# Tumor Growth Dynamics Simulation Based on Cellular Automata

Zhouji WU[1] and Priyasha PAUL[1]

[1] *Universite Evry, Paris Saclay**

## Abstract

Mathematical oncology aims to use continuous or discrete models to mathematically describe cancer-related phenomena. While these methods are typically expressed in terms of differential equations, the composition of tumors involves specific cellular structures, which can be modeled using their probabilistic properties. Cell-based models allow the monitoring of independent single parameters, which may vary in both time and space. This report, based on the original paper, presents a cellular automaton(CA)-based simulation strategy to model four possible basic behaviors of tumor cells: proliferation, migration, apoptosis, and quiescence. Although these behaviors are simple, the model can simulate complex global tumor features depending on different parameter settings. This report demonstrates five different scenarios, highlighting the model's ability to express tumor dynamics, such as hidden periodicity, spatial resource dependence, clonality, and death instability. By omitting biochemical details, the model achieves the capability to perform large-scale simulations, effectively capturing the long-term tumor dynamic features.

**Keyword: Tumor Dynamics, Cellular Automata, Tumor Heterogenesis**

## 1 Introduction

Cellular Automata (CA) is a kind of discrete model that works by dividing space into a grid, where each unit follows simple rules and changes over time steps based on its local neighborhood. From simple local rules, Cellular Automata are able to produce complex global behavior, a phenomenon known as emergence. With this feature, CAs are efficient for simulating complex biological processes such as tumor growth because of their ability to model spatially-distributed systems with local interactions.[1]

### 1.1 Conventional Cellular Automata

In a typical CA, cell updates its state based only on its local neighborhood which simplifies its individual behaviors and make it naturally suited for large-scale parallel computation and efficient for simulating complex systems. They also provide a powerful framework for modeling localized interactions in various domains such as physics, biology, and social systems. Remarkably, certain Cellular Automata, like Conway's Game of Life, are Turing complete, meaning they can simulate any computation given the right initial conditions.[2]

A standard CA can be defined as a quadruple (C, n, S, f) as:

- $C$ is a set of cells, not required to be finite.
- $n$: $C \times C \rightarrow 0, 1$ is a neighborhood function that can be seen as a relationship (usually reflexive and symmetric) between cells.
- $S$ is a set of states. Each cell will have an associated state, in each moment.
- $f$: $S|N| \rightarrow S$ is a transition function.

### 1.2 Tumor Dynamics

Tumors are complex structured entities composed of heterogeneous cells that grow uncontrollably and interact with their surrounding microenvironment. These cells are influenced by factors like nutrient availability, oxygen levels, and immune responses, leading to diverse and dynamic behaviors such as cell proliferation, migration, and invasion. As tumors grow, they form patterns like invasive fronts and necrotic cores, which are influenced by spatial interactions.

To model these complex dynamics, Cellular Automata (CA) offer a suitable approach. CA's grid-based structure and local interaction rules allow for the simulation of tumor growth,[3] invasion patterns[4] and cellular heterogeneity[5] in a computationally efficient way. The emergent behavior from simple rules makes CA an ideal tool for studying tumor progression and exploring potential treatments.

### 1.3 Tumor Heterogenesis

Tumor cell heterogeneity refers to the presence of diverse cell populations within a tumor, each exhibiting distinct genetic, phenotypic, and functional characteristics. This variability arises due to genetic mutations, environmental pressures, and clonal evolution, making tumors highly dynamic and complex.[6] Despite its significance, tumor cell heterogeneity is often overlooked in many cancer research studies, which tend to focus more on tumor growth and the invasion of normal tissues. While these aspects are critical for understanding cancer progression, they fail to capture the full complexity of tumors. The diverse cell populations within a tumor can behave differently, responding variably to treatments and influencing disease outcomes,. As a result, therapies that target the bulk tumor mass without considering cellular diversity may be less effective. A deeper understanding of tumor cell heterogeneity is essential for developing more personalized and effective cancer treatments.[7]

In this project, we created a simulation of how tumors grow and behave using cellular automata. Our model treats different types of tumor and only tumor cells differently, based on how they grow (proliferation), move (migration), stay inactive (quiescence), or die (apoptosis). These behaviors are decided by probabilities, helping us mimic the complex and varied nature of real tumors.(To avoid confusion, we refer to the fundamental grid elements of the automaton as "units" instead of "cells," since we are modeling biological cells.)

## 2 Modelization

### 2.1 Lattice

The model works on a simple 2D grid that behaves like the environment where the tumor grows. Each spot on the grid can either be empty or occupied by a cell. We use a Moore neighborhood,

*Local CA Engine Provided by Frank Delaplace, Universite Evry, Paris Saclay

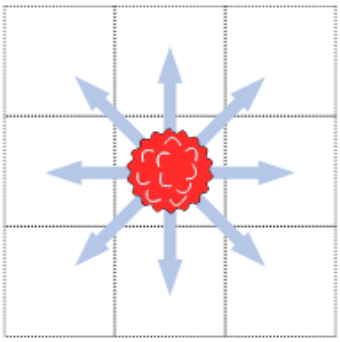

**Figure 1:** Lattice Definition

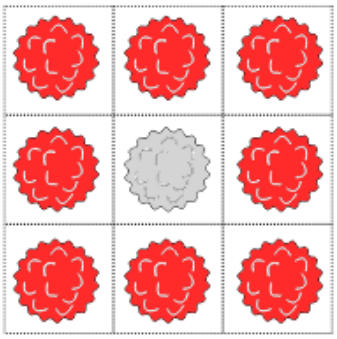

**Figure 2:** Quiescence by Completely Surrounded

meaning that each unit interacts with the eight surrounding positions, the lattice is a $3 \times 3$ grid as Figure 1. The length of each lattice element is 10 m, which is comparable to the size of a regular cell. This choice allows for more biologically realistic behaviours like multi-directional migration and division.

To allow for continuous tumor expansion, the lattice is designed to dynamically grow. When tumor cells approach the border, the grid is expanded by adding new rows and columns, ensuring that growth is not restricted by fixed boundaries.

### 2.2 Unit Types and Behaviors

**Unit Types:** $RTC$, $STC$, $TSTC$, $Empty$
In our cellular automata model, each unit in the lattice represents a potential space that may or may not be occupied by a tumor cell. We define four types of unit states to simulate tumor dynamics:

- RTC (Regular Tumor Cell): These cells make up most of the tumor and can only divide a certain number of times before they die. This limit reflects how regular cancer cells eventually lose the ability to keep multiplying, unlike stem cells that can go on dividing indefinitely.
- STC (Stem Tumor Cell): These cells are immortal and can divide an unlimited number of times. However, they only produce RTCs upon division, acting as a continuous source of growth.
- TSTC (True Stem Tumor Cell): This type can perform asymmetric division, producing either another STC or an RTC. They are rare but crucial for sustained tumor growth and heterogeneity.
- Empty: Represents unoccupied space on the lattice. These are potential target positions for cell proliferation or migration.

**Four Basic Behaviors** The spatial arrangement of units is fundamental to how the tumor evolves. Units interact locally, meaning that the behavior of one unit depends on the state of its neighbors. This local rule system creates global patterns over time, such as tumor clustering or necrotic cores.
At each time step, a unit (tumor cell) can perform one of the four actions:

- Apoptosis: The cell dies and the unit becomes empty.
- Proliferation: The cell divides, and a new cell is placed in the neighbour empty unit.
- Migration: The cell moves to a neighbouring empty unit.
- Quiescence: If no action is taken, the cell remains in place and accumulates inactivity time. But if it is wrapped inside as Figure 2, it can not return to active unless at least one adjacent cell moves or dies.

### 2.3 Probabilistic System and Time Step

The actions that are mentioned above are controlled by probabilities. Such probabilities are affected by parameters like cell cycle time, mobility, and division limits.

- $_{P_A}$ (Apoptosis)
- $_{P_P}$ (Proliferation), $_{P_P} = CCT* \Delta t/24$
- $_{P_M}$ (Migration), $_{P_M} = \mu$ * $\Delta t$
- $_{P_S}$ (Symmetric Stem Proliferation)

The simulation advances in discrete time steps. Each step represents a fixed time interval (e.g., 1 hour or 1/24 day). During each step, all units are updated simultaneously based on their current state and neighbour configuration. The use of a fixed $\Delta t$ also ensures synchronization between probabilistic rules and biological timing.

| Parameter | Value | Unit |
|---|---|---|
| Time step ($\Delta t$) | $1/24$ | day |
| Cell cycle time ($CCT$) | $24$ | hours |
| Proliferation probability | $4.17\%$ | per time step |
| Lattice cell width | $10$ | $\mu m$ |

Table 1: Typical Parameters for Studied Scenarios

## 3 Implementation

To implement a CA for tumor modelization, technics can vary considering study boundary. Biological cells are more than pack of small units, because they can have communication or distanced regulation which can not be supported by standard CA protocols. There has been many extended versions of CA fitting for modelizing different aspects of tumor researches.[8]

### 3.1 Global CA

Global CA (GCA) allows the introduction of global variables or rules—such as total population count, overall density, or global

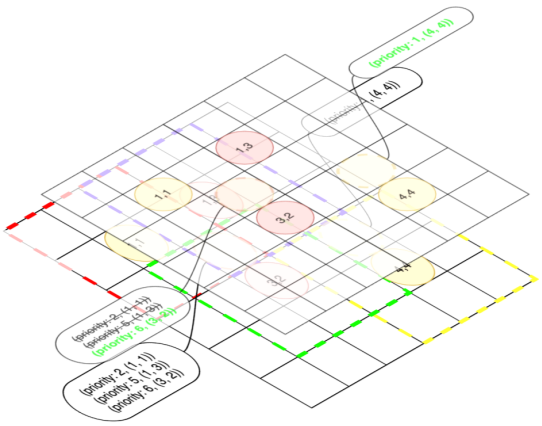


**Figure 3:** Global Negotiation for Conflicts Dissolve

state distribution—as additional inputs for updating each cell's state.[9] GCA provides greater flexibility, making it well-suited for modeling complex phenomena involving non-local coupling, global resource constraints, and collective feedback mechanisms.
To be more specific in our model design, two behaviors are not able to take place under conventional CA constraints. Due to limited time, we managed to utilize the local CA engine provided by Frank Delaplace*. Since for behaviors of apoptosis and quiescence, cell only operate on its own unit which is compatible with local CA engine. As for migration and proliferation, if the correct timing and empty units in its neighborhood, it will manage to turn it into a cell. Units have to possess the ability of operating neighbors directly or communication with them to trigger their transformation. For more complex scenarios, more than 1 cell can randomly choose a same unit because of the overlapping lattices. Only one behavior can validate while others should be blocked. We proposed a scheme that each cell should determine its behavior according to local neighborhoods. If they are going to migrate or proliferation, a flag containing its behavior and source indices can be put to the target unit. For even same behaviors executed by different types of cells, the priority can be different.[10]

| Behavior\Cell Type | TSTC | STC | RTC |
|---|---|---|---|
| Replication | 6 | 5 | 2 |
| Migration | 4 | 3 | 1 |

Table 2: Behaviors Priorities for TSTC, STC, and RTC Cells

So priority can be distinctive for both behaviors and type of source cell, then the flag format can be $(priority : int, row, col)$. In level of local behavior decisions, cells do not have to be aware of other competitors on the target. Once they decide to migrate or proliferate to a neighboring empty unit, they just put a flag formatted as above.

A global negotiation strategy can be adopted to dissolve the conflicts as Figure 3. After all local behaviors, migration and proliferation are pending. A global scan decorator is applied on local behaviors of one timestep to randomly pick one flag among those at highest priority within each empty unit with flags. Then only preference caused by behavior and cell type exists here rather than bias from order of asynchronized operations which prevents systematical bias accumulation.

### 3.2 Two Levels Time Steps

With the conventional CA engine, only one uniform granularity for time step is used arranging the frequency of both units behavior and simulation data update. The graphical UI based on $matplotlib$ library using backend of $Tkagg$ and tumors are believed starting with one single tumor cell which requests manually setup of simulation. The resource-costy graphical interface seems unavoidable to preserve. The timestep for cells' behaviors is fixed to an hour, while the sampling time gap of simulation can vary but default set to 1 day(24 hours). This setting allows rich features of cell living activities to be captured and balancing cost of simulation components.

## 4 Simulation Scenarios

For most of tumor entities, they are believed originated from single cancer cells. Within a tumor, the composition of cells of different types is both a phenomenon and cause of heterogenesis. Then an idea occurs that starting at different types of tumor cells, would the morphological and physiological features of the tumor differ. Simulation scenario settings start from single cells of 3 types, $RTC$, $STC$ and $TSTC$.

### 4.1 Scenario 1, 2 and 3: Tumor Growth from Different Single Cells

According to existing research, tumors originate from tumor stem cells, not ordinary tumor cells. Ordinary tumors may proliferate, differentiate and form different cell groups in the tumor, but the continued growth and recurrence of tumors are often closely related to the presence of tumor stem cells. Therefore, tumors cannot originate from cells that are not tumor stem cells.[11]

#### 4.1.1 Scenario 1: Start from a RTC

Even though a tumor is not likely originates from a regular tumor cell clinically. It still can be worthwhile to understand it from the dynamics and modeling. Experiments follow parameters mentioned in Table 1 and 3 (If no specific remarks).

| Parameter | Value | Unit |
|---|---|---|
| Apoptosis Probability ($P_A$) | 0 | % |
| Migration Ability ($\mu$) | 10 | cell width/day |
| Symmetric Stem Proliferation ($P_S$) | 1 | % |

Table 3: Default Simulation Parameters

The tumor starting from a RTC shrinks in 20 hours told from the snapshots in Figure 4 even though exempting them from apoptosis. This could be another tolerance of cancerousness in comparison to immunology and apoptosis, namely that even some mutations are cancerous and regular tumor cells emerge. While they are neither immortal nor mutation aggregated and would fade out in hours.

#### 4.1.2 Scenario 2 & 3: Start from a STC and TSTC

In more realistic cases, a tumor is able to be clinically diagnosed can only originate from a stem tumor cell. In the 2nd and 3rd scenarios, tumor growth from a single STC and TSTC were simulated shown in Figure 5. Since in $scenario2$, it started from a STC which is not able to symmetrically proliferate to another STC. The STC count

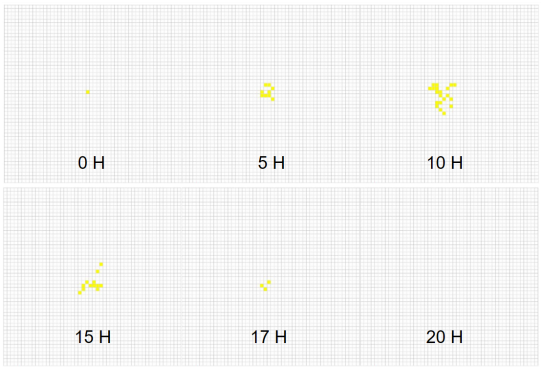


**Figure 4:** Scenario 1 Simulation Snapshots(by hours)

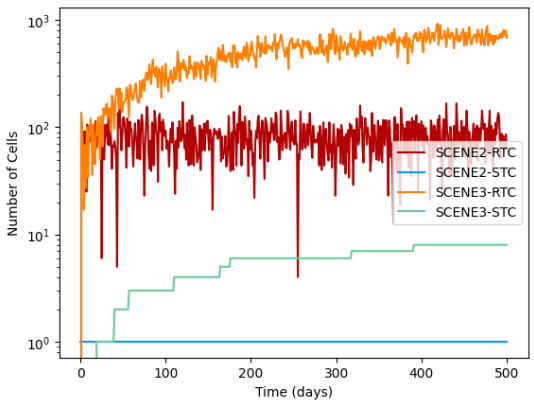


**Figure 5:** Tumor Growth from single STC and TSTC

in $scenario2$ remains at 1 while in $scenario3$ it climbs to about 10 after 500 days. And both RTC counts sharply rise to about $10^2$ in 10 to 20 days. The one in $scenario2$ keeps fluctuating around $10^2$ in rest of time, while the one in $scenario3$ continue increasing at a fading slope till about $10^3$ .

In early stages, similar proliferation potentials are observed in STC and TSTC. But later on, STC clone shows heavy self-limitation while TSTC can proliferate to STC which is immortal as well and able to form new clones. Still migration ability is too low or too limited the resources are to avoid competition among clones, total RTC count in $scenario3$ would come to an upper bound in the end.

## 4.2 Scenario 4: Tumor Growth with Different Apoptosis Rates

Starting from $scenario4$, tumor cells are not exempted from apoptosis anymore. In each time step, they are under the risk of apoptosis at a probability ($P_A$) of 0%, 1%, 10% and 30% respectively. In comparisons of RTC counts and STC counts across 4 apoptosis probabilities, can a anti-intuitive speculation be proposed that a proper death rate retrieves resources and boosts tumor expansion. The RTC counts of $P_A = 1\%$ and $10\%$ exceed the convergent upper bound $10^3$ of that in case $P_A = 0$. As for STC, curves in $P_A = 10\%$ and $30\%$ are approaching $10^2$, while in $P_A = 0$, it is merely $10^1$. The optimal Apoptosis Probability for tumor is around $10\%$. Of course, the more apoptosis happens, the STCs are more prosperous because of their immortality and the sacrifice of RTCs. But the moral rate of RTCs is way faster than proliferation of STCs if too frequent apoptosis which is not worthy for tumors globally.

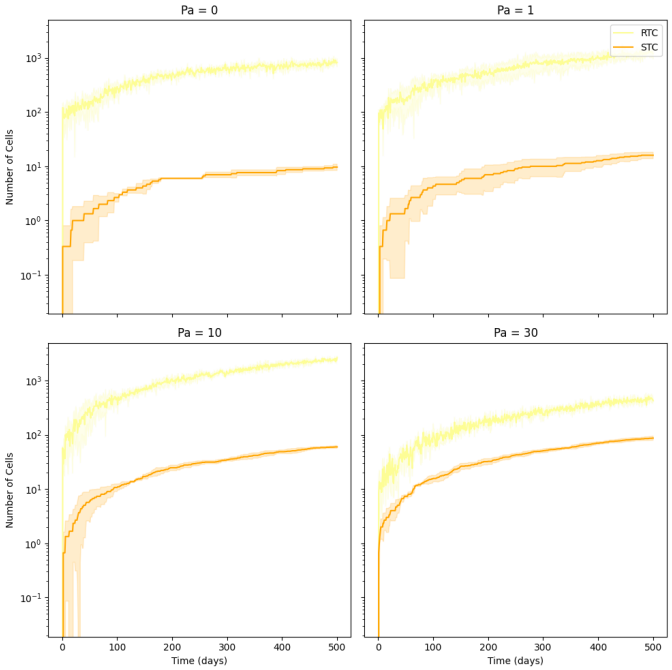


**Figure 6:** Apoptosis Influence on Tumor Growth
(Here and in the following, shaded area: $\bar{N} \pm 1\sigma$, $Dup = 3$)

As interpreted, too low apoptosis of RTCs forestall resources like spaces in neighborhood of TSTC preventing proliferation of STCs.

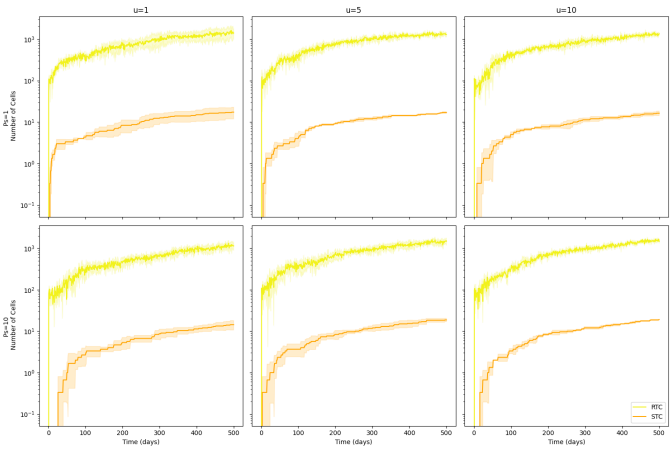


**Figure 7:** Migration and Stem Symmetrical Proliferation Settings

## 4.3 Scenario 5: Influence of Migration Potential and Stem Symmetrical Proliferation

In $scenario5$, we discuss a more complex scenario considering different migration potential ($P_M$) at 1, 5, 10 $cell\ width/day$ and stem symmetrical proliferation ($P_S$) at 1% and 10% respectively. ($Prob.\ Apoptosis$, $P_A = 1\%$)

According to Figure 8, symmetrical stem proliferation only affects low migration potential cases. In low migration, $P_M = 1$ cell width per day, higher symmetrical stem proliferation results into both lower RTC and STC counts. While in higher mobility sets, no significant difference is observed. High stem proliferation probability could lead to an unaffordable number of STC in early

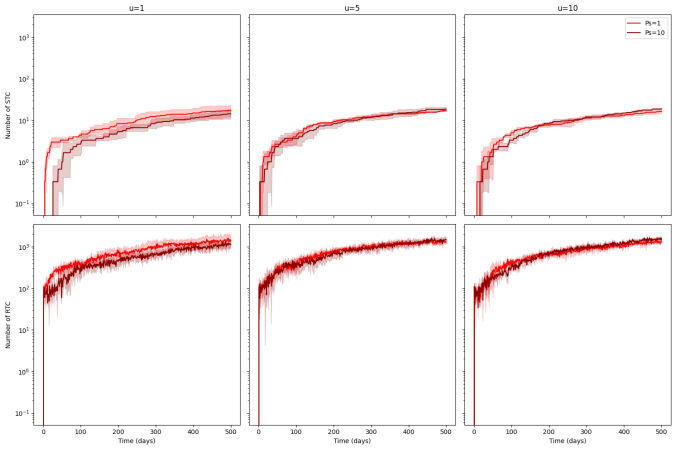


**Figure 8:** Influence of Stem Symmetrical Proliferation

stage which will rapidly expand excessive RTCs uninterruptedly occupying the neighborhood of TSTC and prohibit its further stem proliferation. Unless TSTC and STC escape from there, otherwise due to limited resources, no birth of STC to form new clones. Both counts of RTCs and STCs will convergent.

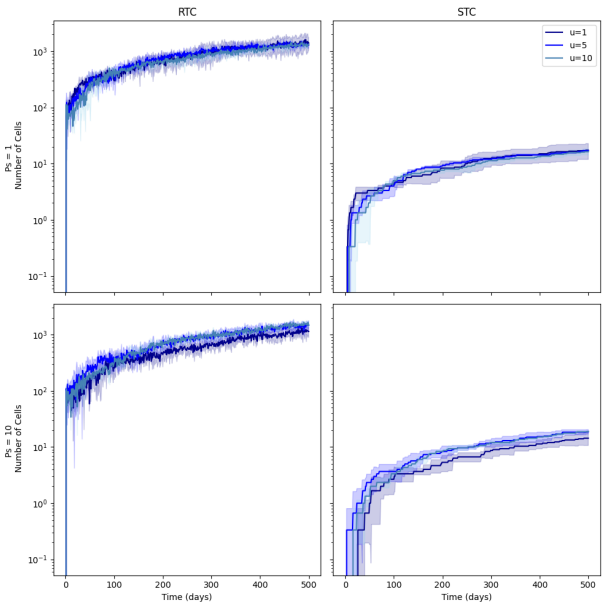


**Figure 9:** Influence of Migration Potential

Then different migration potential is studied as Figure 9. In the case of low symmetric stem proliferation ($P_S = 1$), migration potential do not lead to significant differences. As for stem proliferation increased, both RTC and STC counts curves of migration potential($\mu$) at 5 and 10 cell width per day are floating above that of ($\mu = 1$). The migration is a factor of paramount importance for tumor expansion. Tumors with stronger ability of migration can be more invasive than those only with high proliferation.

## 5 Limitations and Prospects

The limitation of this model is as clear as its pros because of the total decoupling from biochemical features. For better simulation performance on large scale and long term settings, only a probabilistic system was abstracted. In this case, the model is not able to involve micro environment except spaces. Some specific phenomenons like tumor cavitation can not be observed.

The configuration of parameters can be tricky as well. All parameters other than proliferation are neither measured nor able to be easily estimated based on wet lab data. Some parameters need to be jointly toned or combined to study. Vast parameter domains need to be explored with little support of previous data.
In the original paper, they also studied influence of life duration of RTC varying among 10, 15 to 20 CCT. It may change the critical conditions, but similar phenomenons and conclusions are attained. Due to limited pages and time, we did not combine $P_{\max}$ into adjusted parameters in our tested scenarios. To more finite this model and better modelize tumor dynamics, test on more parameter settings should be conducted later and correspond to tumor progress data from clinics.

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