

1. What are the major parameters of the tumor model in Module 3?

The researchers found that there are three major types of intervention impacting the density of cycling or non-cycling CSCs and DCs:

- Reducing DC lifetime or lifespan of DC (and the minimal and maximal age of the initial DC subpopulation) increases cycling CSC density. It decreases DC density and macroscopic growth rate (no effect on non-cycling CSC density).
- Reducing the proliferation rate or decreasing the probability of entering the cell cycle (p_0) decreases cycling CSC, DC density, and macroscopic growth rate (no effect on non-cycling CSC density).
- Increasing differentiation reduces the number of non-cycling CSCs and the macroscopic growth rate (no effect on cycling CSCs or DCs), which could be accomplished by:
 - increasing the maximal differentiation rate (p_{\max}).
 - Increasing the density of CSC neighbors by decreasing the dampening coefficient k .
 - Decreasing a ; the number of CSC neighbors giving the half-maximal differentiated rate.

2. What are the main features of the total number of tumor cells as a function of time?

The total number of tumor cells over time follows a dynamic pattern influenced by CSC proliferation, differentiation, and DC death rates.

Three phases were identified:

- The initial growth phase.
- Followed by an intermediate phase approximated by a parabola with a quadratic coefficient qualified as a “macroscopic growth rate”.
- The final phase occurs when population growth tapers off to a “quasi-steady state,” at which point the number of cells remains roughly constant.

3. What is the main novelty of the approach discussed in the lecture from earlier cancer treatments?

The model predicts that for targeting differentiation to be successful in curing cancer, it must be combined with antiproliferative agents. Additionally, this approach differs from previous models by incorporating environmental feedback and the influence of neighboring cells on differentiation.

4. What is the relation between the extreme (max and min) values of the differentiation rate and the extreme values of the cell density?

The probability of differentiation p_d follows a sigmoid-like function, meaning that it remains relatively stable at extreme values of CSC density. When the number of neighboring CSCs falls below a certain threshold, the probability of differentiation reaches its minimum value p_{\min} , and does not decrease further as CSC density continues to drop. Similarly, when CSC density exceeds an upper threshold, the differentiation probability approaches its maximum value p_{\max} ; and remains at this level even as CSC density increases further.

$$p_d = p_{\max} - \frac{a^m(p_{\max} - p_{\min})}{a^m + (\text{den}(A))^m}$$

a is the CSC density in the neighborhood that gives the probability $(p_{\min} + p_{\max}) / 2$, and m is the steepness coefficient.

5. What is the relation between the proliferation rate and the number of vacancies around the cell?

The capacity of a cell to divide depends on the availability of a neighboring space used by the CSC for one of its two daughter cells it divides into. This relationship is linear, the probability of proliferation is directly proportional to the initial probability of entering the cell cycle, p_0 , times the number of vacancies around the cells, n ($n = \text{dens}(S) = N1 + N2 / k$; $N1$ and $N2$ are first and second-degree vacant neighbors of the cell S):

$$p_c = 1 - (1 - p_0)^n = np_0 + o(p_0)$$

P_0 is the basic probability of entering the cycle when only one empty neighboring vacant space is available. If there are no empty, all automata cells in the cell's neighborhood are occupied, the cell remains a non-cycling CSC, and the proliferation rate is 0.