Investigating How Calcium Diffusion Affects Metabolic Oscillations and Synchronization of Pancreatic Beta Cells

UMBC REU Site: Interdisciplinary Program in High Performance Computing

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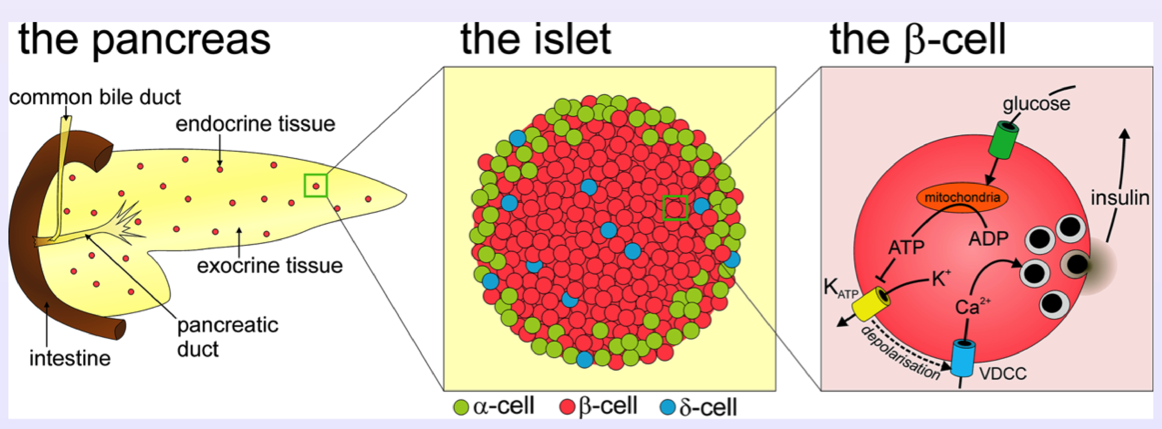
Problem

In order to further understand diabetes mellitus, it is necessary to investigate the dynamics of insulin secretion into the bloodstream. Beta cell clusters called islets of Langerhans located in the pancreas, are responsible for the production and regulation of insulin based on changes in glucose and calcium concentration levels. Using the Dual Oscillator Model, we examined how calcium handling within individual pancreatic beta cells affects the synchronization of oscillations within electrically coupled cells.



Dual Oscillator Model (DOM)

Electrical Component

$$\frac{dV}{dt} = -\frac{I_{\text{K}} + I_{\text{Ca}} + I_{\text{K(Ca)}} + I_{\text{K(ATP)}}}{C_{\text{m}}}$$

$$\frac{dn}{dt} = \frac{n_\infty - n}{\tau_n}$$

$$\frac{d[\text{Ca}]}{dt} = f_{\text{cyt}}(J_{\text{mem}} + J_{\text{er}})$$

$$\frac{d[\text{Ca}_{\text{er}}]}{dt} = -f_{\text{er}}\sigma_V J_{\text{er}}$$

Glycolytic Component

$$\frac{d[\text{G6P}]}{dt} = k(J_{\text{GK}} - J_{\text{PFK}})$$

$$\frac{d[\text{FBP}]}{dt} = k(J_{\text{PFK}} - \frac{1}{2}J_{\text{GPDH}})$$

Mitochondrial Component

$$\frac{d[\text{ADP}]}{dt} = J_{\text{hyd}} - \delta J_{\text{ANT}}$$

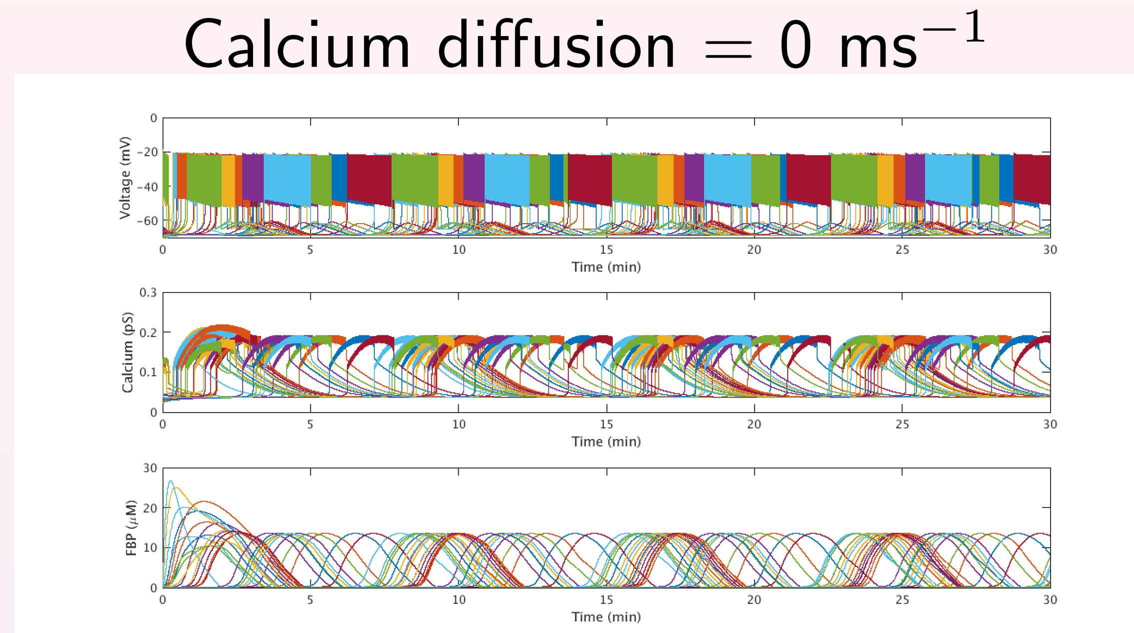
Islet Model with Coupling

$$\frac{dy}{dt} = f(t, y) + Gy$$

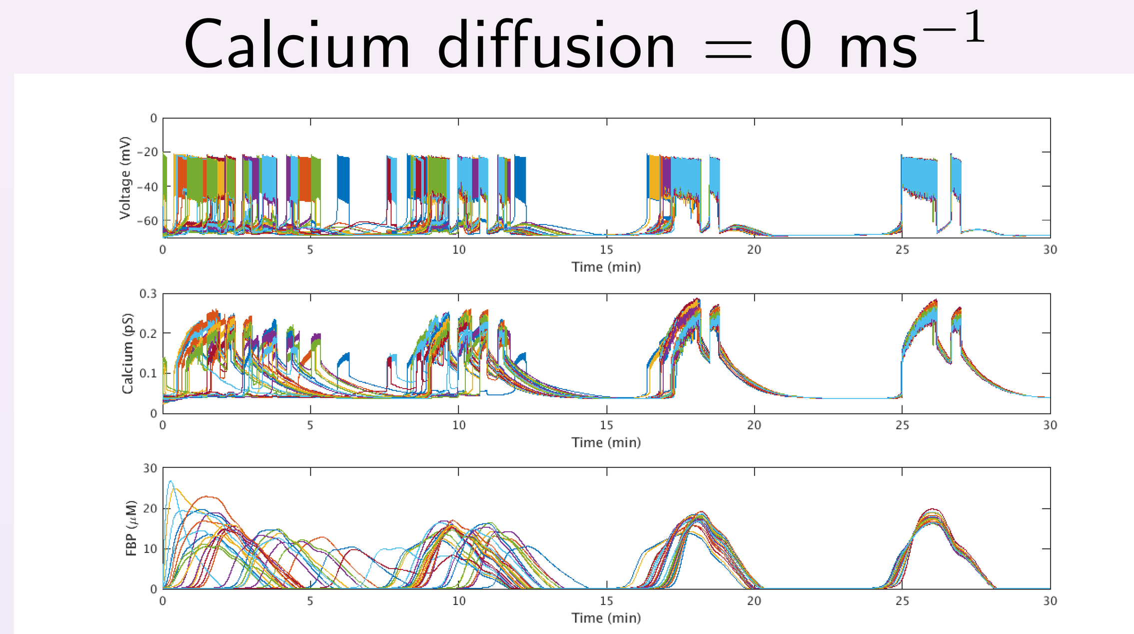
We incorporated voltage coupling and calcium diffusion using adjacency matrix, G, to represent an NxNxN pancreatic islet, where y is a vector containing the seven state variables.

Oscillation Results

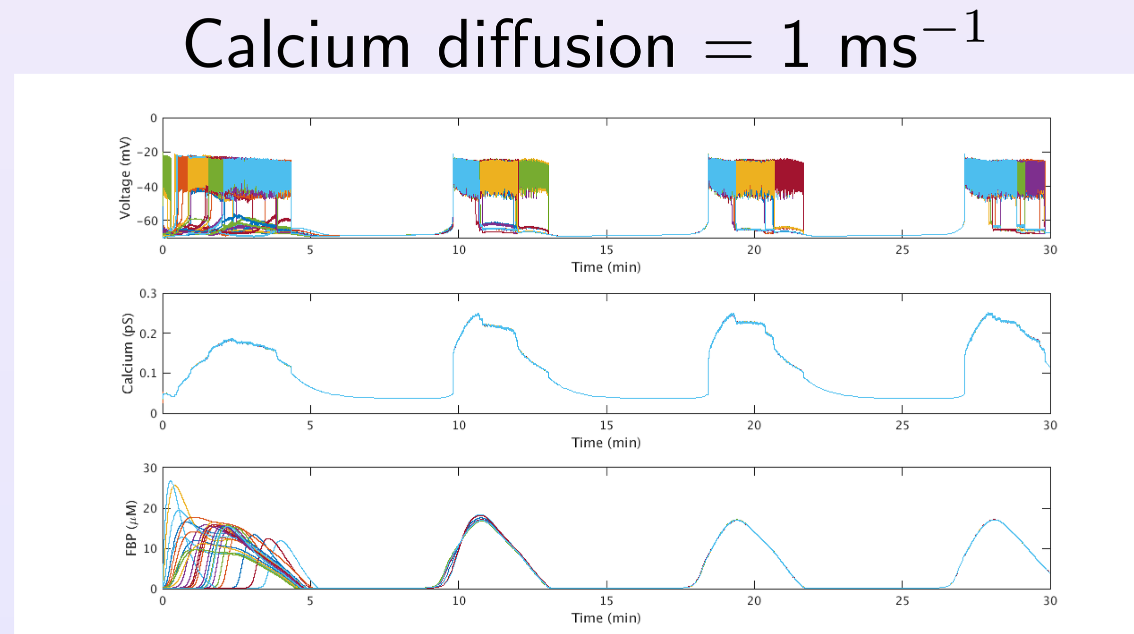
Voltage coupling = 0 pS
Calcium diffusion = 0 ms^{-1}



Voltage coupling = 10 pS
Calcium diffusion = 0 ms^{-1}

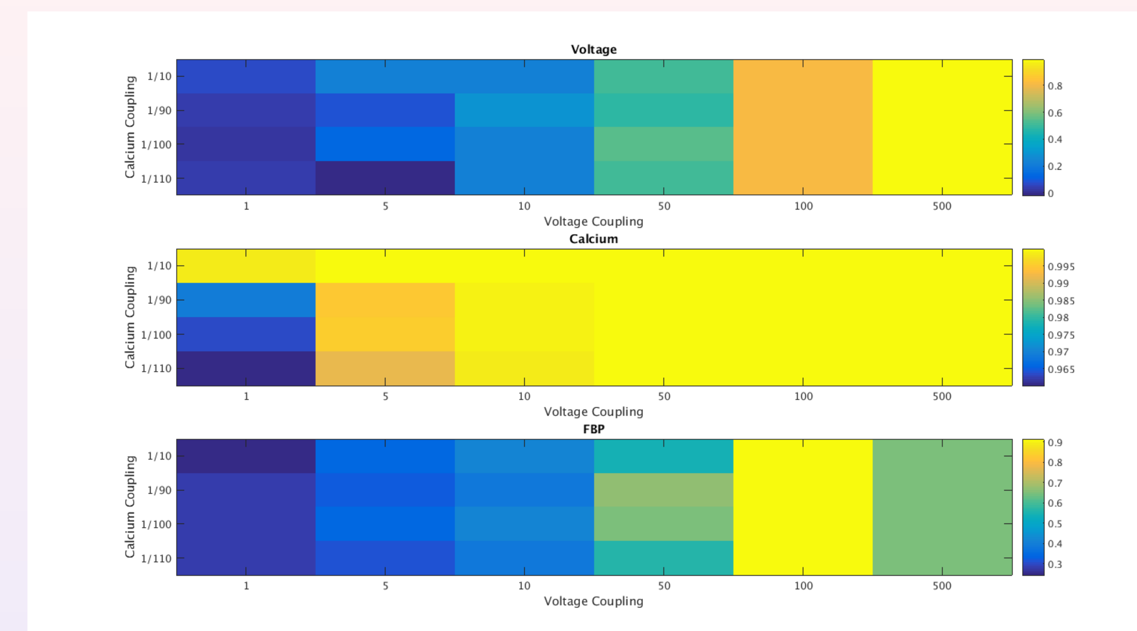


Voltage coupling = 10 pS
Calcium diffusion = 1 ms^{-1}



These plots show the effect of calcium diffusion in a 3x3x3 islet with initial conditions drawn from a normal distribution with 20% standard deviation.

Islet Synchronization



Using the Pearson correlation (Matlab `corr` function) and the minimum row mean, we measured the synchronization of pancreatic islets with various amounts of voltage coupling and calcium diffusion. (Synchronization: Yellow - High, Blue - Low)

Conclusions

- Calcium diffusion between beta cells in a pancreatic islet synchronizes metabollic oscillations when voltage coupling is low (e.g., 1, 5, 10 pS).
- When voltage coupling is high (≥50 pS), the role of calcium in the synchronization of metabollic oscillations is overshadowed by voltage coupling.

References

1. Full technical report: HPCF–2015–24 `hpcf.umbc.edu` > Publications.
2. Watts, Margaret et al. *SIAM Journal on Applied Dynamical Systems*, 13 (2014).
3. Watts, M. and A. Sherman. *Synchronization of Insulin Secreting Cells.* [Unpublished - PowerPoint].

Acknowledgments

REU Site: `hpcreu.umbc.edu`

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