

Modeling Angiogenesis in Hypoxic Breast Cancer Tumors

Kali Konstantinopoulos¹, Timothy Mahajan¹, Furkan Kurtoglu¹, John Metzcar¹, Daniele Gilkes², Paul Macklin¹

1) School of Informatics, Computing, and Engineering, Indiana University

2) School of Medicine, John Hopkins University

Introduction

- Hypoxic conditions occur in the center of tumor after tumor cells use and deplete oxygen.
- Hypoxic cells secrete signaling chemicals to induce vascularization, such as vascular epithelial growth factor (VEGF).

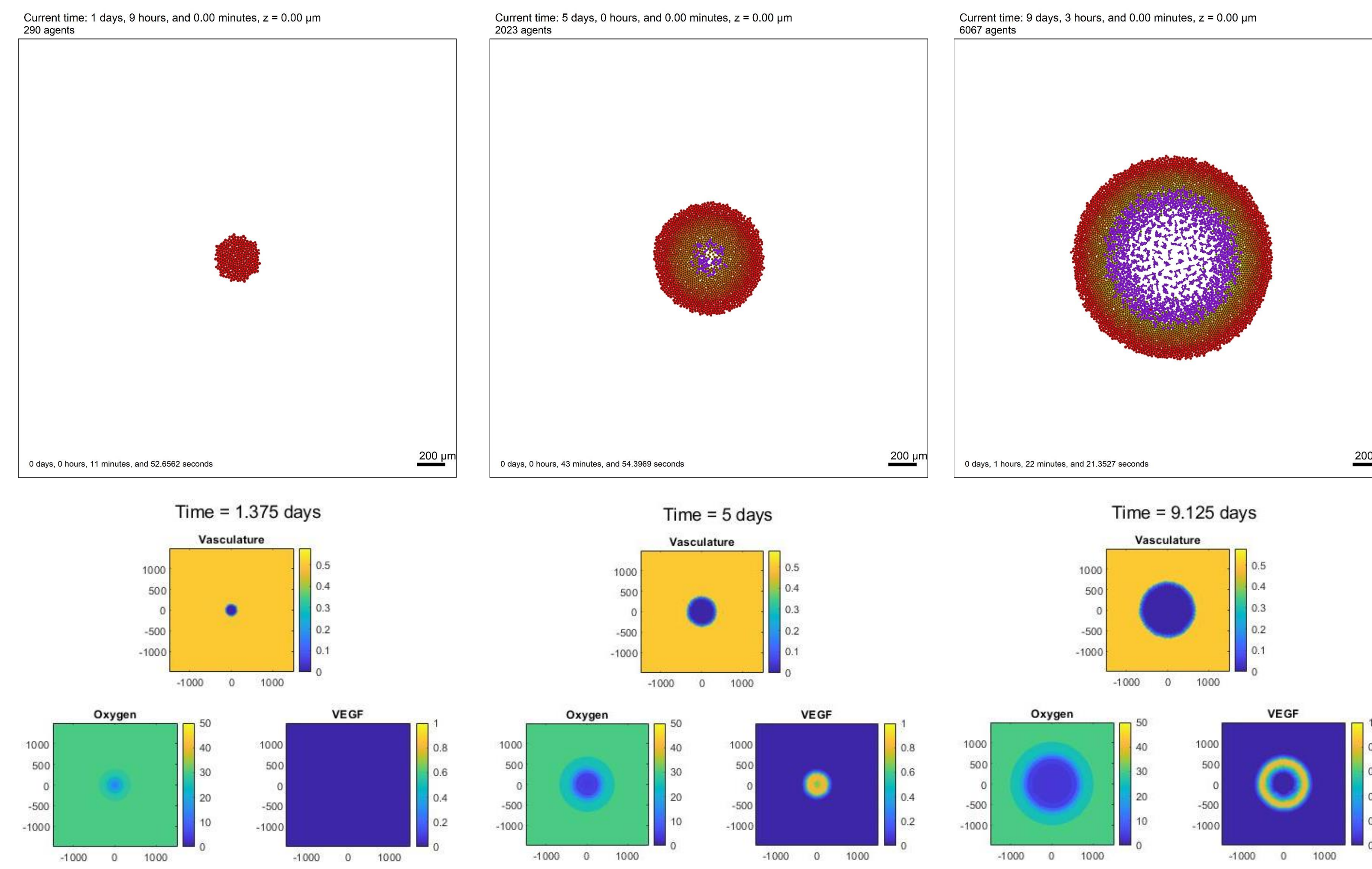
Methods

- This model is developed with using agent-based multicellular system simulator which is called PhysiCell¹.
- Cells are changing behavior according to oxygen level. After they become hypoxic, their genes are regulated.
- Our model accounts for this vascularization by increasing VEGF secretion by hypoxic cells.
- Vasculature is controlled by three mechanisms, which are grow, death, and advective flux.
- Blood supplies or uptakes metabolites from microenvironment according to blood target values.

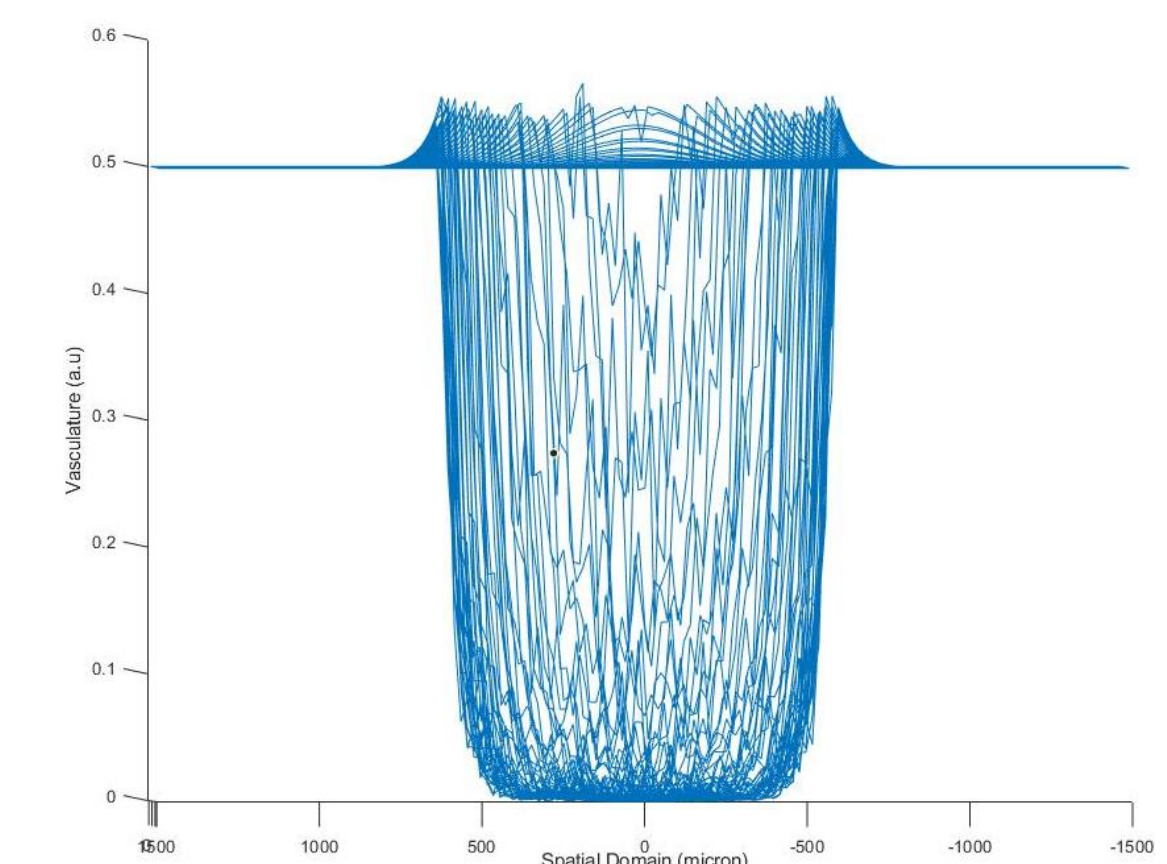
$$\frac{\partial \rho_v}{\partial t} = -\nabla \cdot \mathbf{J} + S$$

$$\text{Advective Flux: } \mathbf{J} = \mu_v \nabla \rho_v \frac{\nabla \mathbf{a}}{\|\nabla \mathbf{a}\|} \quad \left| \quad S = \overbrace{\beta b_v \left(1 - \frac{\rho_v}{\bar{\rho}_v}\right) \rho_v}^{\text{Vascular Birth}} - \overbrace{d_v \frac{\rho_v}{\bar{\rho}_v} \rho_v}^{\text{Vas. Death}}\right.$$

Results



- Tumor has a necrotic core that has nearly no oxygen.
- Cellular layering is formed as:
Necrotic, *Hypoxic*, *Normoxic*
- VEGF concentration through tumor has ring-like distribution which is consistent with literature³.
- A small vasculature accumulation near to tumor is observed. This was an expected behavior in order to modeling equations.



Future Work

- This model will be uploaded to NanoHUB to be able to run in cloud with user interface².
- Also, angiogenesis will be an external module that can be added to simulation which will be build in NanoHUB.

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References

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