Seminar of SFB 910

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Perturbations both trigger and delay seizures due to generic properties of slow-fast relaxation oscillators

The mechanisms underlying the emergence of seizures are one of the most important unresolved issues in epilepsy research. In this work, we analyze white and how perturbations, exogenous or endogenous, may promote or delay seizure emergence [1], following previous observations in vivo, in vitro and in silico [2]. To this aim, due to the increasingly adopted view of epileptic dynamics in terms of slow-fast systems, we perform a theoretical analysis of the phase response of a generic relaxation oscillator. As relaxation oscillators are effectively bistable systems at the fast time scale, it is intuitive that perturbations of the non-seizing state with a suitable direction and amplitude may cause an immediate transition to seizure. By contrast, and perhaps less intuitively, smaller amplitude perturbations have been found to delay the spontaneous seizure initiation. By studying the isochrons of relaxation oscillators, we show that this is a generic phenomenon, with the size of such delay depending on the slow flow component. Therefore, depending on perturbation amplitudes, frequency and timing, a train of perturbations causes an occurrence increase, decrease or complete suppression of seizures. This dependence lends itself to analysis and mechanistic understanding through methods outlined in this paper. We illustrate this methodology by computing the isochrons, phase response curves and the response to perturbations in several epileptic models possessing different slow vector fields. While our theoretical results are applicable to any planar relaxation oscillator, in the motivating context of epilepsy they elucidate mechanisms of triggering and abating seizures, thus suggesting stimulation strategies with effects ranging from mere delaying to full suppression of seizures.

[1] Alberto Pérez-Cervera, Jaroslav Hlinka. Perturbations both trigger and delay seizures due to generic properties of slow-fast relaxation oscillators. PLOS Computational Biology, 17(3): e1008521, 2021.

[2] Chang, Wei-Chih, et al. "Loss of neuronal network resilience precedes seizures and determines the ictogenic nature of interictal synaptic perturbations." Nature neuroscience 21.12 (2018): 1742-1752.

The Seminar will take place online via Zoom as part of the Oberseminar "Nonlinear Dynamics" organized by Bernold Fiedler (FU Berlin), Isabelle Schneider (FU Berlin), Eckehard Schöll (TU Berlin) and Matthias Wolfrum (WIAS). For information on how to access the event, please contact any of the above or: henning.reinken@itp.tu-berlin.de

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