Rhythms in the Hypothalamus and Pituitary

organized by
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Workshop Summary

Overview

Neuroendocrinology is at the intersection of neuroscience and endocrinology, i.e., the study of the brain and the study of the hormone-releasing endocrine glands. Of the many endocrine glands in the body, the one that is under the most direct neural control is the *pituitary gland*. This is located directly below the brain region called the *hypothalamus*. The anterior region of the pituitary consists of several cell types, each of which is electrically excitable (like neurons) and which secretes a hormone when activated. Neurons within the hypothalamus act on the pituitary cells to evoke hormone secretion at the proper times and under the proper physical stimuli. The pituitary hormones then act on other endocrine glands (like the pineal glad, the adrenal gland, the ovaries, and the testes) to influence secretion of hormones from these glands. All of the hormones influence the activity of neurons within the hypothalamus (and other brain regions), closing the loop. Additional mathematical richness is added to the system by the fact that hormones are secreted from the hypothalamus and pituitary in pulses on several time scales, and the frequency and amplitude of these pulses vary on slower time scales. Mathematical Neuroendocrinology is a very new field (we just coined the term during the workshop) that uses mathematical modeling and analysis to help interpret neuroendocrine data and design new experiments. Models have been developed at the cellular level, as well as the system level (using mean field models).

Goals of the Workshop

This workshop was the first meeting between neuroendocrinologists and mathematicians currently working in or interested in working in this field. The first goal was to do this and provide a forum for interactions between and within the two groups of participants. The second goal was to identify open problems in neuroendocrinology where mathematics might be of help. The third goal was to initiate collaborations between mathematicians and experimentalists, directed partially at applying mathematics to problems that were identified during the workshop. The final goal was to come up with a plan for maintaining the momentum started by the workshop.

Workshop Achievements

1. Goal 1: Provide a forum for multidiscipline interaction. The workshop attracted roughly equal numbers of mathematical and experimental scientists. There were some connections between these groups due to existing collaborations, but few of the mathematicians knew more than two or three of the experimentalists, and vice versa. Also, the workshop attracted several young participants who had had very

little prior exposure to the more senior participants from either group. The structure of the workshop was ideally suited for mixing of the two populations of participants. One big achievement of the workshop was therefore to establish a small community of scientists with an interest in mathematical neuroendocrinology.

2. Goal 2: Identify open problems amenable to mathematics. During the lectures and the breakout sessions several open problems were identified that could be amenable to mathematical modeling and analysis. These include the synchronization of oxytocin neurons within the hypothalamus; synchronization of gonadotropin releasing hormone neurons of the hypothalamus; separation of daily rhythms from hourly rhythms in cortisol hormone levels; understanding the multi-scale time dynamics of secretion from pituitary cells; investigating the role of secretion priming in pituitary response to rhythmic stimuli (this may provide a rationale for why oscillations are important – they help the secretory vesicles recover); and using network parameters such as level of connectivity and level of randomness to fit data, thereby giving insight to network architecture. Mathematical techniques that could be used to address these open problems were discussed during the afternoon breakout sessions of the workshop.

3. Goal 3: Initiate collaborations. While it will take time to see what collaborations emerge from the workshop, the initial indications look good. Possible new collaborations that we have observed are Bertram-Tabak-Stojilkovic, Zeeman-Mollard-Bonnefont, Zeeman-Stojilovic, Li-Leng, DelNegro-Stojilkovic, Bertram-Tabak-DelNegro, Lyles-Sherman-Selgrade, and Fletcher-Stojilkovic-Li.

4. Goal 4: Plans for the future. Due to the success of this workshop, and the unanimous support of the participants, we have decided to organize a second workshop on mathematical neuroendocrinology. This would be held in summer 2010, most likely at the NSF-funded Mathematical Biosciences Institute at Ohio State University. Bertram and Sherman have agreed to organize this workshop, and they have been in contact with the director of the MBI. A proposal for this workshop has been submitted. There was also discussion of organizing a get-together at Neuroscience 2008, and of running minisymposia on Mathematical Neuroendocrinology at other national meetings. For example, Tsaneva-Atanasova and Tabak are planning to submit a proposal for a minisymposium at the bi-annual meeting of the SIAM activity group on Dynamical Systems in May 2009. Other promising meetings would be national and international meetings of the US and European Neuroendocrine societies. Another plan is to set up a web site where participants of the AIM workshop, as well as others interested in the field, could go for information on upcoming activities, and where data bases for computer codes, experimental data, and links to relevant journal articles would be established. Bertram has contacted David Farmer at the AIM about this. There was high enthusiasm for a special issue of the *Journal of Neuroendocrinology*, dedicated to modeling in Neuroendocrinology. Several participants committed to submitting papers to such an issue. Leng will contact the senior editors to explore the possibilities. Finally, Li and Leng plan to write an article for SIAM News about the workshop, with the hope that this will encourage other mathematicians to enter the field.