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Molecular biology and basic cellular physiology(24AIM112)& Ethics, innovative research, businesses & IPR(24AIM115)

# OXYGEN-BASED TUMOUR GROWTH MODEL

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# INTRODUCTION

- Develop a Python-based model to visualize tumor growth dynamically.
- Correlation between the features in the data.
- Research Paper: “**Oxygen-Driven Tumor Growth Model: A Pathology-Relevant Mathematical Approach** “.

# BIOLOGICAL FOUNDATION

**Tumor Cells:**

- Uncontrolled division, bypassing checkpoints.
- Resistance to Apoptosis.
- Altered Metabolism and immune evasion.
- Angiogenesis.

**Role of Oxygen in Tumour Growth:**

- High Oxygen → **Proliferation.**
- Low Oxygen (Hypoxia) → **Quiescence.**
- Severe Oxygen Deprivation → Necrosis - The premature death of cells due to lack of oxygen or nutrients.

# RESEARCH PAPER:

- The paper presents the Oxygen-Driven Model (ODM), a mathematical model aimed at understanding tumor growth, hypoxia, and necrosis based on oxygen diffusion.
- The model was tested using 38 xenografted cell lines and 5 patient-derived xenograft-like models.
- Tumors were classified into two groups based on oxygen uptake and proliferation rate:
  **Group 1:** Slow-growing, poorly oxygenated tumors.
  **Group 2:** Tumors with similar oxygen supply but varying intrinsic growth rates.

| SI.NO | Software/Tool | Issue Encountered |
|---|---|---|
| 1 | PhysiCell | Lack of proper guidance on usage |
| 2 | VCell (Virtual Cell) | Installation and execution issues |
| 3 | CompuCell3D | latest Version not supported by Laptops |
| 4 | MATLAB(simulink) | No Proper libraries for cell simualation |

# MODELLING



## Correlation:

Correlation is a way of measuring the relationship between two factors (also called features or variables). It tells us how changes in one factor are linked to changes in another.

- **Correlation Coefficent**

**Data Set Used:**

| | A | B | C | D | E | F | G | H | I | J | K |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Repr. Sys. | Tumor Typ | k_p (mmH | SE(k_p) (m | k_r (cm^-1 | SE(k_r) (cn | Î”V (cmÂ³/ | Îº | Î³ | Rank | Residual |
| 2 | Gastric | SGC70 | 0.001537 | 6.30E-05 | 5.645459 | 22.90991 | 0.10401 | -24395.2 | 1523.081 | -3.47814 | -0.05214 |
| 3 | Breast | 7860 | 0.001412 | 0.001793 | 4.040413 | 27.89 | 0.021053 | -22229 | -976.076 | 13.42916 | 0.164252 |
| 4 | Lung | A2058 | 0.000516 | 0.001056 | 8.530466 | 11.69119 | 0.123879 | -12005.3 | -451.428 | 1.311797 | 0.242613 |
| 5 | Colon | Ri1 | 0.001357 | 0.001676 | 5.115475 | 24.73491 | 0.049121 | -52878.5 | 4534.125 | 6.926747 | 0.284354 |
| 6 | Kidney | HCC1954 | 0.002139 | 0.002081 | 10.61301 | 5.428485 | 0.093142 | 107348.7 | -2418.91 | 6.097443 | 0.091611 |
| 7 | Cervix | H3255 | 0.000592 | 0.00414 | 0.279427 | 17.71612 | 0.086047 | -19532.6 | 2547.102 | -2.8631 | 0.052742 |
| 8 | Other | SGC31 | 0.000491 | 0.001445 | 13.94095 | 33.78201 | 0.086527 | -69655.3 | 3805.214 | 13.56603 | 0.194466 |

This dataset captures tumor specific growth and oxygen dependency across multiple cancer types.

## Key Parameters

- **k_p (mmHg)** → Proliferation rate
- **k_r ($cm^{-1}$ s)** →oxygen uptake rate
- **V ($cm^3$)** → Tumor volume

doi:10.1371/journal.pcbi.1004550.t00

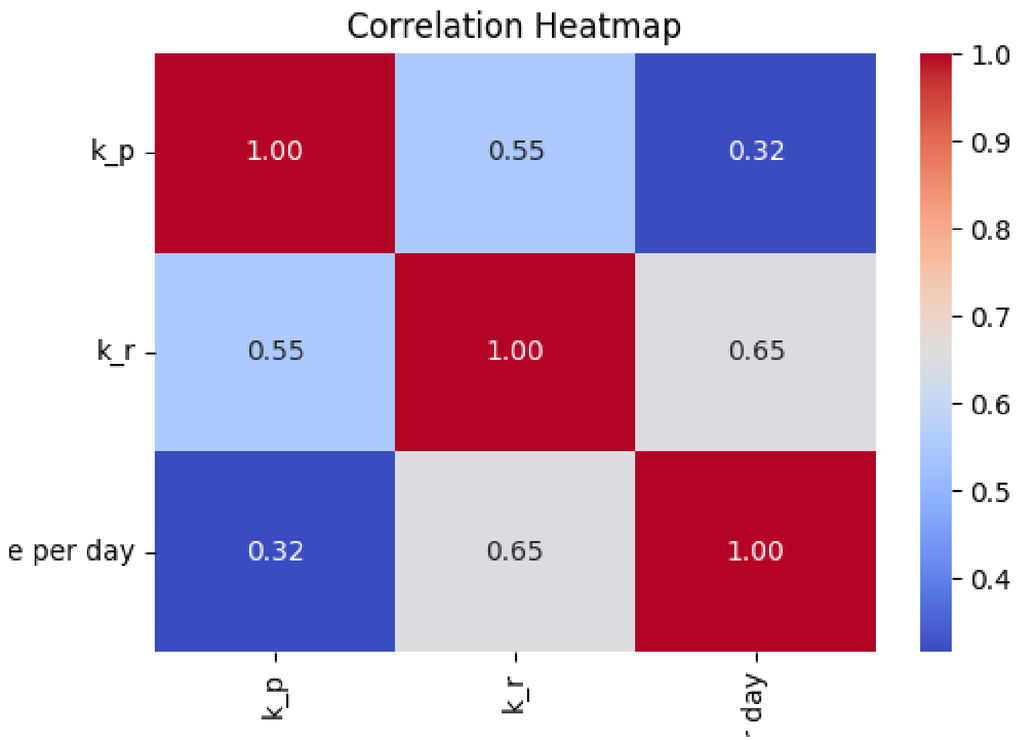
# OUTPUTS

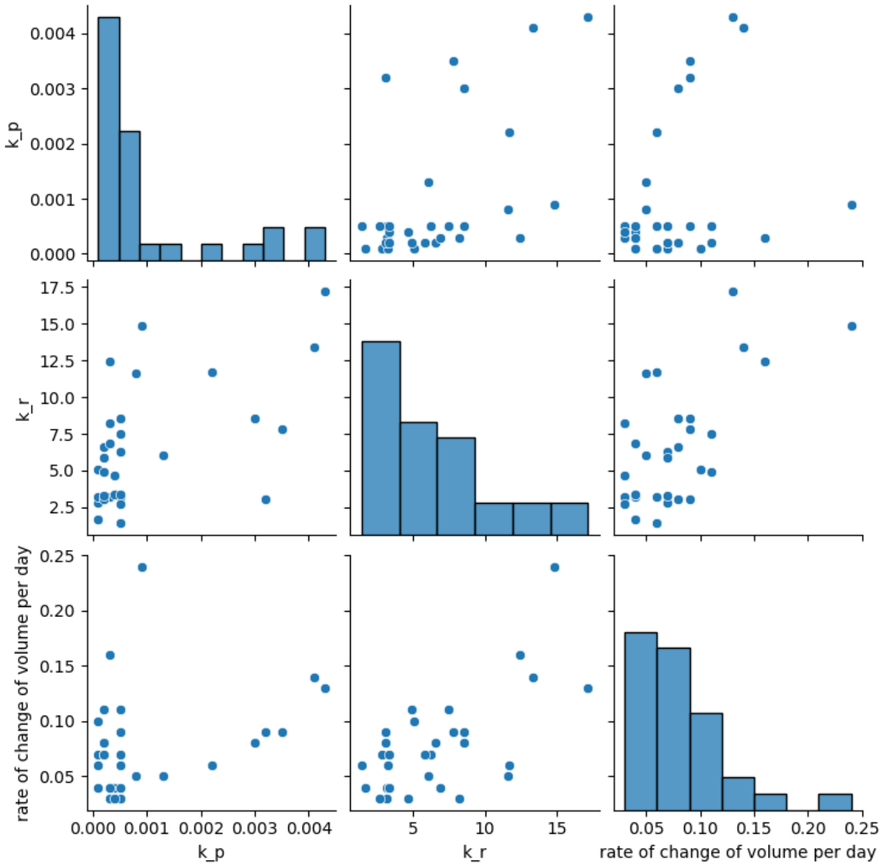


## Correlation Matrix:

| | k_p | k_r |
|---|---|---|
| k_p | 1.000000 | 0.548791 |
| k_r | 0.548791 | 1.000000 |
| rate of change of volume per day | 0.315765 | 0.651345 |

| | rate of change of volume per day |
|---|---|
| k_p | 0.315765 |
| k_r | 0.651345 |
| rate of change of volume per day | 1.000000 |



# ETHICS AND IPR

## Patent 1

### SYSTEM AND METHOD FOR DETECTING FORESTALLING AND TREATING CANCER PATIENTS USING ARTIFICIAL INTELLIGENCE

- **AI-Powered Detection –** Uses deep learning (Back Propagation Network) to analyze cancer test results.
- **Patient Data Collection –** Collects data from the two patients and processes data .
- **Cancer Stage Detection:** Compares new results with past cases.
- **Patient Classification:** Groups patients based on disease severity.
- **Outcome:** Enables personalized, accurate, and efficient cancer care.

# Patent 2:

## METHODS FOR DETERMINING TREATMENTS FOR CANCER PATIENTS

- Determination of Clinicopathological Markers.
- Input into a Gradient Boosting Machine Learning Model: The model is trained to analyze the markers to assess the patient's prognosis.
- Prediction of Short-Term Mortality.
- Therapeutic Decision-Making based on the prediction.

SUMMARY OF THE INVENTION

**[0009]** As described below, in a first aspect, the present disclosure provides a method of treating a patient having cancer, comprising: a) determining concentrations of multiple clinicopathological markers of the patient; b) providing, to a gradient boosting machine learning model, the determined concentrations of the multiple clinicopathological markers; c) receiving, from the gradient boosting machine learning model, a prediction of whether the patient is likely to die within a period of 12 weeks; and d) administering an anticancer therapeutic to the patient if the prediction indicates that the patient is not likely to die within the period of 12 weeks.

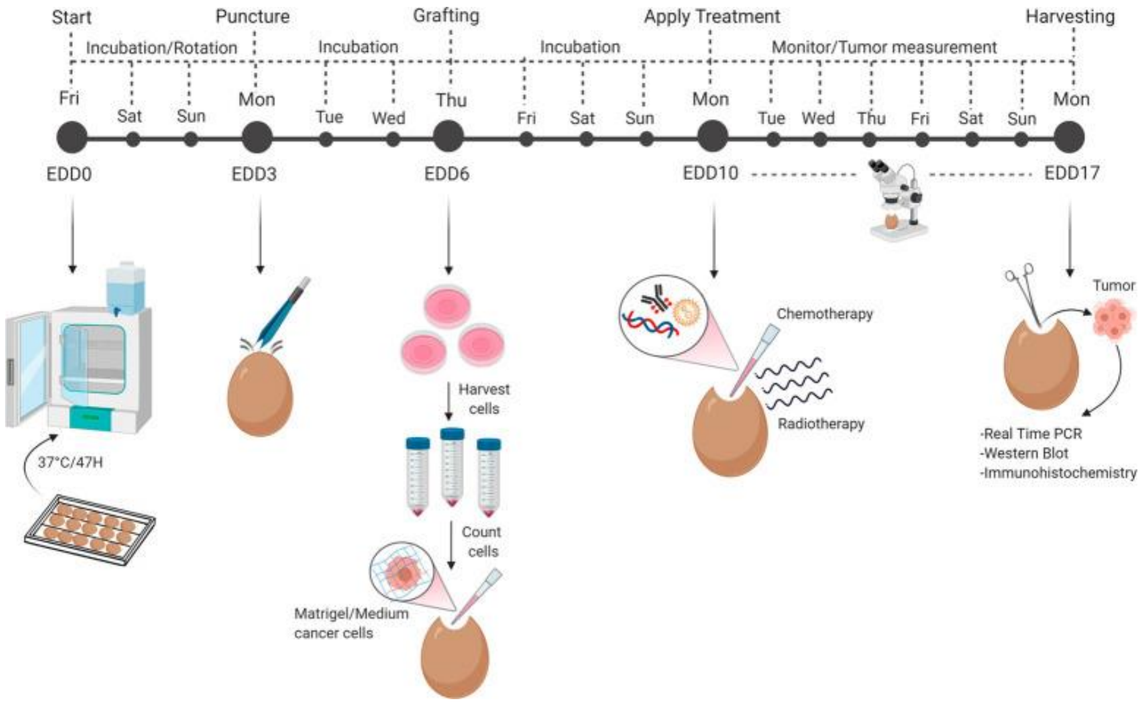
Dataset Identification

**[0232]** A comprehensive set of ICI trials was utilized with individual patient concentration data (Table 9) for developing the 3i score model. The trials were selected so that the training and tuning sets would include data for patients with a diverse range of tumor types and across different lines of therapy.

Dataset Separation, Labelling

**[0250]** Acquired datasets were pre-processed internally according to internal data management standards. Patients who died within 12 weeks (i.e. time from randomization/first dose to death ≤12 weeks) were labelled as EM. Patients who survived beyond 12 weeks (i.e. time from randomization/first dose to death ≥12 weeks) were not labelled as EM. Patients who were censored within 12 weeks (i.e. patients lost to follow up <12 weeks) were not included in the training set during the development of the model. No other data manipulations were performed.

# CLINICAL PROTOCOL & LEARNING APPROACH




**Clinical Protocol: CAM Model for Tumor Growth (Shortened Overview)**

- Embryonic Day 0 (EDD0): Start incubation.
- EDD3: Puncturing to reposition the air sac.
- EDD6: Graft $2 \times 10^6$ SCC-25 tumor cells (tumor forms by EDD10).
- EDD10: Topical treatment applied.
- EDD10–EDD17: Tumor growth monitored until harvesting.

**Active & Transverse Learning in Tumor Growth Modeling:**

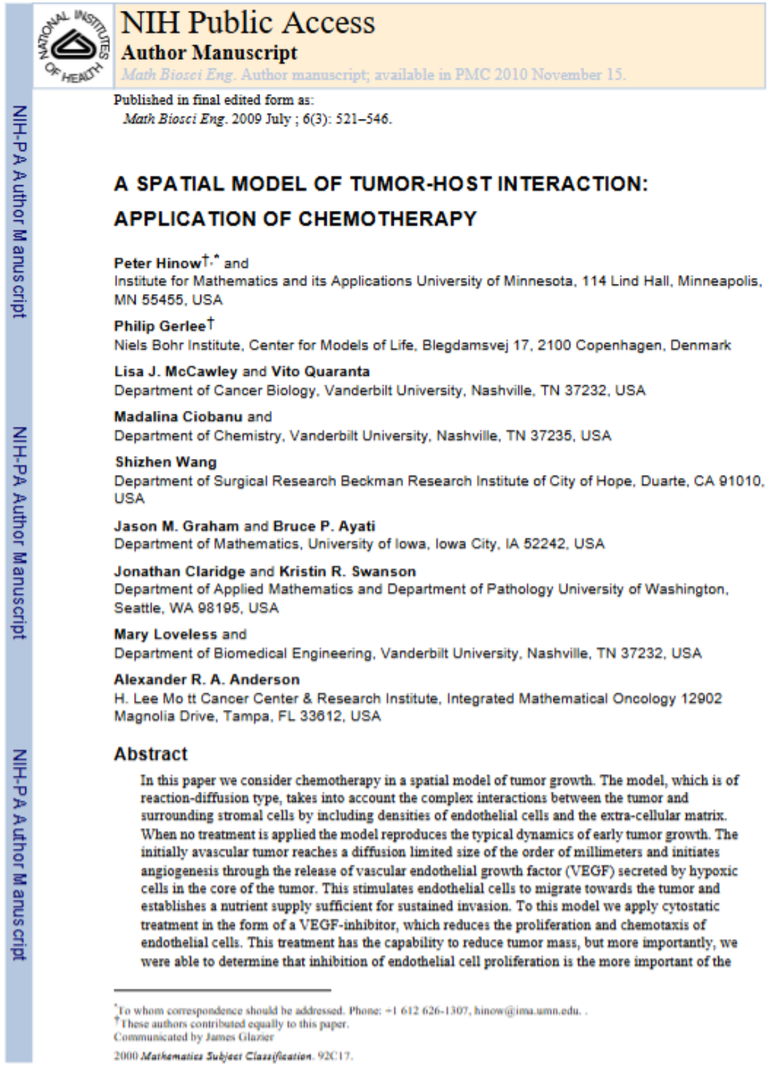
- **Active Learning:** Iterative model refinement by adjusting tumor growth parameters (progression/regression rates) and observing outcomes.
- **Transverse Learning:** Applying oxygen diffusion insights to tumor proliferation modeling, improving prediction accuracy.

Source: (https://pmc.ncbi.nlm.nih.gov/articles/PMC8205242/)
Sarogni P, Mapanao AK, Marchetti S, Kusmic C, Voliani V. A Standard Protocol for the Production and Bioevaluation of Ethical In Vivo Models of HPV-Negative Head and Neck Squamous Cell Carcinoma

# CASE STUDY

## Key Points: Spatial Tumor–Host Interaction Model (Hinow et al., Math Biosci Eng. 2009)

- **Mathematical Model of Tumor Growth:** Uses reaction-diffusion equations to model oxygen-dependent tumor expansion.
- **Oxygen & Hypoxia Influence:** Shows how low oxygen (hypoxia) slows tumor growth and triggers angiogenesis.
- **Tumor-Host Interaction:** Models the balance between tumor proliferation and oxygen supply in the microenvironment.
- **Extension to Chemotherapy:** Explores how oxygen availability affects treatment response, linking tumor growth to drug diffusion.





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### A SPATIAL MODEL OF TUMOR-HOST INTERACTION: APPLICATION OF CHEMOTHERAPY

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**Abstract**

In this paper we consider chemotherapy in a spatial model of tumor growth. The model, which is of reaction-diffusion type, takes into account the complex interactions between the tumor and surrounding stromal cells by including densities of endothelial cells and the extra-cellular matrix. When no treatment is applied the model reproduces the typical dynamics of early tumor growth. The initially avascular tumor reaches a diffusion limited size of the order of millimeters and initiates angiogenesis through the release of vascular endothelial growth factor (VEGF) secreted by hypoxic cells in the core of the tumor. This stimulates endothelial cells to migrate towards the tumor and establishes a nutrient supply sufficient for sustained invasion. To this model we apply cytostatic treatment in the form of a VEGF-inhibitor, which reduces the proliferation and chemotaxis of endothelial cells. This treatment has the capability to reduce tumor mass, but more importantly, we were able to determine that inhibition of endothelial cell proliferation is the more important of the

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# THANK YOU