

Agent-Based Biomechanical Modelling of Lung Adenocarcinoma and its Tumour-Immune-Microenvironment using PhysiCell



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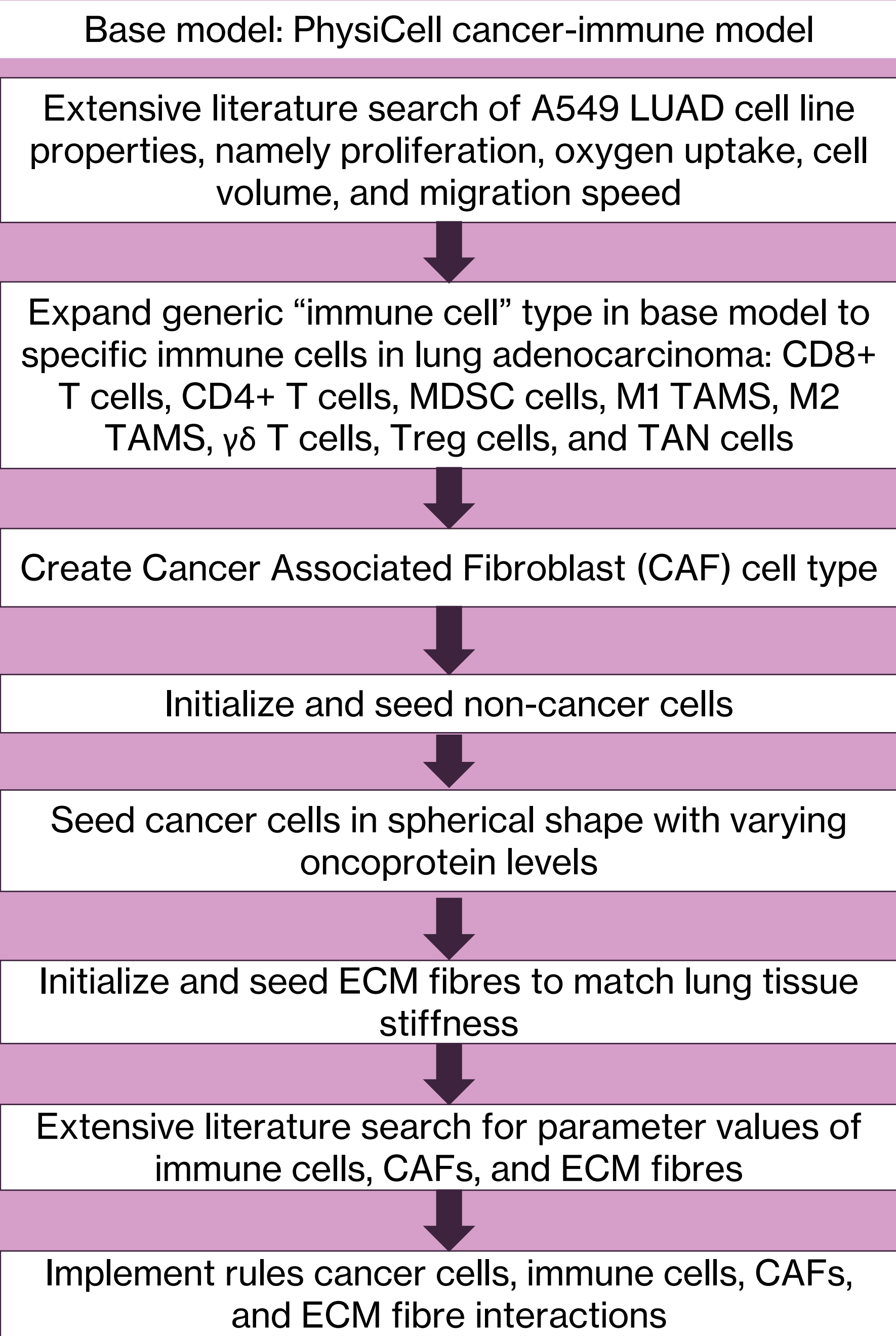


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Abstract

Lung cancer, of which **lung adenocarcinoma (LUAD)** is a subtype, is the leading cause of cancer death in the world¹. The tumour-immune-microenvironment (**TIME**) contains complex interactions between **cancer cells, immune cells, and extracellular matrix (ECM) proteins** that contribute to tumour growth³. Immune cells can have **both pro- and anti-tumour roles**³. In LUAD the ECM increases in stiffness and density, thus promoting tumour growth⁴. There is a gap in **in-silico modelling of the comprehensive TIME of lung cancer** using agent-based modelling, which this model seeks to address. The model presented expands the existing PhysiCell cancer-immune model to simulate **early LUAD**, through agent-based modelling of cancer cells, immune cells (CD8+ T, CD4+ T, *MDSC, M1 *TAM, M2 *TAM, $\gamma\delta$ T, *Treg, and *TAN cells), CAFs, and ECM fibres. This can be used in conjunction to in-vivo or in-vitro experiments to **predict tumour growth, simulate patient specific prognostic predictions, and trial cancer therapies**. This project also provides a **stepwise methodology** for comprehensive simulation of specific cancer types including the TIME.

Methodology



Legend

- cancer cell
- MDSC
- $\gamma\delta$ T cell
- TAN
- CD8+ T cell
- M1 TAM
- Treg
- ecm
- CD4+ T cell
- M2 TAM
- CAF

What is PhysiCell?

PhysiCell is software used to build mechanistic, multicellular, off-lattice agent-based models, predominantly for cancer. It is written in C++ and is open-source⁵.

Mechanistic: based on scientific laws and rules⁵

Agent-based: each cell/fiber is an independent object with individual rules⁵

Off-lattice: cells not confined to predefined coordinates on a grid⁵

Each cell type is programmed with parameter values for cell cycling, apoptosis, necrosis, solid and fluid volume changes, mechanics, and motility, secretion/uptake, and rules for cell-cell interaction⁵. Custom parameters/rules can be added⁵.

Results

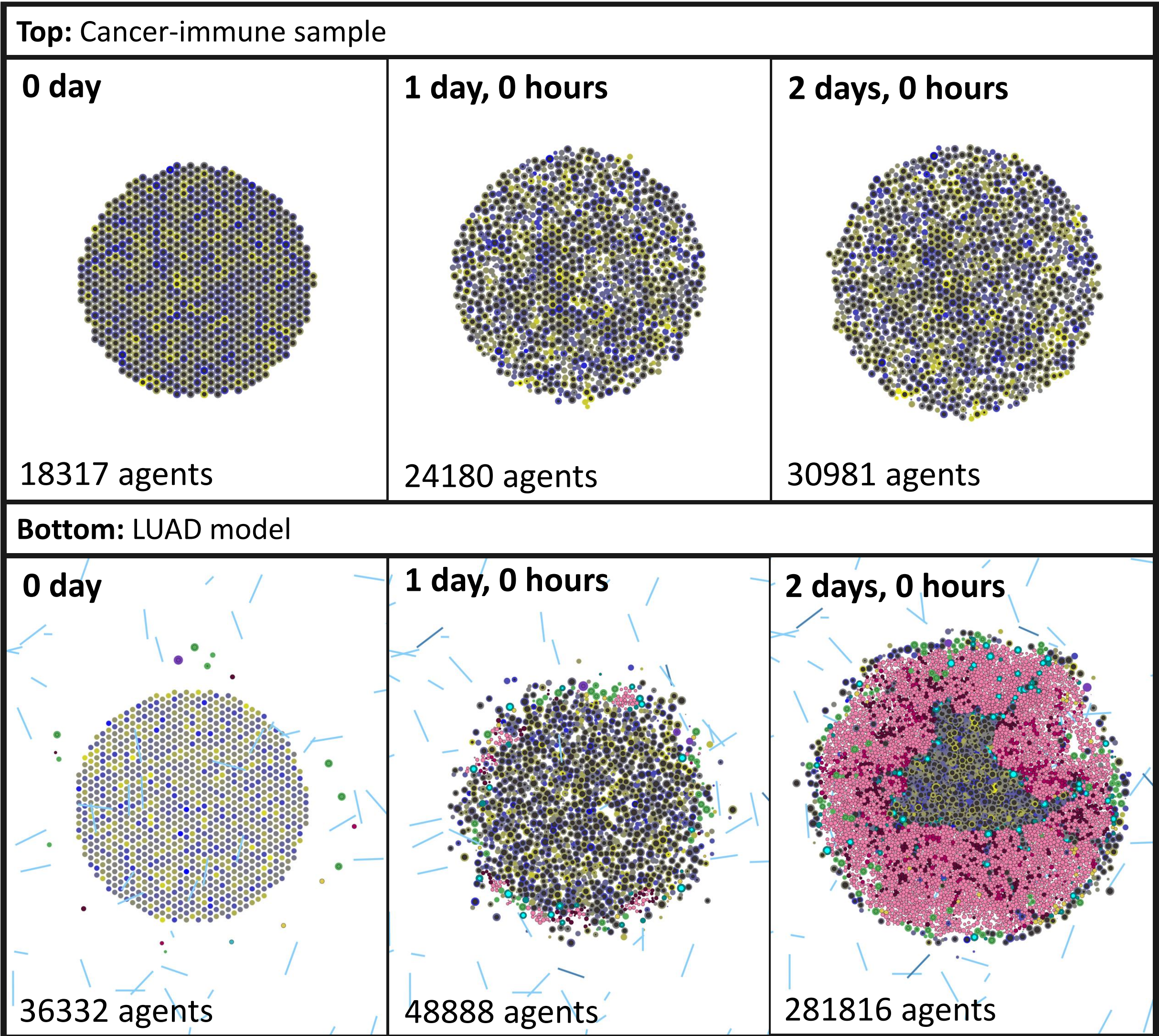


Figure 1. Cross section of simulated LUAD and TIME at various timepoints.

Future Directions

1. **Ensure 3D simulation functionality and validity**
2. **More accurate spatial arrangement of cells** → Seed non-cancer cells in between cancerous cells
3. **ECM fibre subtypes** → expand generic ECM cell type to specific subtypes

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*MDSC = myeloid-derived suppressor cell, TAM = tumour-associated macrophage, Treg cell = regulatory T cell, TAN = – tumour-associated neutrophils

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