# CARTopiaX: Extending a Next-Generation Platform for Computational Cancer Biology

Progress update of Google Summer of Code Project 2026



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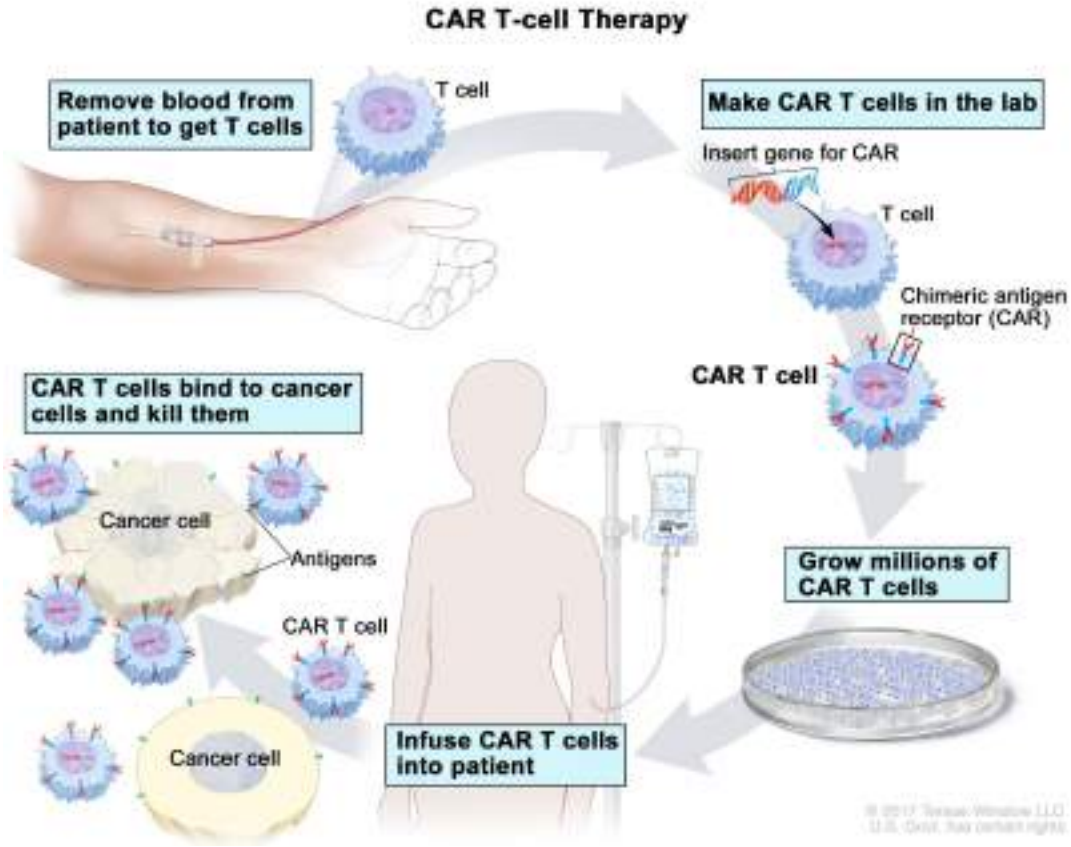
# CAR T-cell Therapy




**CAR T-cell therapy**: A type of immunotherapy that engineers T-cells to recognize and kill cancer cells.

Image ref: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy

# CAR-T Treatment Modeling: CARTopiaX

- While CAR-T therapy is **highly effective in hematological cancers** (e.g., leukemia) and supported by numerous mathematical models, it still **struggles in solid tumors**, where robust simulation **models remain scarce** despite their importance for optimizing treatment strategies.
- **CARTopiaX** is an **agent-based model** (ABM) built on BioDynaMo, implementing the **mathematical framework** proposed in Nature paper "*In silico study of heterogeneous tumour-derived organoid response to CAR T-cell therapy*" (2024)
- It provides a platform for simulating **tumor–immune interactions**, **testing hypotheses** and **evaluating CAR-T treatment strategies in silico**.
- Goal: Extend and calibrate CARTopiaX to **reproduce state-of-the-art CAR T-cell experiments**, **demonstrating** it as a **flexible** and **robust framework** for in silico hypothesis testing that **accelerates research** and **reduces reliance on costly wet-lab** experiments.

CARTopiaX

CARTopiaX repository

# The Selected Paper: Evaluating CAR-T Cell Therapy in a Hypoxic 3D Tumor Model

- Experimental Setup: The study utilized HER2+ SKOV3 **ovarian cancer cells** in a 3-D GelMA hydrogel, comparing a **hypoxic environment** (created by a **polycarbonate cap**) **against normoxia** (no cap).
- Treatment Protocol: **Anti-HER2 CAR-T cell** efficacy was evaluated at a **20:1 effector-to-target (E:T) ratio** over a total experimental duration of **72 hours**.
- Limited T Cell Infiltration: Despite high tumor mortality, CAR-T cell infiltration into the 3-D hydrogel bulk was negligible, with most immune cells remaining at the edges.
- Key Finding, Bystander Killing Mechanism: **Tumor death at a distance (in the core)** was driven by metabolic competition; activated **CAR-T cells at the periphery** rapidly consume glucose and oxygen, **starving the already stressed cancer cells in the center**.
- Aim: Extend CARTopiaX to **replicate their results** in silico.

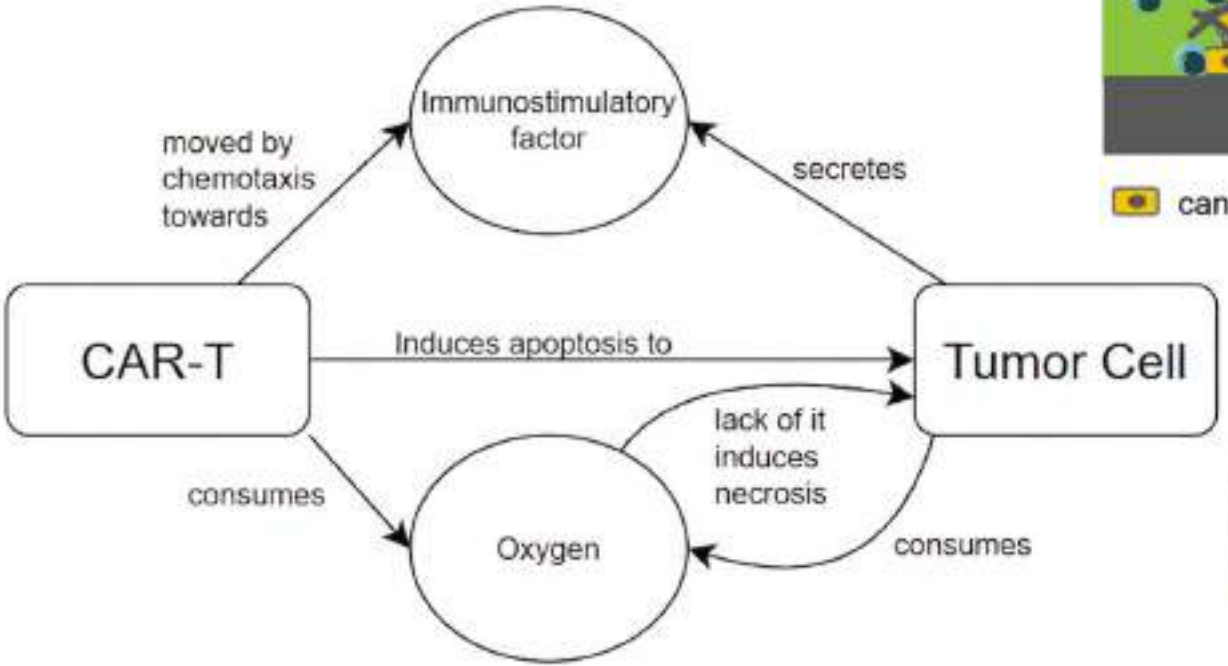

HHS Public Access

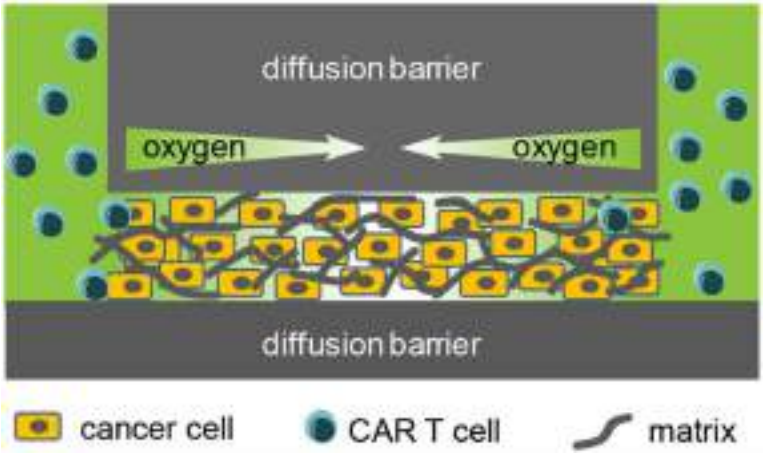
Evaluating CAR-T Cell Therapy in a Hypoxic 3-D Tumor Model

Abstract

Ando Y, Siegler EL, Ta HP, Cinay GE, Zhou H, Gorrell KA, Au H, Jarvis BM, Wang P, Shen K. Evaluating CAR-T Cell Therapy in a Hypoxic 3D Tumor Model. Adv Healthc Mater. 2019 Mar;8(5):e1900001. doi: 10.1002/adhm.201900001. Epub 2019 Feb 8. PMID: 30734529; PMCID: PMC6448565.

# The model: cylindrical tumor mass



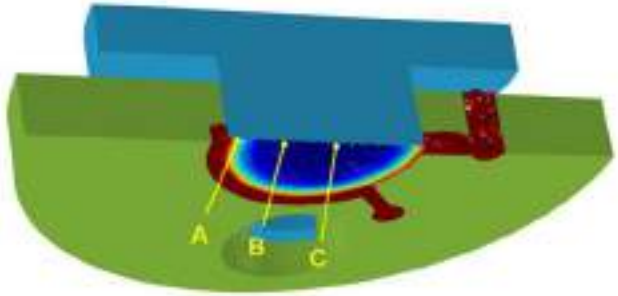
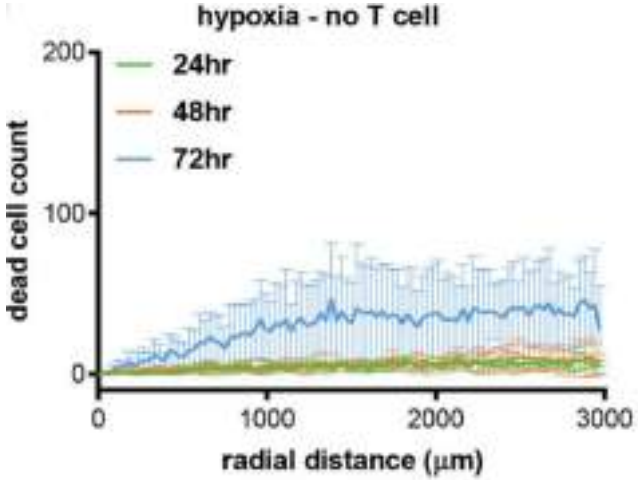
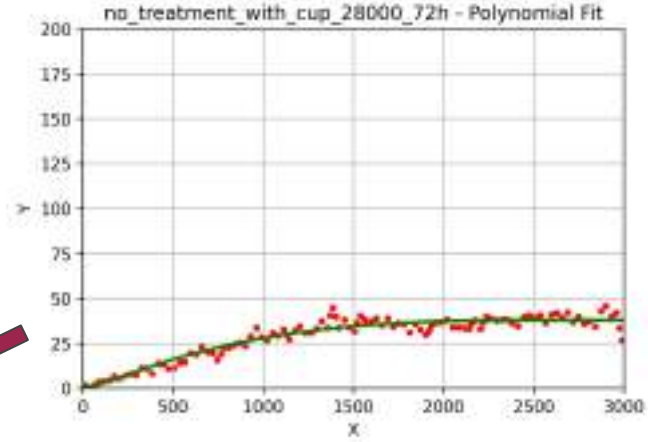
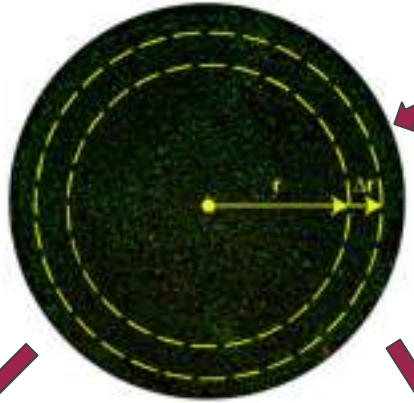



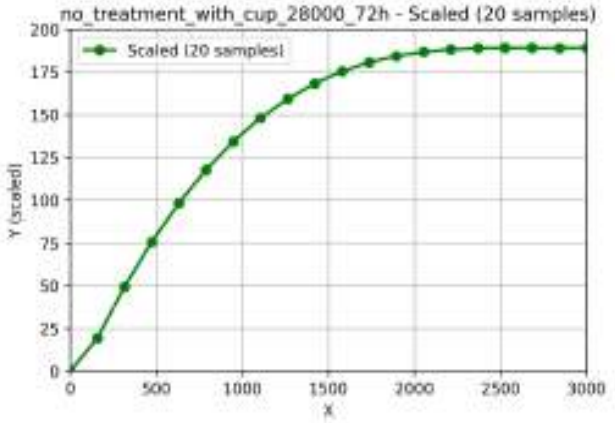

Image ref: https://pubmed.ncbi.nlm.nih.gov/30734529/

# Data obtention

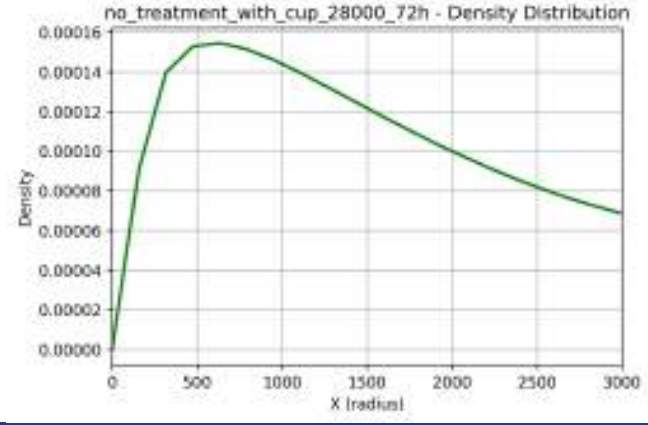


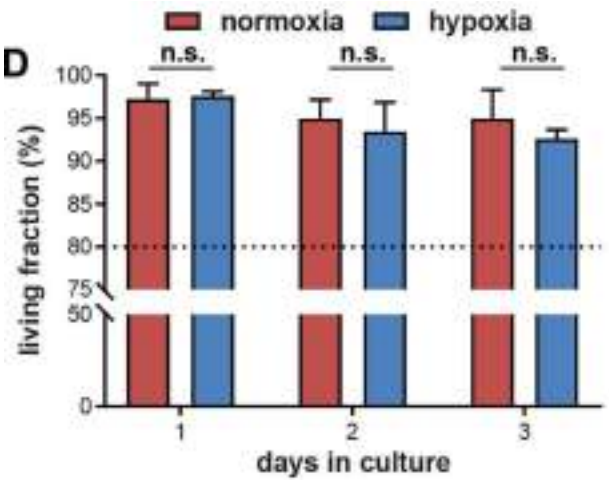

Area normalization of the absolute numbers



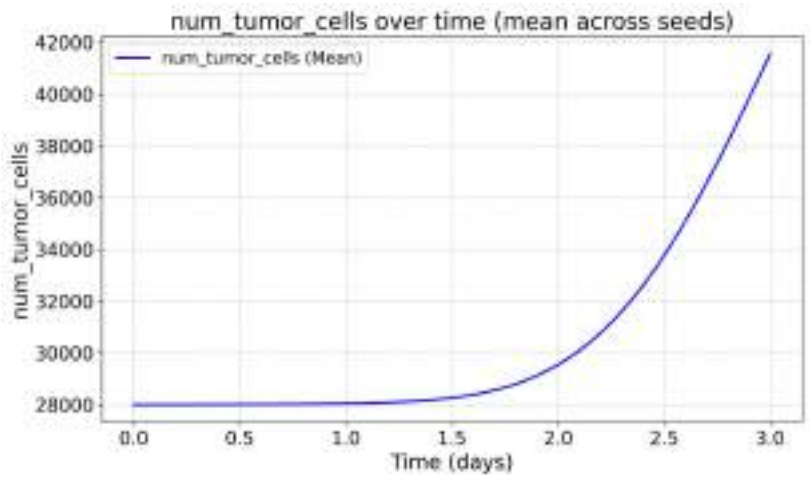
# Number of cells computation

**Dead cells count**

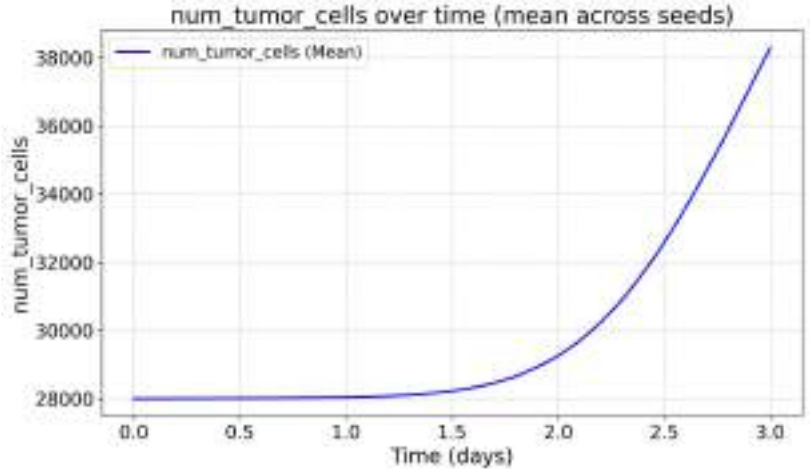
+



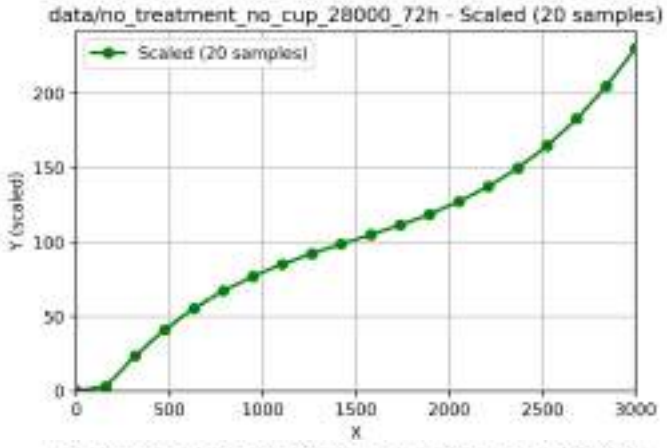

normoxia

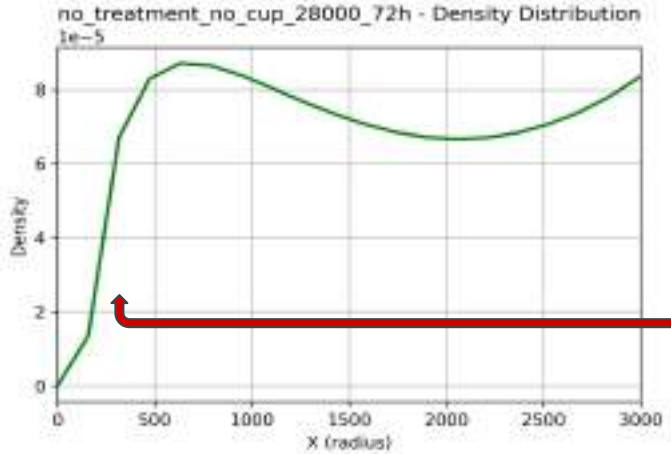



hypoxia



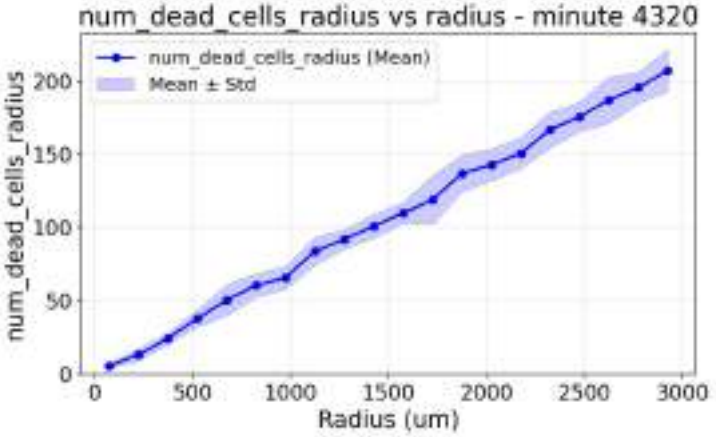
# Density of 10 million cells/mL, no cup (normoxia)

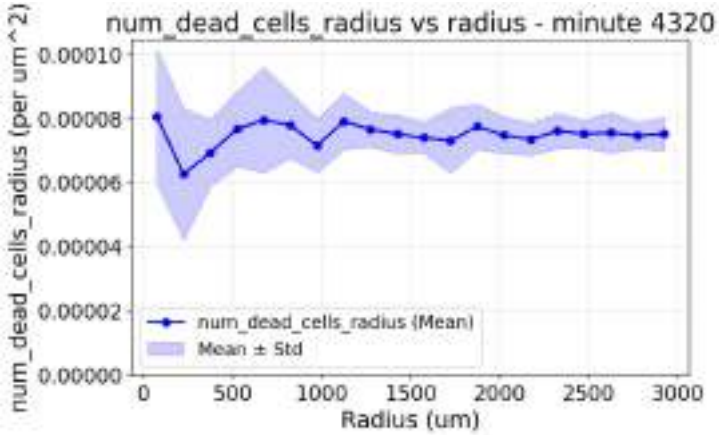



**Absolute count is misleading**: deaths are **uniformly distributed**

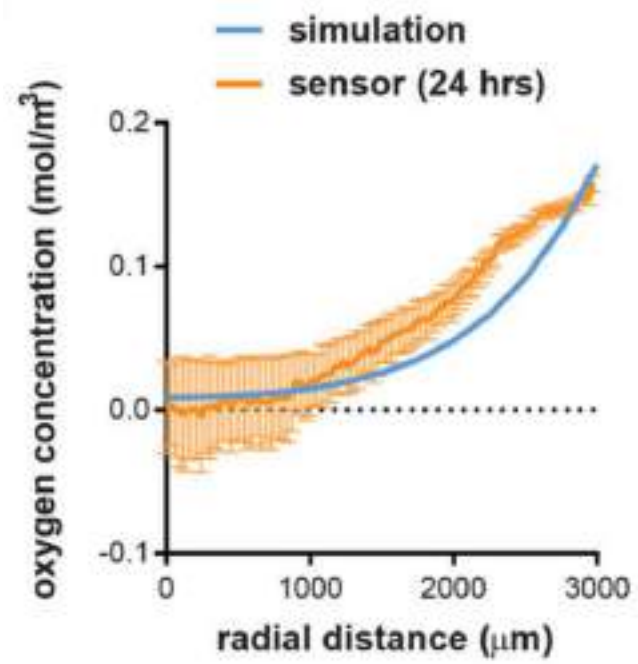
Anomalies caused by near-zero values and a very small radius containing too few cells



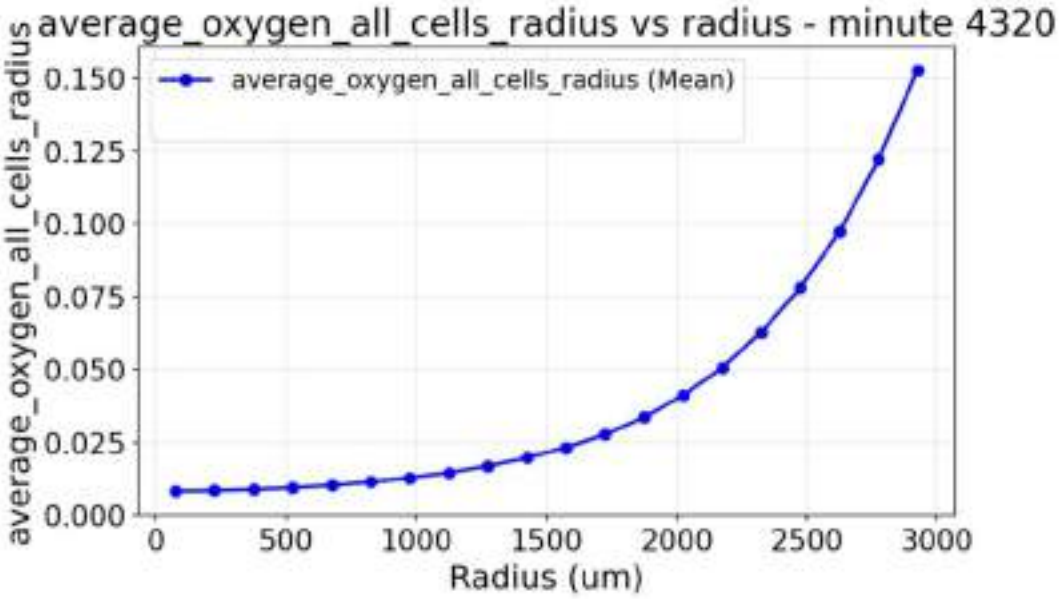



# Density of 10 million cells/mL, with cup (hypoxia)

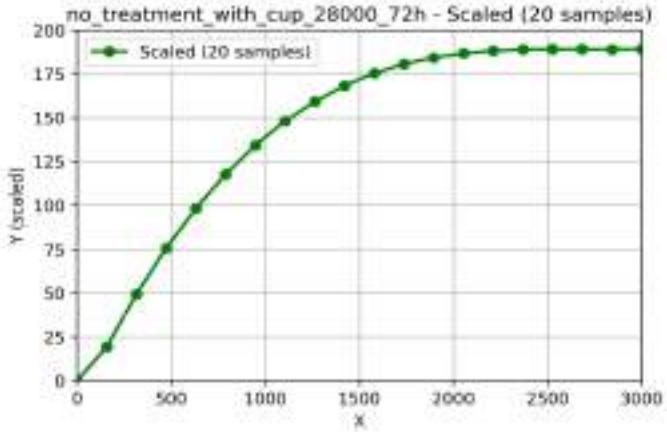
Paper's reported oxygen levels (orange). The authors also modeled them using a simple differential equation model (blue), but this is unrelated to CARTopiaX

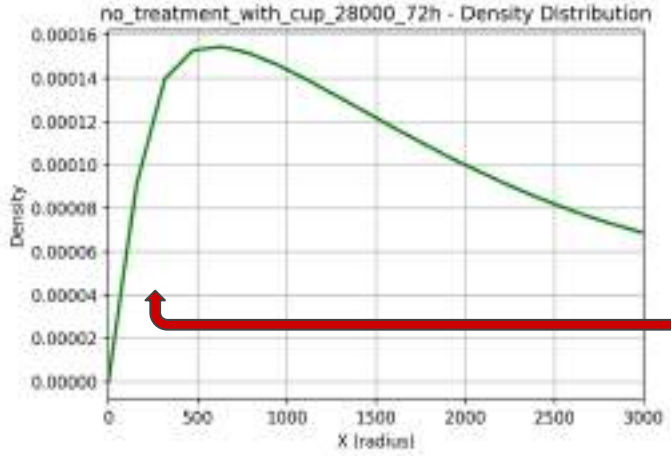



**Decreasing oxygen that flows from the border** of the cylinder (3000μm)



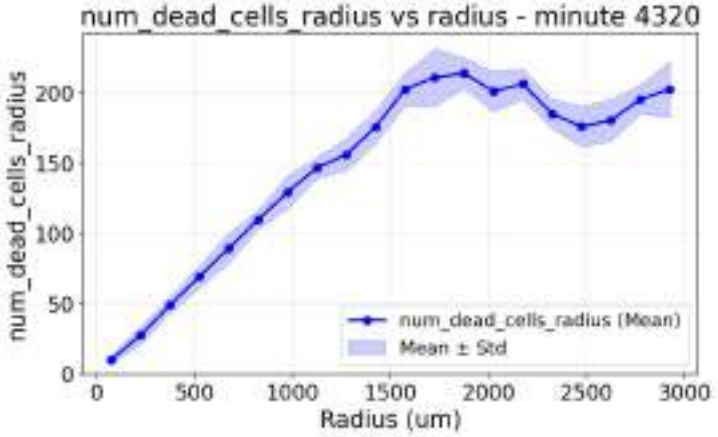
# Density of 10 million cells/mL, with cup (hypoxia)

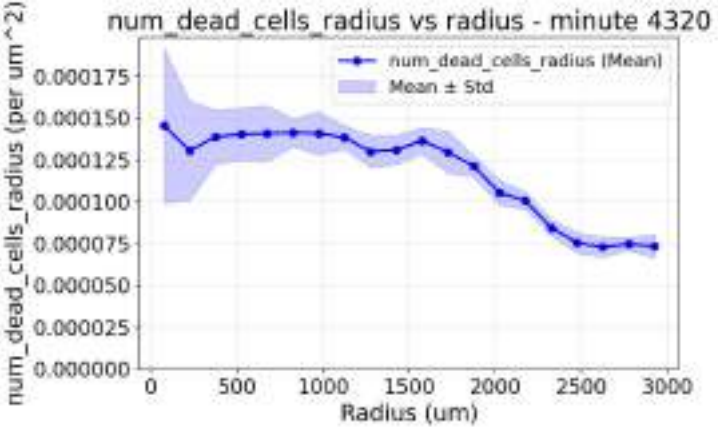


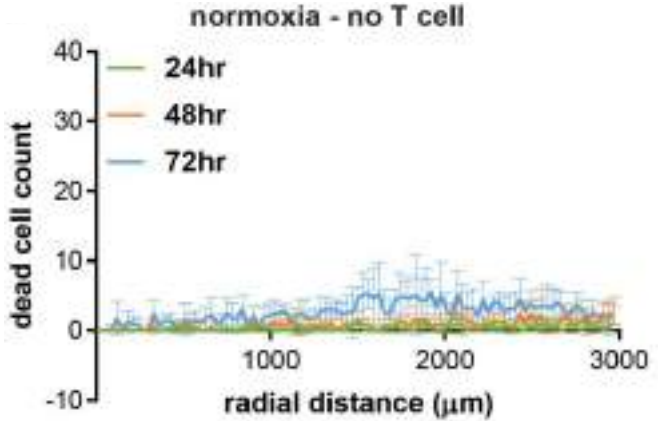

**Cells tend to die at the center**, where oxygen levels are lower

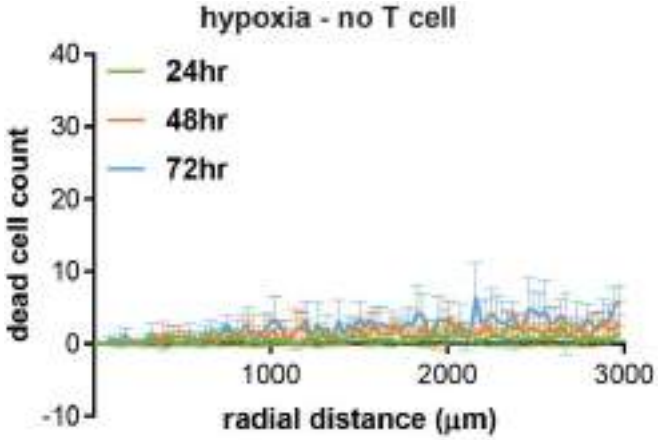
Anomalies caused by near-zero values and a very small radius containing too few cells



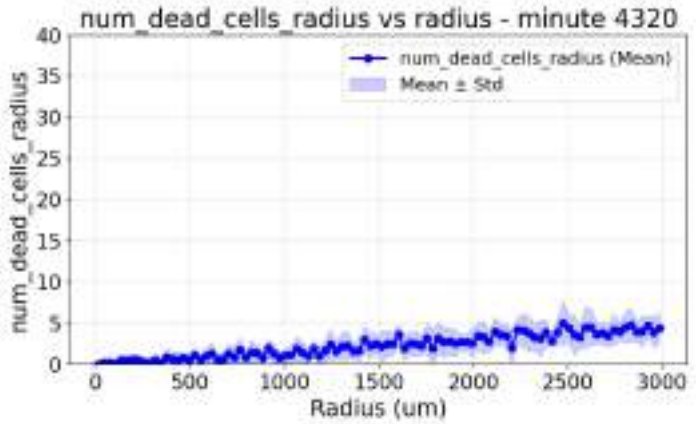



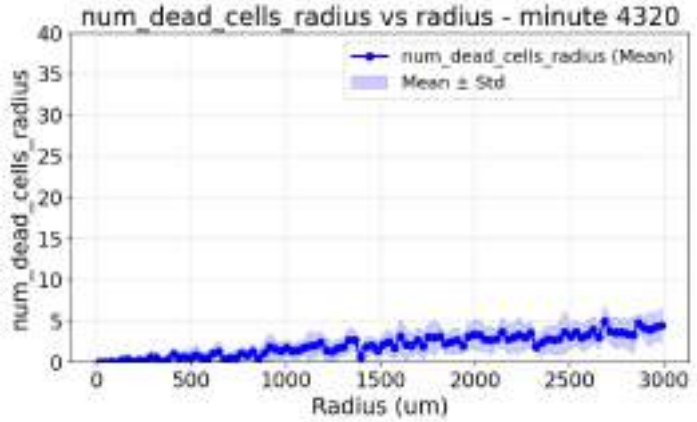
# Density of 1 million cells/mL




**Very few cells** are present. Therefore, both the normoxic (without cup) and hypoxic (with cup) conditions **are effectively normoxic**, resulting in **no significant differences**.



# Conclusion: Next steps & Impact

- Already achieved: **Hypoxic tumor** model successfully **replicated**.
- Present: Replicating the behavior of a **20:1 CAR T-cell therapy (already in progress)**, including:
  - A new **glucose** gradient.
  - **Medium viscosity** and its effect on CAR T-cell motility and interaction forces.
  - CAR T-cell **cytotoxicity** and **tumor immune evasion** under hypoxia.
  - Activated CAR T-cell **oxygen consumption**.
- Main goal: Establish **CARTopiaX as a flexible and extensible framework** for computational oncology.
- Further step: Already planning the **structure of a manuscript** presenting CARTopiaX through quantitative validation against wet-lab experiments for **publication in a scientific journal**.