gPC-based robustness analysis of neural systems through probabilistic recurrence metrics | Uros Sutulovic

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Abstract:
Neuronal systems exhibit an astounding complexity; yet, they manage to preserve their characteristic function and signaling patterns despite large uncertainties, variability, and external disturbances. In fact, their associated models embed uncertain parameters that are hard to estimate and often impossible to measure directly. Robustness analysis is a powerful method for understanding how key characteristics of the model's network structure and sets of uncertain parameters enable the persistence of desired dynamical patterns and properties. In particular, probabilistic robustness analysis provides tools that quantify not only whether a property holds, but also with which likelihood, given uncertain parameters with a known probability distribution. Probabilistic analysis typically relies on Monte Carlo (MC) methods, which employ many simulations with sampled random variables and then compute summary statistics from the random realizations, to quantify the likelihood of the emergence of a desired pattern. However, MC methods suffer from poor scalability: especially for complex systems in neuroscience, they would require prohibitive computational power to adequately conduct probabilistic analysis, thus making large parameter spaces or combinations inaccessible.

To make probabilistic robustness studies more efficient and scalable for complex neuroscience models, we explore the effectiveness of surrogate models as an alternative to MC approaches. We employ generalized polynomial chaos (gPC) methods, which represent stochastic processes as a series expansion with respect to an appropriate basis of orthogonal polynomials related to the distribution of the uncertain system parameters; these methods leverage the linearity associated with the spectral representation to directly compute the summary statistics of interest, thus allowing fast, efficient and accurate extraction of statistical moments for any system.
We apply various gPC methods on widely used models of neural dynamics that can exhibit multiple dynamical regimes, at different

scales: the Hindmarsh-Rose (HR) model for single-neuron, the Jansen-Rit (JR) model for neuron networks and the Epileptor model for whole brain regions. We assess the trade-off between efficiency and accuracy of different gPC approaches, selecting the most performing computational settings to study the effects of parametric uncertainty on the average signaling of these neural models.
To perform a comprehensive exploration of parameter spaces, we develop a novel pipeline. Since standard metrics in neuroscience, such as inter-spike intervals and firing rates, fall short for stochastic time series, we quantify probabilistic robustness with a novel methodology that combines recurrence plot analysis and automated persistency analysis. This new method has two main benefits: first, within the parameter space of interest, it quantifies the level of uncertainty for which a certain regime gets disrupted; second, it systematically identifies “regions of safe operation”, i.e., areas in the parameter space where a certain regime, quantified by the persistency of the associated pattern in the recurrence plot, holds despite stochasticity.

The results obtained for the HR and JR models enrich the biological insight generated with bifurcation analysis, by clarifying the effect of uncertainties and stochasticity and allowing to formulate new hypotheses and possibly falsify models. The proposed methodology enables new possibilities to unravel the robustness properties of complex systems in neuroscience and provides a powerful and versatile tool to all researchers in the field.