

Nonlinear Signal Analysis Applied to Neural Circuits in the Hippocampus and Retina

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Nonlinear signal analysis techniques (Wiener kernel analysis) were applied to study processing changes in epileptic rat hippocampus and mechanisms of contrast gain control in catfish retina:

1) For the hippocampal preparation, 2-3 month old Wistar rats were implanted with stimulating electrodes in the perforant path and recording electrodes in the granule cell layer. Animals received up to 60 min of stimulation as a model for status epilepticus/epileptogenesis, and responses to paired-pulse or white noise inputs were monitored sequentially. Loss of inhibition with brief 1-3 min of stimulation, measured by increase paired-pulse ratio (P2/P1 ISI 40ms) from $.25 (\pm .27)$ pre- to $1.02 (\pm .18)$ post-stim ($p < .001$), lasted $43 (\pm 15)$ min. For 30-60 min of stimulation, the paired-pulse ratios were $0.088 (\pm 0.11)$, $1.59 (\pm .036)$, $0.06 (\pm .11)$, $0.82 (\pm .22)$ for pre-, immediate post-, 1 week post-, and 1 month post-stimulation, respectively ($p < 0.025$). Compared to pre-stimulation values, Wiener kernel amplitudes for immediate, 1 week, and 1 month post-stimulation were $24\% (\pm 13\%)$, $72\% (\pm 17\%)$ and $31\% (\pm 21\%)$, respectively ($p < 0.05$). Wiener kernels one month post-stimulation showed response prolongation with increased opportunity for excitatory interactions of inputs (particularly those separated by 4 ms). In conclusion, brief perforant path stimulation causes sustained loss of inhibition in the dentate, possibly an early event in the transition to status epilepticus. Stimulation for 30-60 min causes chronic changes in paired-pulse and white noise (Wiener kernel) responses. Transient recovery occurs by 1 week, but later new features appear (including delayed/late inhibition and potential excitatory cross-talk) that might favor epileptic seizures.

2) For the retinal preparation, sharp electrode recordings were obtained from transient amacrine cells using white noise photic stimulation to generate 1st and 2nd order Wiener kernels. Transient amacrine cells receive inputs from both ON- and OFF- bipolar cells and the kernels were fit using an analytic form for a parallel path L_1 -N- L_2 "sandwich" model. The model is able to predict time series response of transient amacrine cells to white noise and step inputs well (MSE $< 20\%$ in selected cells). Results suggest the strong even-order nonlinear behavior of amacrine cells suitable for contrast detection emerges from summation of even but cancellation of odd order terms, a result of the convergence of parallel inputs of opposite polarity. The model also suggests kinetic differences between the ON- and OFF-bipolar inputs to transient cells, with the ON-bipolar impulse response being 6 msec later than that of the OFF-bipolar pathway. A greater scaling in the 2nd order kernel relative to the 1st order kernel (on the order of being squared) is observed with increasing variance of the white noise input, suggesting that contrast gain circuitry adjustments occur at the pre-filter level before the nonlinearity. In conclusion, Wiener analysis and modeling of kernels reveals the highly nonlinear behavior of these cells to result from convergence of parallel inputs of opposite polarity. In addition, the mechanism for contrast gain adjustment to light levels of different modulation depth involves circuitry feedback from the inner retina to bipolar cells.