Study of Dependency of Synchronization of Beta-cells Insulin Secretion on Size of Langerhans Islets

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The simulations of intra-cellular processes such as metabolic networks or gene expression control mechanisms have been widely covered in many tools available today[1,2] however the simulation of multiple cells interacting in a common environment such as tissues is not yet fully available.

Tsim (Tissue Simulator) was initially developed for the study of early growth of tumours inspired on works previously done in the area but unlike these studies, the simulation process in Tsim happens both inside and outside the cells.

The regulation of glucose in blood is achieved by glucose sensing cells named beta-cells located in human pancreas, their function is to secrete insulin to signal to muscle and liver they should capture glucose from blood and convert it to glycogen.

This signaling is composed of pulses that are synchronized among the cells within the islets of Langerhans. In this study we propose that there's a lower and upper limit for the size of these clusters so their synchronization and response time will comply with the time constants of human body.

In order to quantify these dimensions, hybrid automata simulation models were created in Tsim with cells disposed in a spatial array as proposed in literature[4] and glycolysis and insulin secretion mechanisms were simulated using the kinetic equations from previous studies[3]. This model is based on a 2-dimensional array of cells, blood vessels and extra-cellular matrix space as well as on differential equations for diffusion of inter-cellular species and intra-cellular metabolism kinetics.

The final results were compared to data obtained by other mathematical models based on deterministic equations[5] and in vivo data in order to evaluate the consistency of this study.

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