Modeling Vascular Diffusion of Oxygen in Breast Cancer

Senior Project By Tina Giorgadze   Advisors: Kerri-Ann Norton, Ethan Bloch

Abstract

Oxygen is a vital nutrient necessary for tumor cells to survive and proliferate. It is diffused from our blood vessels into the tissue, where it is consumed by our cells. This process can be modeled by partial differential equations with sinks and sources. This project focuses on adding an oxygen diffusion module to an existing 3D agent-based model of breast cancer developed in Dr. Norton's lab. The module includes 2D and 3D partial differential equations (PDEs) and their numerical evaluations using the finite difference method. The vascular diffusion process occurred in four steps: 2D point source diffusion, 2D line source diffusion, 3D cubic patch diffusion, and vascular diffusion of oxygen.

$$\boxed{U_{i,j,k,t+1} = U_{i,j,k,t} + Dt \times \alpha \frac{U_{i+1,j,k,t} + U_{i-1,j,k,t} + U_{i,j+1,k,t} + U_{i,j-1,k,t} + U_{i,j,k+1,t} + U + i, j, k-1, t - 6U_{i,j,k,t}}{Dx^2}}$$

$$\boxed{U(X,t)_t = \vec{\nabla}^2 U(X,t) + F(X,t)}$$

Figure 1: Top: Approximation of the oxygen concentration matrix U at time step t+1 at 3D location i,j,k using the finite difference method Bottom: diffusion equation. U represents the quantity of oxygen at time t at location X. F is the supply/sink function

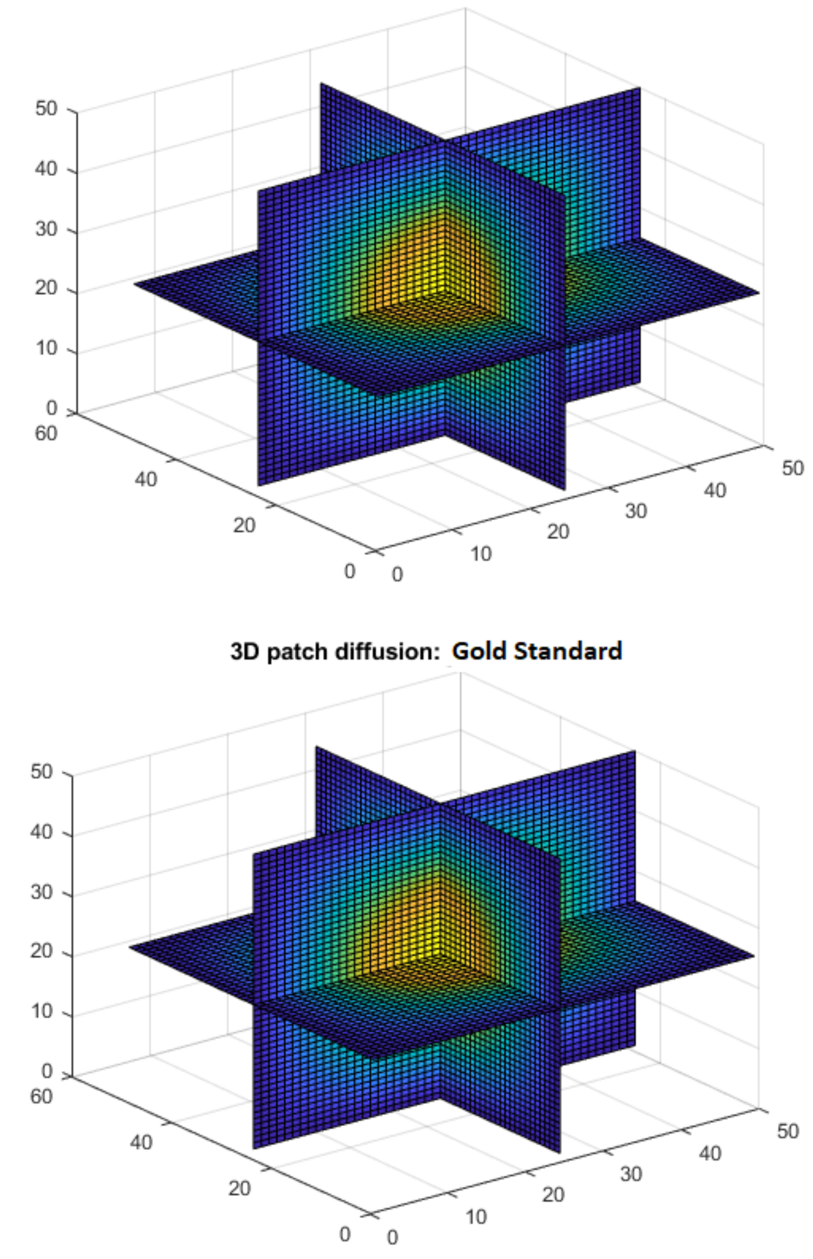

Figure 5: Top: TG model slices of cubic patch diffusion. Bottom: Cubic patch diffusion slices from the gold standard

Methods

•Programmed 2D steady-state diffusion of a point source
- supply rate of 100 nd units placed
- at center of a 50 × 50 grid
- computed error between my O2 matrix and "Gold Standard"

•Programmed 2D diffusion of line source
- supply rate of 100 nd units
- at top boundary of the 50 × 50 grid
- computed error between my O2 matrix and "Gold Standard"

•Obtained a diffusion radius in range 100-200 microns

•Programmed 3D diffusion of a cube source (7 x 7 x 7)
- supply rate of 1000
- at center of a 50 × 50 × 50 grid
- validated 3D patch diffusion using an existing 3D diffusion program

•Programmed 3D vascular diffusion of oxygen
- 8 blood vessels (Figure 6)
- 500 × 500 × 500 grid

•All diffusions were modeled by a diffusion PDE, and evaluated numerically using Finite Difference Method approximations (Figure 1).

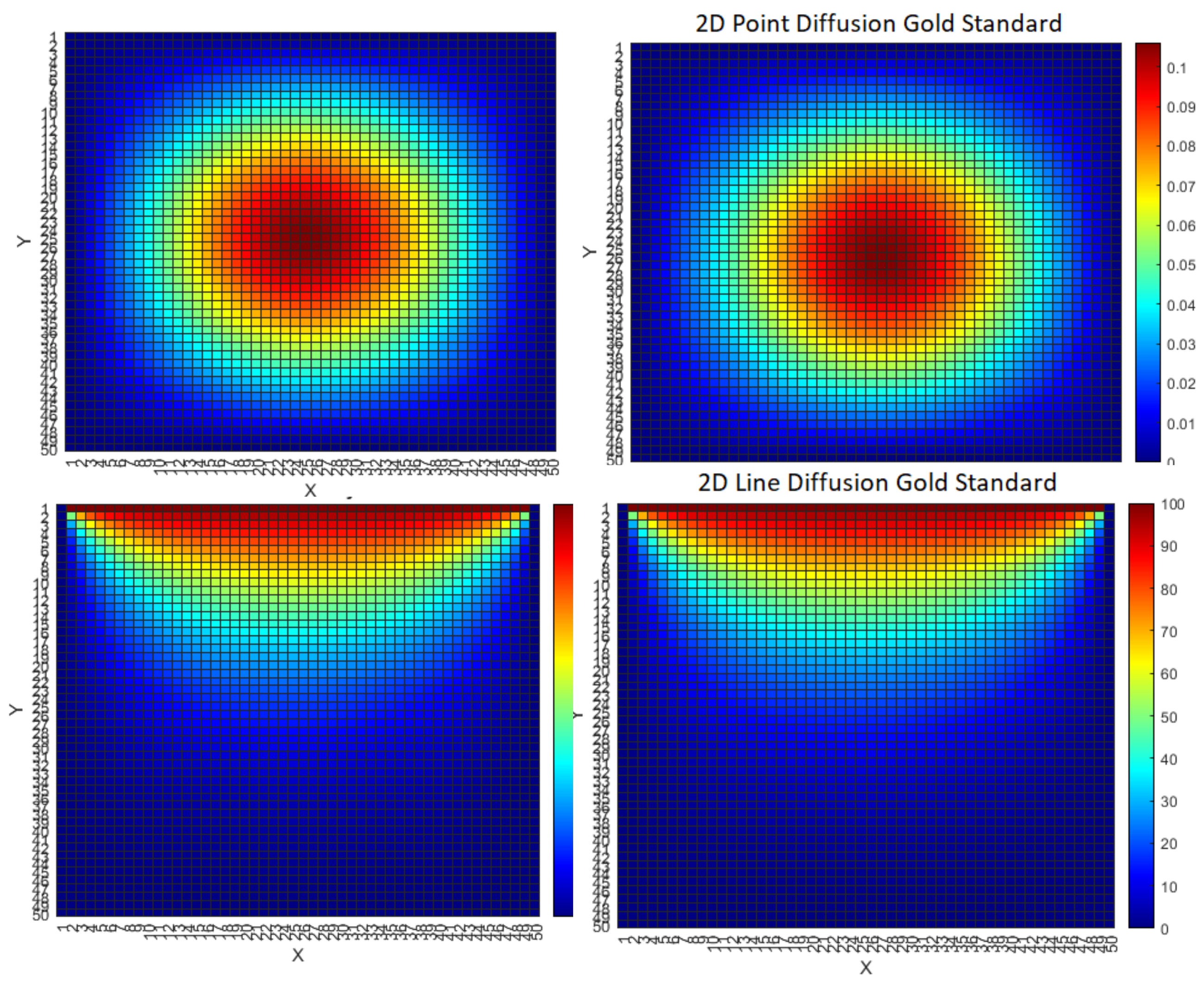

Figure 2: Left column: TG model of point-source diffusion (top) Point Source Diffusion Gold standard (bottom). Right column: TG model of line source diffusion (top) Line Source Diffusion Gold standard (bottom).

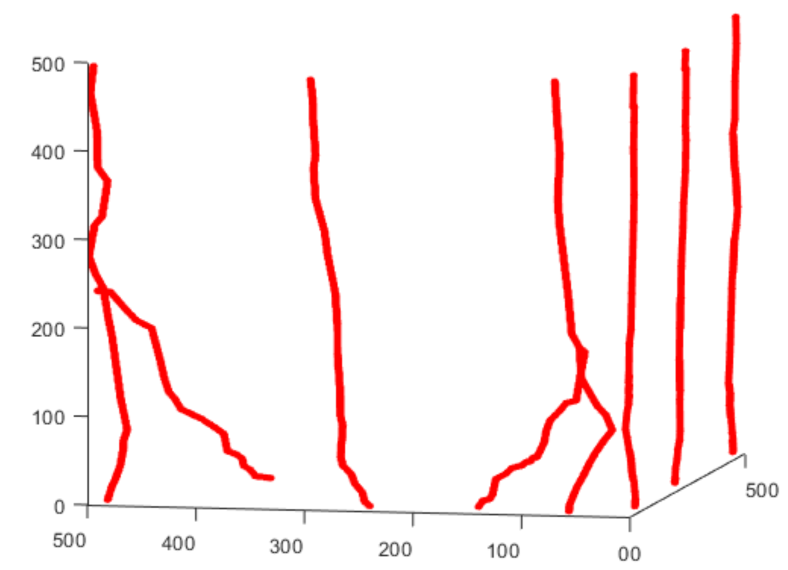

Figure 6: Initial Vasculature

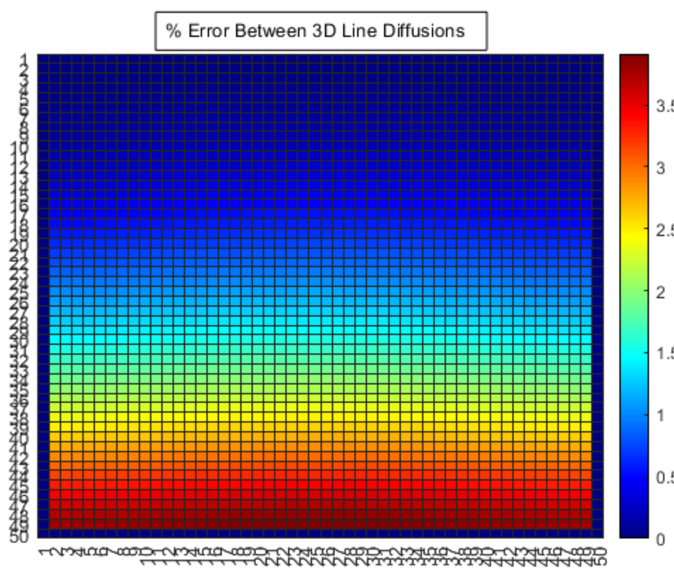

Figure 3: Error Map for 2D Line Diffusion

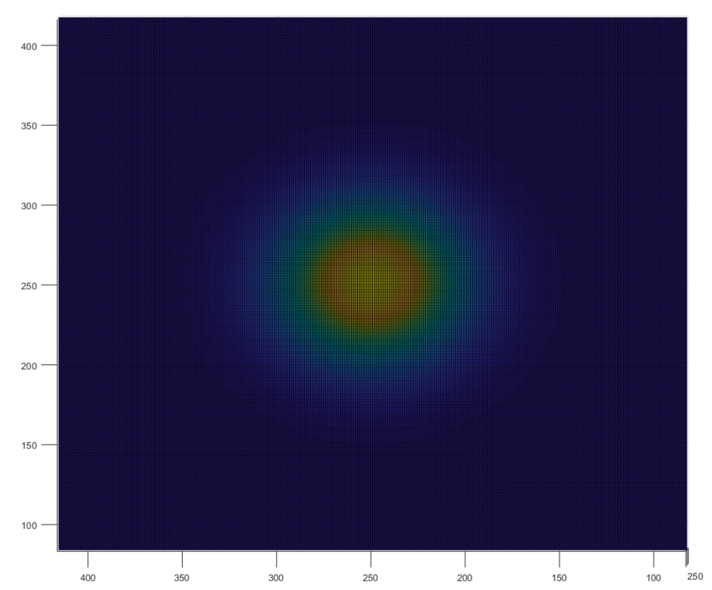

Figure 4: Diffusion radius of 100 microns

Results

•Both 2D point source and line source diffusions were successful.
- Point source: Average error was under 0.4% (Figure 2)
- Line source: Average error was 1.3% (Figure 2)
  - This was due to buildup of error from one row to the next (Figure 3)

•Obtained diffusion radius of 100 microns (Figure 4)

•3D cubic patch diffusion was also successful.
- O2 diffused equally in all three dimensions as a sphere (Figure 5)
- 3D cube source: Average error was 0.3%

•The vascular diffusion of oxygen looks realistic (Figure 7)
- red blood vessels diffuse oxygen into the grid, see cross-sections in Figure 7
- diffusion concentrations are highest where vessels cross through the plane

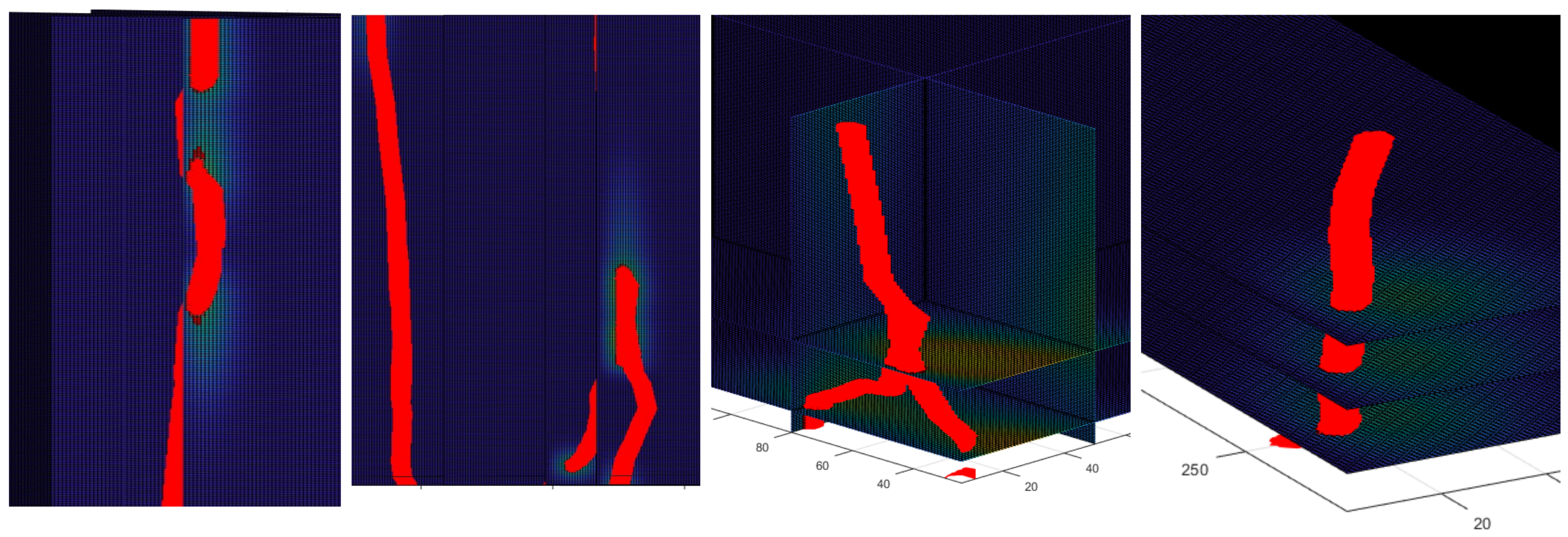

Figure 7:   Four examples of vascular diffusion of oxygen

Bibliography

1 Jana Gevertz, Zahra Aminzare, Kerri-Ann Norton, Judith P´erez-Vel´azquez, Alexandria Volkening, and Katarzyna A Rejniak, Emergence of anti-cancer drug resistance: exploring the importance of the microenvironmental niche via a spatial model, Applications of dynamical systems in biology and medicine, 2015, pp. 1–34.

2.Tina Giorgadze, Henning Fischel, Ansel Tessier, and Kerri-Ann Norton, Investigating Two Modes of Cancer-Associated Antigen Heterogeneity in an Agent-Based Model of Chimeric Antigen Receptor T-Cell Therapy, Cells 11 (2022), no. 19, 3165

3.Alex Pedcenko, 3D Heat equation solution with FD in MATLAB, 2023, https://github. com/aa3025/heat3d/ releases/tag/1.0.5.

4.G Nervadof, Solving 2D Heat Equation Numerically using Python, https://levelup. gitconnected.com/solving-2d-heat-equation-numerically-using-python-3334004aa01a.