Simulating Survival and Insulin Secretion in Pancreatic Islet Tissue Constructs

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Introduction

- Patients with type 1 diabetes lack functional pancreatic islets.
- Pancreatic islets are clusters of endocrine cells which consume oxygen and glucose and produce hormones such as insulin to manage blood sugar levels.
- Transplantation of pancreatic islets into diabetic patients using hydrogel carriers may aid in restoring normoglycemia.[1]
- Hydrogels provide mechanical support and protection from the recipient immune system but inhibit the diffusion of oxygen, glucose, and insulin.

Goals

- Predict islet survival and insulin secretion inside hydrogel tissue constructs
- Optimize the seeding density of islets inside hydrogels

Methods

Islets are modeled using Hill equations to describe the consumption of oxygen and glucose and the glucose dependent production of insulin as previously published by Buchwald.[2,3]

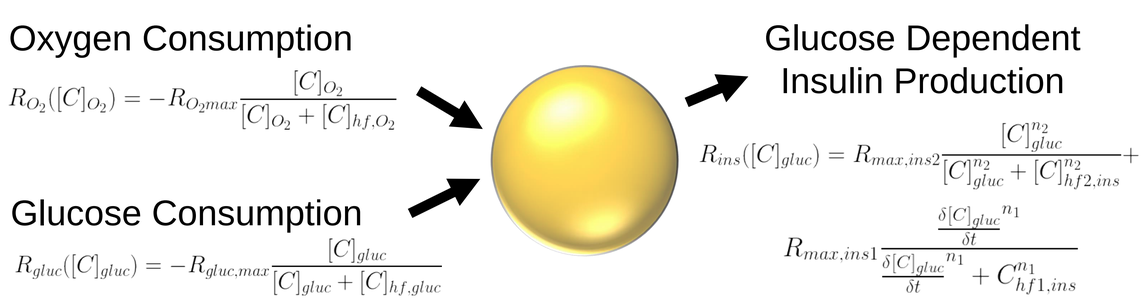

Figure 1. Islet Model

The transport of diluted species module was used with diffusion coefficient constants to simulate the diffusion of oxygen, glucose, and insulin.[3,4] The stationary solver was used to simulate islet survival and the time dependent solver was used to observe insulin secretion for the tissue constructs. Hydrogel constructs were created using fibrin at 10mg/mL in plate wells.

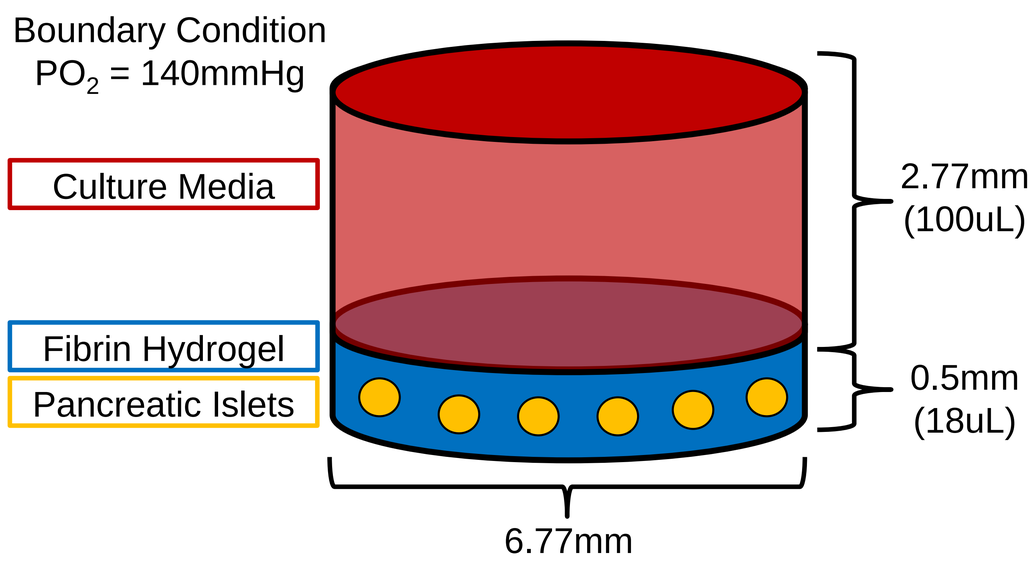

Figure 2. Model Setup and *In Vitro* Experimental Setup

Results

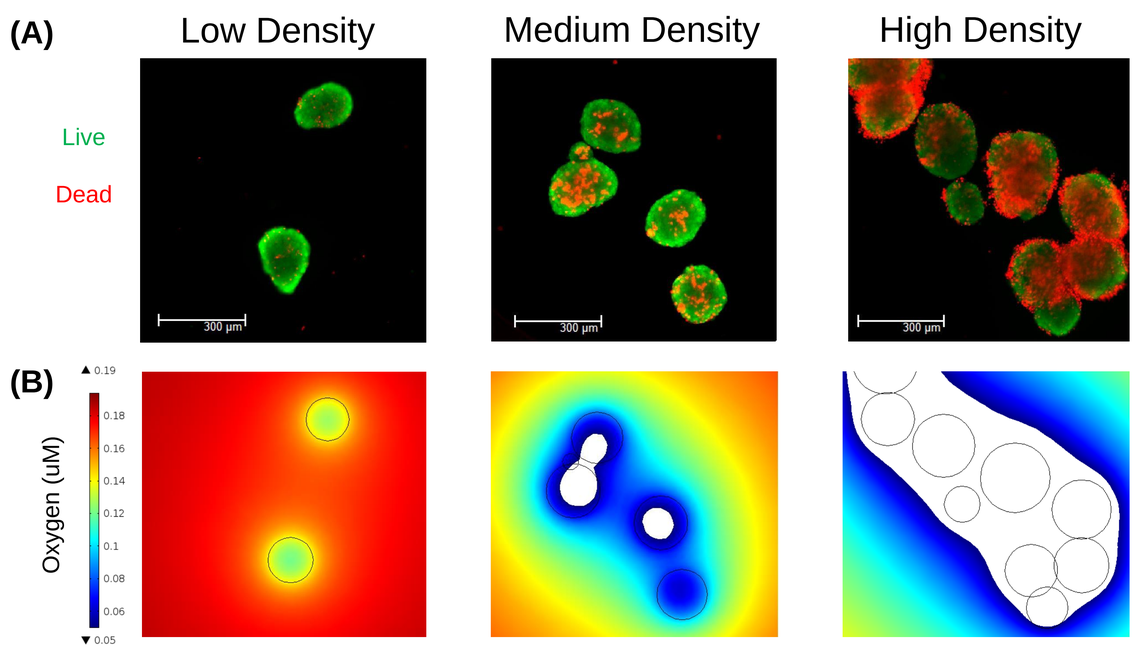

Figure 3. O_2 model validation (a) Islets cultured in Figure 2 setup and stained using a live-dead assay (b) Corresponding 2D cross sections for oxygen simulations with islets. White designates hypoxic areas with <0.05uM O_2

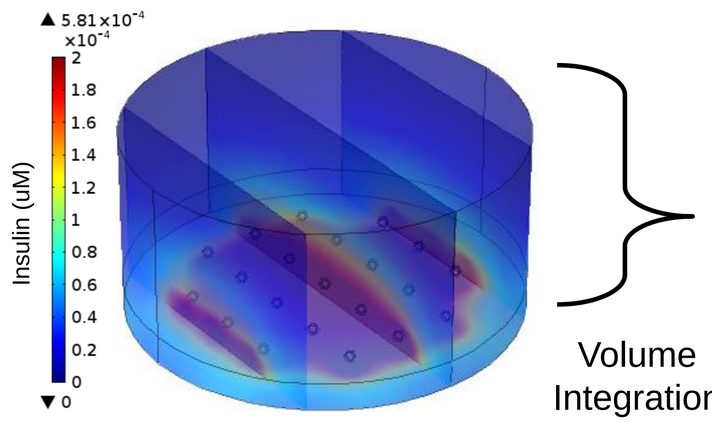

Figure 4. Simulated Insulin release from 20 islets

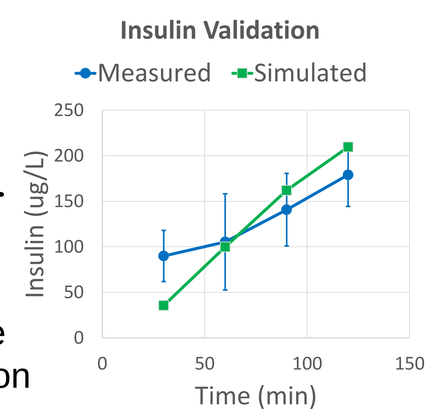

Figure 5. Comparison between experimentally measured insulin and simulated insulin

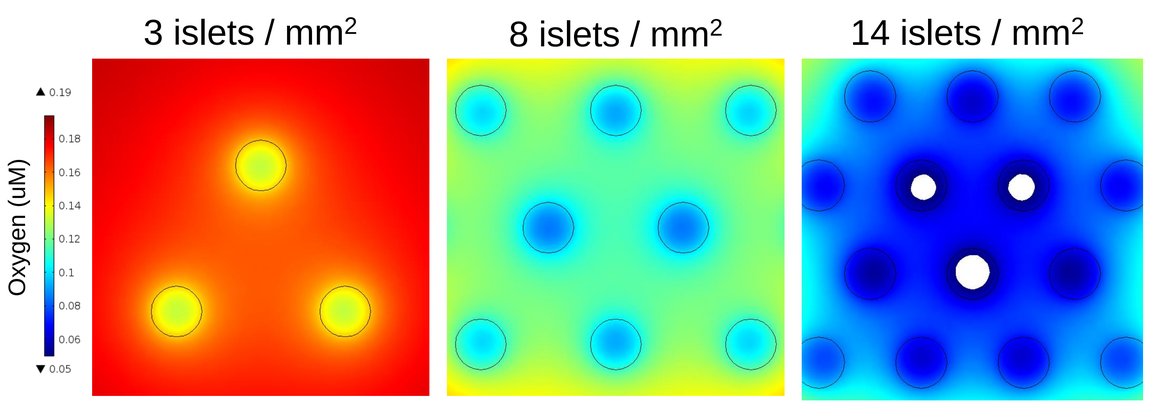

Figure 6. Simulations performed at different islet densities to predict optimal seeding densities. White designates hypoxic areas with <0.05uM O_2

Conclusions

Utilizing COMSOL Multiphysics® to simulate pancreatic islet behavior generates results that can be verified with *in vitro* experimentation. Future work will focus on utilizing this model for designing tissue constructs capable of facilitating adequate nutrient and oxygen diffusion to allow for pancreatic islet survival and functionality after transplantation.

References

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3. P. Buchwald, S. R. Cechin, J. D. Weaver, and C. L. Stabler, "Experimental evaluation and computational modeling of the effects of encapsulation on the time-profile of glucose-stimulated insulin release of pancreatic islets," *BioMedical Engineering OnLine,* vol. 14, p. 28, (2015)
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