

Nonlinear Systems Model of Hippocampus  
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Abstract:

A combined theoretical/experimental approach based on principles of nonlinear systems analysis for developing biologically realistic models of brain systems will be presented. The approach is applied to study of the hippocampus, a region of the brain responsible for the formation of long-term memories. The hippocampus is typical of most neural systems found in the mammalian brain in that it is composed of several populations of nerve cells, each with a distinct set of functional properties that include higher order nonlinearities, and are interconnected through a variety of feedforward and feedback circuits. Because of its special role in memory formation, the strengths of connections between hippocampal neurons also are subject to activity-dependent modification, i.e., system properties can be nonstationary. Collectively, these characteristics present a unique set of challenges to developing a biologically realistic model at the systems level which also provides a basis for understanding the relation between system dynamics and the underlying biological processes.

A strategy for developing a nonlinear systems model of the hippocampus will be outlined, as first applied to the intact rabbit brain. Methods for characterizing third, fourth, and higher order nonlinearities, as well as nonstationary second order nonlinearities, will be reviewed. These results will be compared to data and resulting models for progressively reduced rabbit hippocampal preparations, demonstrating and quantifying the contribution of "long-loop" feedback pathways to global system properties. Additional results using pharmacological and micro-surgical manipulations in rabbit brain slice preparations elucidate the role of "short-loop", inhibitory interneurons. Extension of the nonlinear systems analytic approach to cellular processes will be demonstrated with an application to characterization of the voltage-dependent blockade of the NMDA receptor-channel, and the segregation of AMPA and NMDA receptor-channel contributions to glutamatergic excitation of hippocampal dentate granule cells. Methods based on higher-order Laplace transforms are being developed to "synthesize" a global hippocampal systems model from the various components characterized through the parallel, experimental and theoretical decomposition studies. Finally, implementations of hippocampal second and third order nonlinearities in VLSI will be reviewed.