Abstract BARCCSYN 2026

Epileptic seizures do not occur randomly: their onset depends on slow circadian rhythms and fast fluctuations in brain state. Neurotransmitters and neuromodulators that regulate neuronal excitability both modulate and are modulated by these processes, collectively creating time-varying permissive conditions for seizure onset. However, the precise neurochemical landscape governing the transition to ictal activity remains poorly understood, while recent studies suggest that interneurons play distinct roles in this process [1]. We address this gap by developing a multiscale neural mass model (NMM) that captures how excitability evolves across different timescales. We consider one of the most well-established NMMs for epilepsy [2] that couples an excitatory pyramidal neuron population with two GABAergic interneuron subpopulations, PV+ (somatic inhibition) and SOM+ (dendritic inhibition). As a first step, we focus on GABA as the key modulator of the excitation/inhibition balance. Our investigation reveals that distinct dynamical regimes, including interictal, ictal, and resting states, occupy well-separated regions of GABAergic parameter space. This raises a central question: can transitions between these regimes arise autonomously from GABAergic fluctuations? To investigate this, we extend the conventional NMM [2] by introducing a slow subsystem that reformulates GABAergic concentrations. Using bifurcation analysis, we identify candidate mechanisms by which the inhibitory landscape drifts toward seizure-permissive states. Our approach provides a mechanistic framework for understanding how neurochemical timescales interact to control seizure onset. In future work, we will validate the model using experimental recordings and extend it by incorporating equations for neuromodulators relevant to seizure occurrence, enabling a fuller representation of the neurochemical landscape governing seizure susceptibility.

References:

1. Magloire, V., Cornford, J., Lieb, A., Kullmann, D. M. & Pavlov, I. KCC2 overexpression prevents the paradoxical seizure-promoting action of somatic inhibition. *Nat Commun* **10**, 1225 (2019).

2. Wendling, F., Bartolomei, F., Bellanger, J. J. & Chauvel, P. Epileptic fast activity can be explained by a model of impaired GABAergic dendritic inhibition. *European Journal of Neuroscience* **15**, 1499–1508 (2002).