
Computational/Experimental Study of Hypothalamus-Pituitary Interactions
(1R01DA019356-01-FY04)
Richard Bertram
Florida State University

The overall aim of this project is to combine experimental studies with mathematical modeling to understand the interactions between the hypothalamus and the pituitary gland that lead to rhythmic secretion of the hormone prolactin. This work will be done in close collaboration between experimental labs and a mathematical modeling lab. The primary goal of this research is to understand how neurosecretory cells within the hypothalamus interact with the pituitary gland to produce daily rhythms of prolactin secretion in the rat during pregnancy. Prolactin is one of the most versatile hormones of mammalian organisms, with over 300 separate biological activities. The prolactin secreted following the mating stimulus has many targets, including other endocrine glands, and is important for maintaining a normal pregnancy in the rat. Prolactin is secreted by pituitary lactotrophs. Secretion from these cells is tightly regulated by the hypothalamus, a region of the brain that transmits time-of-day information to the rest of the body. The interaction between hypothalamic neurons and lactotrophs is complex; the neurons influence each other as well as the lactotrophs, and prolactin from lactotrophs feeds back onto and influences the hypothalamic neurons. Such a complex system is ideal for mathematical modeling, which can provide insight into the influence of the various network interactions, and can be used as a tool for integrating information. There are four specific aims in this proposal. First, a mathematical model will be developed for pituitary lactotrophs. This model, based largely on experimental data on cultured lactotrophs from our lab, will provide a mechanistic understanding of the activity patterns of these cells. Second, mathematical models will be developed of hypothalamic dopamine- and oxytocin-secreting neurons, using hypothalamus slice data from our lab. These neurosecretory cells regulate prolactin secretion from lactotrophs, and are themselves under the influence of neurons within the suprachiasmatic nucleus (SCN). The third specific aim is to develop a mathematical model of the network interactions among the various hypothalamic neurons and pituitary lactotrophs. Fourth, the role of rhythmic clock gene expression in dopamine- and oxytocin-secreting neurons will be investigated.

PI Website

http://www.math.fsu.edu/~bertram/

Publications

M. Egli, R. Bertram, M. T. Sellix, and M. E. Freeman, *Rhythmic Secretion of Prolactin in Rats: Action of Oxytocin Coordinated by Vasoactive Intestinal Polypeptide of Suprachiasmatic Nucleus Origin*, Endocrinology, 145:3386-3394, 2004.

M. Egli, N. Toporikova, M. T. Sellix, W. Blanco, M. D. Bosworth, R. Bertram, M. E. Freeman, *Prolactin Secretory Rhythm of Mated Rats Induced by a Bolus Injection of Oxytocin*, submitted, 2005.