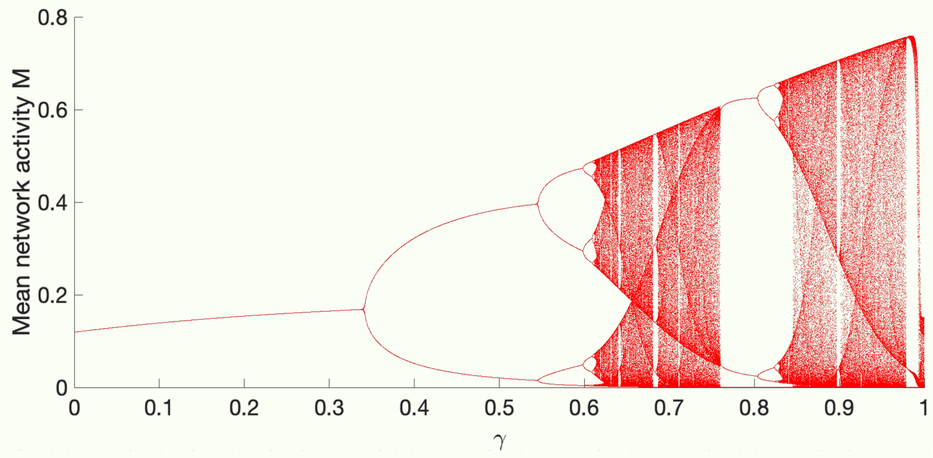
Mathematical model



- Fully connected **network** of inhibitory (I) and excitatory (E) neurons representing a neuronal pool under the TMS coil.
- We derive equations for the membrane potential V_i^K of each neuron, $K \in \{I, E\}$.
- Neurons fire when their membrane potential exceeds a threshold θ_i^K.
- To account for variability, we draw the firing threshold from distribution ρ_K.



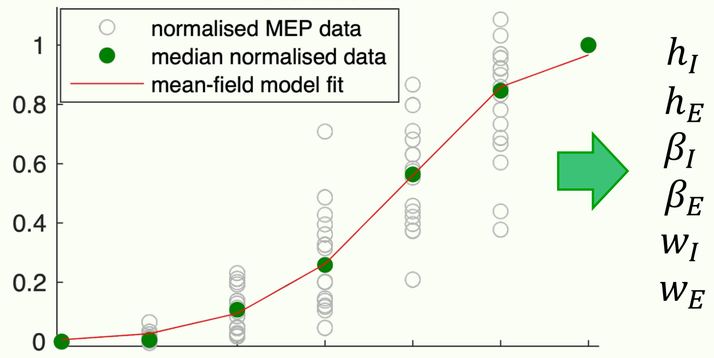
- We interpret normalised MEP curves as the percentage of neurons firing.
- Using a **mean-field** approach, we obtain equations for the mean network activity $M(t)$ and take its steady state M^* as the representative value.



- Bifurcation diagrams help identify the parameters' space ensuring the system stabilises. We assume membrane time constant $\gamma \approx 0$.

Model fit to data

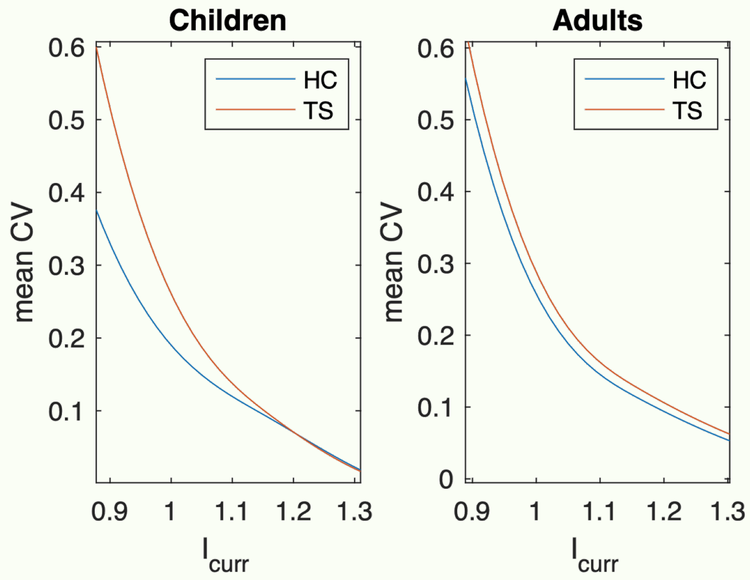
- We find the parameter values that best match model to data, using the least squares method.



- Considering the median of each group's data as the reference curve, we fit the model to it and obtain the groups' parameters.

Model CV

- By fitting, we get each individual's parameters and can compute their model CV by simulating the network model multiple times.



Results and Future work

- Our model suggests that connection strengths $|w_I|, w_E$ of inhibitory and excitatory neurons might be weaker in TS individuals than in age-matched controls.
- By fitting the model to the MEP data before and after iTBS stimulation, we observe an increase in h_I in 70% of individuals, consistent with iTBS being excitatory.
- Statistical tests on larger datasets can provide more insights into the parameters' trends between groups.
- In the future, we will explore MEP data before and after the inhibitory continuous theta-burst stimulation.

References

[1] C. Capaday. On the variability of motor-evoked potentials: experimental results and mathematical model. *Experimental Brain Research*, 2021.
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