Banerjee et al. BMC Neuroscience 2010, 11(Suppl 1):P161
http://www.biomedcentral.com/1471-2202/11/S1/P161

BMC Neuroscience

POSTER PRESENTATION | Open Access

Mixed mode oscillations in a gonadotropin-releasing hormone (GnRH) neuron model

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From Nineteenth Annual Computational Neuroscience Meeting: CNS*2010
San Antonio, TX, USA. 24-30 July 2010

Mixed mode oscillations (MMOs) are complex patterns resulting from an inter-mixing of large- and small-amplitude oscillations. Such patterns have been widely observed in experiments as well as mathematical models [1] and are currently an active area of mathematical research. In neurons MMOs often consist of a mixture of spikes and subthreshold oscillations. Our GnRH work leads to a seven-dimensional soma model aimed at investigating the firing properties of GnRH neurons across puberty. The results of our model are supported by published electrophysiological data of Liu and Herbison [2]. The model exhibits robust subthreshold oscillations in addition to action potentials, an observation validated by experimental evidence. Previously identified mechanisms giving rise to MMOs in mathematical models include canard-based mechanisms such as folded node singularities and singular Hopf bifurcations [3,4]. MMOs arising out of these mechanisms have characteristic patterns of variation in oscillation amplitudes; in the case of folded nodes there are also bounds for the maximum number of subthreshold oscillations per cycle. The MMOs in our system do not follow these patterns but are instead "exotic" MMOs. In this work we use geometric singular perturbation theory to analyze the source of these MMOs in the model and compare to known mechanisms; we also explore the possible physiological function of MMOs in GnRH cells.

Bifurcation analysis of our system was performed with the help of the simulation and continuation tool XPPAUT. Our analysis suggests that MMOs in our model persist near a saddle-node of periodic orbits and the geometry further points to a tangency between an unstable manifold and a family of periodic orbits. In order to facilitate a more detailed analysis of this phenomenon we reduced to a three dimensional fast-slow system with two slow variables that exhibits qualitatively similar MMOs. We note here that MMOs in three or higher dimensional systems have been observed to occur robustly when two of the variables evolve on a much slower time-scale than the rest [3-5] unlike in two dimensional systems where they occur over an exponentially small parameter interval. The bifurcation analysis of our reduced model provides insights into the geometry of stable and unstable invariant manifolds of our system and their role in the generation of the exotic MMOs.

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Acknowledgements
This work was supported by HD-060818.

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Published: 20 July 2010

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doi:10.1186/1471-2202-11-S1-P161
Cite this article as: Banerjee *et al.*: **Mixed mode oscillations in a gonadotropin-releasing hormone (GnRH) neuron model.** *BMC Neuroscience* 2010 **11**(Suppl 1):P161.