THE UNIVERSITY OF ALBERTA

Department of Mathematical and Statistical Sciences

Special Talk

Part 1: Modeling the Pulsatile Secretion of Gonadotropin Releasing Hormone (GnRH) by Synchronized GnRH Neurons.

Part 2: Low Avidity Versus High Avidity T-Cells: Their Role in the Progression and Treatment of T1D.

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Thursday, January 17, 2008
CAB 657 @ 2:00 p.m.

Abstract:

Part 1:

Gonadotropin Releasing Hormone (GnRH)secreted by GnRH neurons in the hypothalamus plays key roles in the onset of puberty and the regulation of hormone secretion from the pituitary. It has been demonstrated experimentally that the temporal profile of the GnRH signal must be pulsatile and episodic to be effective in preserving mammalian fertility and that GnRH neurons are intrinsically capable of generating this profile. Moreover, it has been discovered that GnRH neurons possess GnRH receptors allowing GnRH to regulate its own release. Based on this recent discovery, a new biochemical mechanism has been proposed. We shall introduce, in this part of the talk, a mathematical model based on this mechanism and analyze its characteristics including 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 are required to be active oscillators to generate pulsatility. The effects of recruitment and parameter averaging will be also discussed. Several model predictions explaining the type of behaviour observed experimentally in vivo upon the injection of exogenous GnRH will be stated. Finally, a brief description of our current work examining the 8-minute Calcium oscillation and the GnRH surge will be also presented together with additional future goals.

Part2:

Type 1 Diabetes (T1D) is an autoimmune disorder in which the body's own immune cells (cytotoxic T lymphocytes, CTLs) target the insulin-secreting beta cells in the pancreas. CTLs possess receptors that help them recognize beta cells. Those CTLs with high affinity receptors (also called high avidity T-cells) destroy around 90% of beta cell repertoire that eventually lead to the elimination of insulin secretion crucial for regulating the glucose concentration in the blood. On the other hand, CTLs with low affinity receptors (also called low avidity T-cells) seem to play a protective role. In fact, recent experimental evidence suggests that (1) low avidity T-cells tend to obstruct the progression of the disease; and (2) drug treatments that expand low avidity T-cells are quite effective in treating diabetic animals. In the second part of this talk, we shall briefly discuss these phenomena and present our recent model describing the competition between these two types of T-cells. Furthermore, several model predictions and future research plans will be stated.