From Clinical Slides to Mathematical Prediction, a Twofold Approach.

Sergey Klimov[1], Remus Osan[2], and Yi Jiang[2]

***Short Abstract* — integrating actual pathological slides, of pre-invasive cancer, with a mathematical model will allow for a better understanding of the potential tumor biological properties which lead to malignancy. In our work we hope to use image analysis of DCIS to uncover areas of high proliferative cellular densities alongside other physical constraints and compare them alongside a cellular potts model via CompuCell3d.**

***Keywords* — DCIS, KI-67 quantification, Clinical parameterization**

I. Introduction

Ductal Carcinoma in Situ (DCIS) is a commonly computationally modeled cancer due to its potential to preclude invasive carcinoma [1]. In order to better understand possible cellular mechanisms which might explain this malignant transition we integrate a novel 2 part approach. For the first part we an automated method to quantify histological slides (IHC) of DCIS, stained with the proliferative marker KI-67, to find regions of high density proliferation and other spatial qualities. These images also allow us to identify basement membrane geometric structure, location of relevant blood vessels, and survival outcomes that are unique to the specific patient. For the second half we stimulate DCIS growth using a Cellular Potts model, via Compucell3d [2], in order to correlate potential similarities between the clinical slide and mechanistic explanations via the in-situ experiments. For our simulation we investigate if alterations in cell cycle length heterogeneity [3, 4] and cell/basement membrane compressibility/deformation [5], within patient specific glucose and oxygen microenvironments, can result in significant tumor structural alterations.

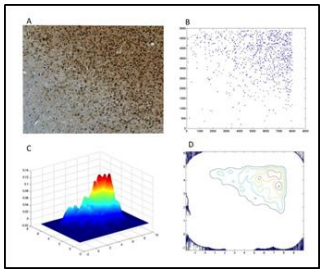
Although calibrations of DCIS models using patient specific IHC [6] and spatial analysis of tumor growth [7] have been done before our model is unique in that it combines membrane deformation, identification of spatial clinical patterns, and spatial alignment of blood vessels.

II. Results

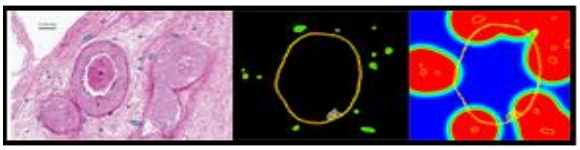
The work is currently in the process of integration, so results are reported alongside the results that we aim for.

A. KI-67 quantification

KI-67 cell pixels were properly stratified by setting a threshold of RGB values that was set at 2 standard deviations around the average of many KI-67 positive cells. The coordinates of these pixels were then ran through a kernel density estimator.



B. Model fit



Integrating CellDraw via CC3D we are able to outline the physical barriers that will be used within our model based on an actual biopsy slide (leftmost panel). The mock simulation of the cell field (middle) shows the basement membrane (red), blood vessels (green), and tumor cells (blue) while the oxygen field (rightmost) shows the potential diffusion limits of oxygen via the blood vessels. We aim to see what parameters can recreate the proliferative densities seen from part A, within the tumors physical constraints.

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[1]Georgia State University, Department of Biology, Atlanta, GA, United States

[2]Georgia State University, Department of Mathematics and Statistics, Atlanta, GA, United States