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Robust Rhythmogenesis in Endocrine GnRH Neurons via Autocrine Regulations in a Common Pool of Extracellular Hormone

Gonadotropin-releasing hormone (GnRH) is a decapeptide hormone secreted by GnRH neurons located in the hypothalamus. It is responsible for the onset of puberty and the regulation of hormone release from the pituitary. There is a strong evidence suggesting that these GnRH neurons are intrinsically capable of generating pulsatile and episodic neurosecretion of this hormone. However, the underlying mechanism for the GnRH-pulse generator remains obscure. The discovery of GnRH receptors allowing GnRH to exert autocrine regulation on its own release, led several experimentalist in NIH to propose in 2003 a mechanism underlying this effect. We developed in 2006 a mathematical model describing the proposed mechanism, then we extended it to explain synchrony observed in GnRH neurons by incorporating the idea of a common pool of GnRH hormone.

In this talk, we shall present this model and analyze several aspects of it, especially robustness. We shall show that the coupling of a heterogeneous family of GnRH neurons will not significantly alter the general dynamics of the pulse generator. Indeed, we shall establish that no more than 50% of these coupled neurons must be active participants in the process to generate pulsatility. The effects of requirement and averaging in parameter-values will be also discussed. Several model predictions explaining the type of behaviour observed experimentally upon the injection of exogenous GnRH will be stated. These results will further demonstrate the essential properties of synchrony observed and the robustness of the model proposed.