

Preparation of 3D In Vitro Models with Predictable Oxygen Distribution

Meaghan D'Arcy, Biomedical Engineering
Mentor: Dr. Vikram Kodibagkar, Professor
School of Biological Health and Systems Engineering



Research Question

Can the oxygen distribution in a 3D *in vitro* model be accurately mapped and predicted using MRI-based oximetry to study cellular response to hypoxia?

Introduction

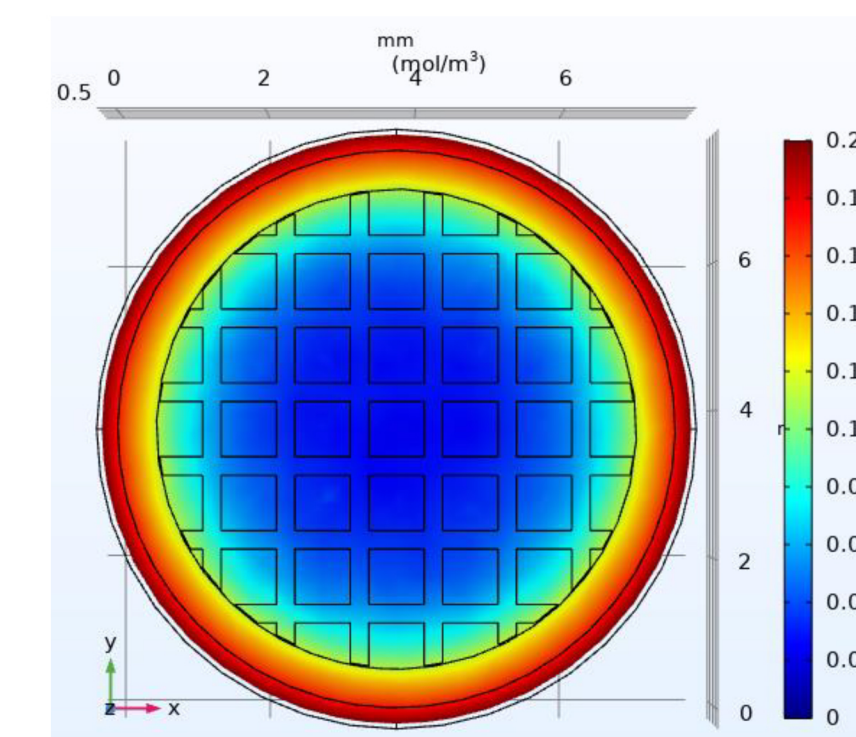
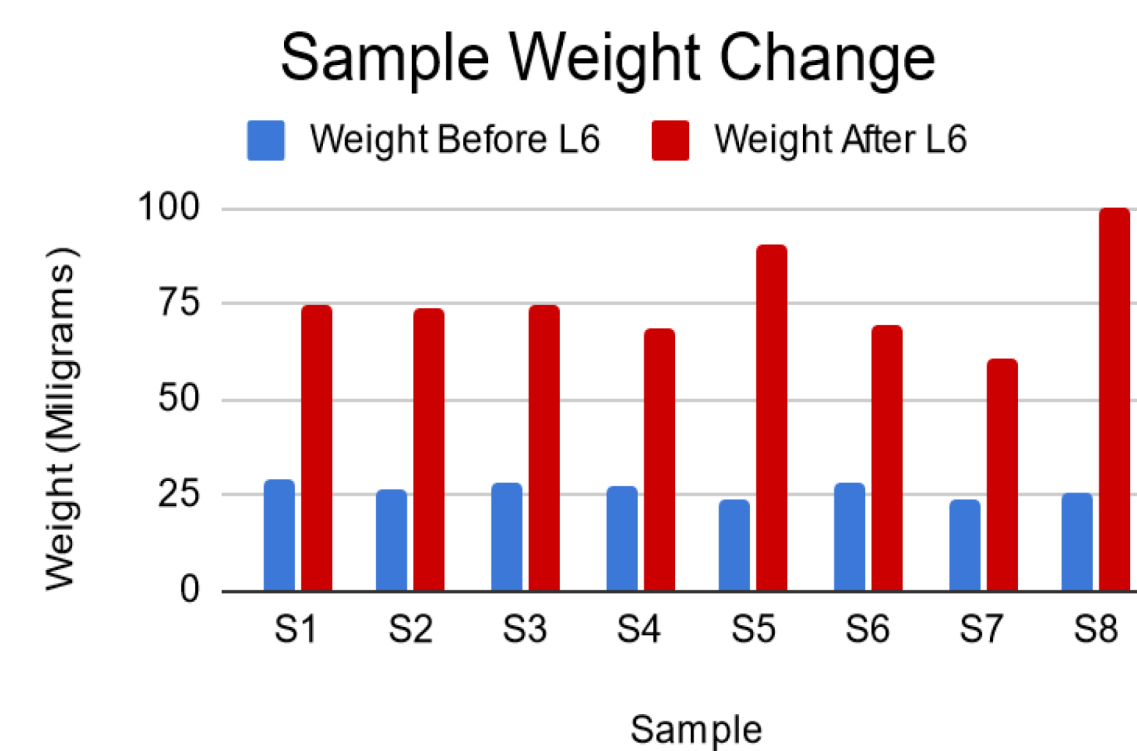
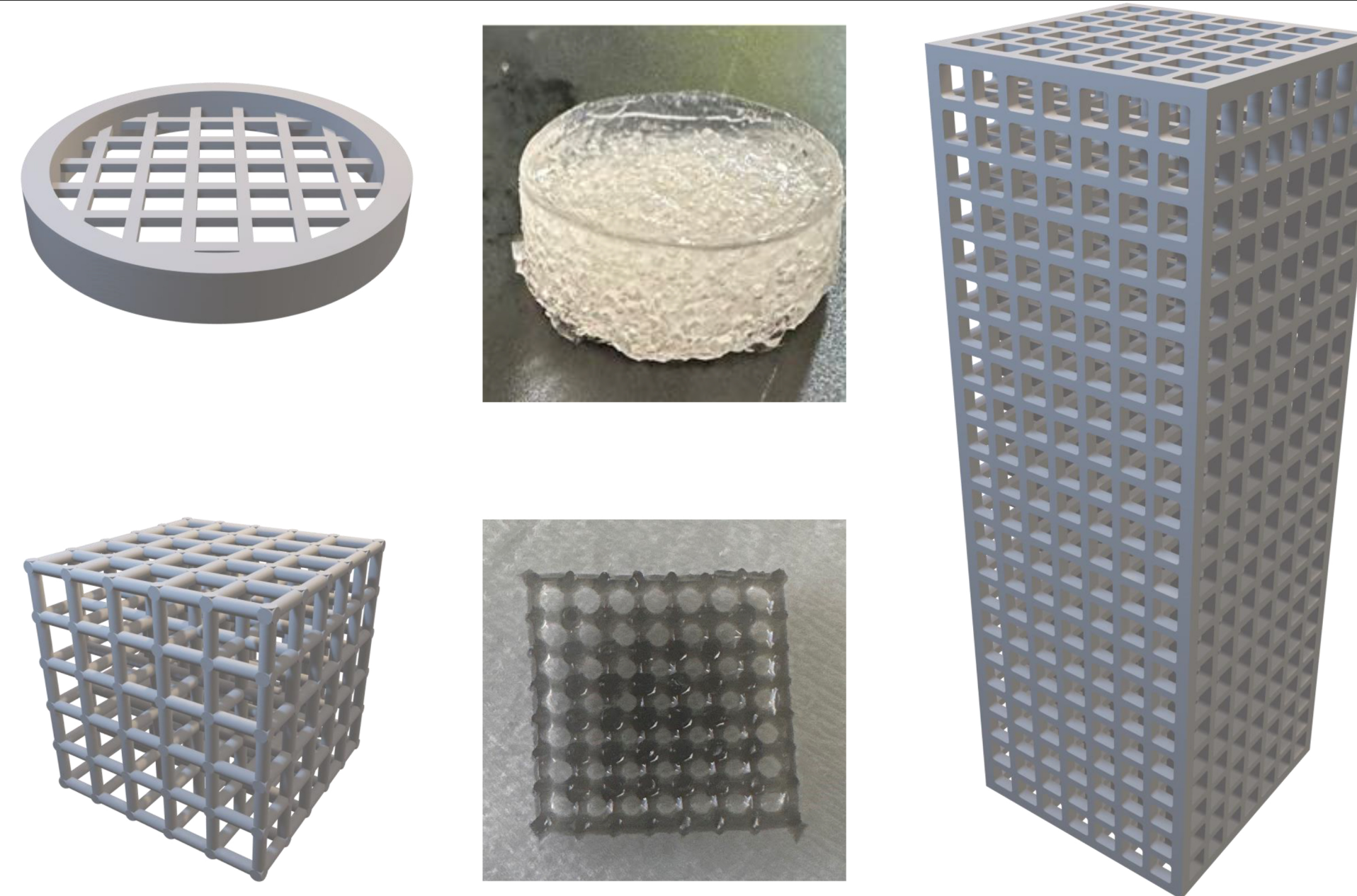
Understanding tissue oxygenation is essential for investigating the role of oxygen distribution in disease progression in cancer, stroke, and traumatic injuries [1]. Cells are sensitive to their surrounding oxygen tension, pO_2 , and their responses impact tissue and organ function [2]. Conventional methods to measure the pO_2 levels in cells include fiber optic probes which are invasive and restricted in certain locations. A 3D *in vitro* model with oxygen-sensitive scaffolding, paired with MRI-based oximetry (PISTOL), can accurately map tissue oxygen distribution, providing insights into hypoxia's impact on cellular behavior [3].

Methods

- 1) Create O_2 sensitive 3D scaffold PDMS sponge
 - a) Original scaffold made from PDMS around a cylindrical array of sugar or salt molecules, then washed, cured, and soaked in L6 treatment
 - b) Final scaffold is a hollow, cylindrical grid 3D printed out of Silicone 40A. Same L6 treatment.

- 2) Comparing COMSOL simulations
 - a) COMSOL simulations for 3D model
 - b) Predict oxygen gradients
- 3) Data Analysis
 - a) Analyze the pO_2 values obtained from the simulated grid

Results



Conclusion

Several O_2 sensitive scaffolds with varied geometries, 2D, and 3D grids were successfully created. The average sample weight increased from $26.4 \text{ mg} \pm 1.9 \text{ mg}$ to $76.4 \text{ mg} \pm 12.7 \text{ mg}$ after L6 soaking, a $191.95\% \pm 58.7\%$ weight increase. The COMSOL simulation of the 3D grid aligns with expected diffusion patterns.

Future Work

I aim to extend this research as my Barrett Honors thesis, focusing on completing the experimental aspects. Specifically, I will culture cells onto the cylindrical grid sponge and apply PISTOL. These results will be compared to the existing COMSOL simulations. This will further validate this system in hypoxia research.

Acknowledgments

A special thank you to Dr. Kodibagkar, Dr. Weaver, and Samrat for their guidance throughout this project. The invaluable assistance of Lakshmi, Charmayne, Shivani, Nihira, and the entire ProBE lab has been instrumental to my success.

References

- [1] Chen, Pai-Sheng, et al. "Pathophysiological Implications of Hypoxia in Human Diseases." *Journal of Biomedical Science*, vol. 27, no. 1, 2020, jbiomedsci.biomedcentral.com/articles/10.1186/s12929-020-00658-7, <https://doi.org/10.1186/s12929-020-00658-7>.
- [2] Giaccia, A. J. "The Biology of Hypoxia: The Role of Oxygen Sensing in Development, Normal Function, and Disease." *Genes & Development*, vol. 18, no. 18, 15 Sept. 2004, pp. 2183–2194, <https://doi.org/10.1101/gad.1243304>.
- [3] Kodibagkar, Vikram, et al. "Proton Imaging of Siloxanes to Map Tissue Oxygenation Levels (PISTOL): A Tool for Quantitative Tissue Oximetry", 23 June 2008, analyticalsciencejournals.onlinelibrary.wiley.com/doi/full/10.1002/nbm.4717.