Modeling the Building Blocks of a Pancreatic Islet

UMBC REU Site: Interdisciplinary Program in High Performance Computing

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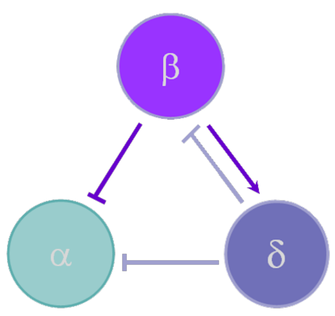
Problem

Diabetes is a pervasive, metabolic disease of elevated blood glucose levels. In order to understand this disease it is important to study the structure and function of units in the pancreas called islets of Langerhans. The cells that make up these islets are responsible for insulin regulation. Our mathematical model focuses on α-, β-, and δ-cells. We have adapted a Tri-Hormone Model into a multicellular computational islet to study 1) the effects of cell-type ratio dependence on secretion through paracrine interactions, 2) paracrine feedback on synchronizing cellular heterogeneity within cell-type, and 3) spatial distribution of cell-types and its effect on secretion.

Background

Tri-Hormone Model: cells are affected by the secretion of neighboring cells

- β-cell inhibition of α-cell secretion
- β-cell stimulation of δ-cell secretion
- δ-cell inhibition of α- and β-cells

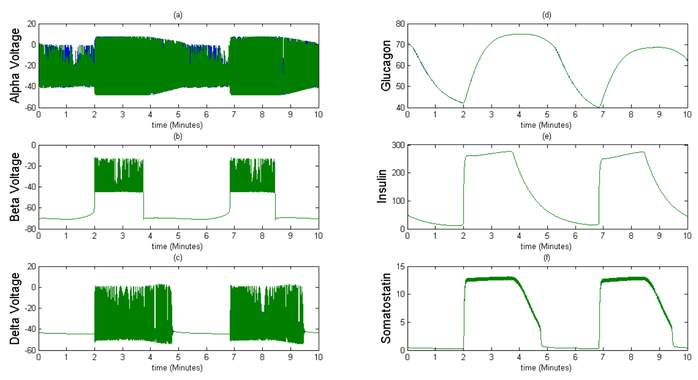


Case Descriptions

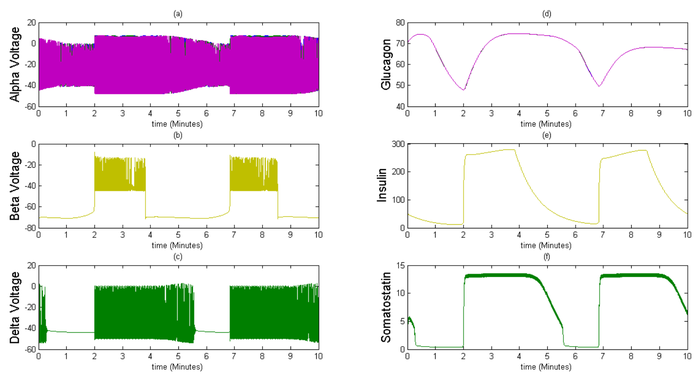
The following plots ($\alpha : \beta : \delta$ and α-cell heterogeneity) have one compartment in their models. Therefore, spatial effects are ignored.

Case Results ($\alpha : \beta : \delta$)

Equal Number of Cells ($9 : 9 : 9$)



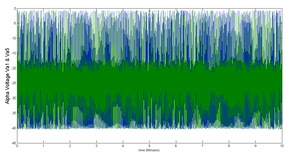
Mouse Islet Representation ($5 : 20 : 2$)



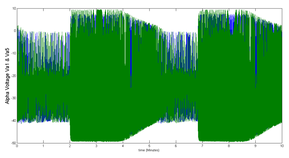
The left column of graphs represents the voltage of α-, β-, and δ-cells. The right column of graphs represents the amount of secreted glucagon, insulin, and somatostatin. The mouse islet shows a lengthening of the bursts in α- and δ-cells with corresponding increase in secretion.

Heterogeneity of α-Cells

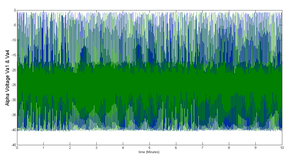
Non-Coupling
$9 : 9 : 9$



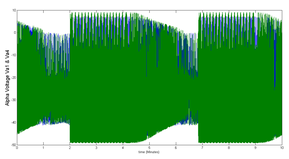
Coupling
$9 : 9 : 9$



Mouse
Non-Coupling
$5 : 20 : 2$



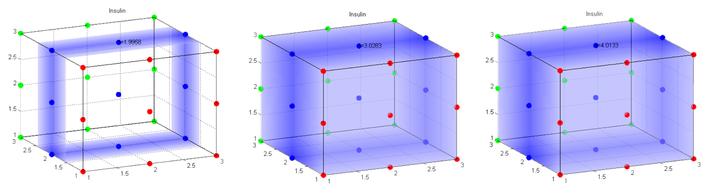
Mouse
Coupling
$5 : 20 : 2$



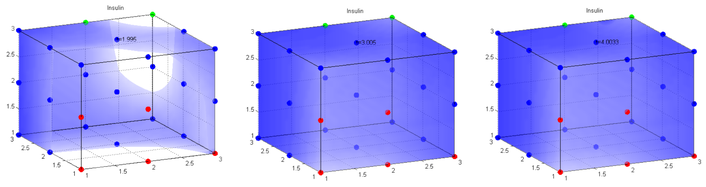
Different GK(ATP) values are assigned to our α-cells and we want to see the effect of paracrine coupling on the behavior of α-cells.

Spatial Islet Diffusion

Insulin Diffusion $9 : 9 : 9$ Islet



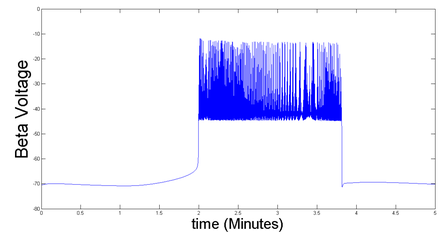
Insulin Diffusion $5 : 20 : 2$ Islet



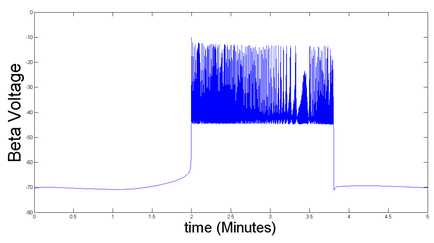
Insulin diffusion during the β-cell voltage bursting. The top graph has an equal number of cells. The bottom graph has mouse islet percentages of cells.

Spatially Dependent Model

β-Cell Bursting



Mouse Islet



The top graph represents an islet of 9 α-cells, 9 β-cells, and 9 δ-cells, with spatial coupling. The bottom graph represents a mouse islet of 5 α-cells, 20 β-cells, and 2 δ-cells, with spatial coupling. The spikes represent β-cell bursting.

References

- See technical report: HPCF–2014–13 at `www.umbc.edu/hpcf` > Publications.

Acknowledgments

- REU Site: `www.umbc.edu/hpcreu`, funded jointly by NSF and NSA
- NSF, NSA, UMBC, HPCF, CIRC