Start

read external parameters from console and initialize all simulation parameters

Write all simulation parameters in *Parameters.txt* file

for each cell in the initial population:
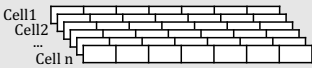
Assign cell's attributes

Each cell is stored as a 7-integer array in a monodimensional vector (cell population vector). The integers represent the cell attributes as follows:
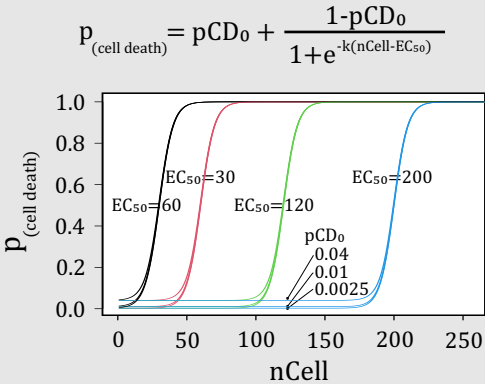
Clone ID	CellCycle Length	CellCycle Timer	position (x)	position (y)	position (z)	Proliferating

Cell1
Cell2
...
Cell n

Clone ID: A unique identifier for the cell's lineage.
Cell cycle length: The cycle length of the cell.
Cell cycle timer: remaining time before the cell is ready to divide.
Position (x, y, z): The 3D coordinates of the cell in the simulated space.
Proliferating: whether the cells is proliferating (1) or resting (0)

for days from 0 to MAXDAYS:

for hours from 0 to 24:

for each cell in the cell population vector:

From xyz cell position determine its voxel in the 3D grid

Increment the cell count in the corresponding density map entry accounting cell's lineage info

A cell-density map is computed by tessellating the continuous space in a 3D-grid and by tallying the number of cells from each lineage within every voxel. This map is subsequently employed to calculate the survival probability of each cell in the following step.

for each cell in the cell population vector:

Calculate the probability of death based on local cell density

does the cell survive?

no — Remove the cell from the population array

yes — update its position by adding a random xyz displacement (migration)

decrease cell-cycle timer by one hour

For any given cell **Q**, death probability is modelled as:

$$p_{(cell\ death)} = pCD_0 + \frac{1-pCD_0}{1+e^{-k(nCell-EC_{50})}}$$

where pCD_0 is the basal cell death probability, k=0.2 and EC_{50} was one of the explored parameters. nCell is the number of cells in the voxel occupied by Q and is calculated as:
$$nCell = nLCell \times Lw + nACell \times Aw.$$
nLCell is the number of cell in the voxel belonging to the same clone of Q (lineage cells).
nACell is the number of cell in the voxel belonging to other clones than that of Q (alien cells).
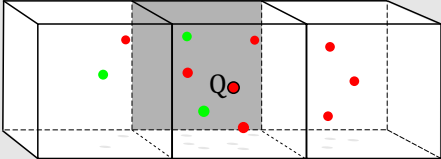
$$nCell = 4 \times Lw + 2 \times Aw$$

Lw and Aw are respectively the weight of lineage and alien cells. When clonal competition is not implemented Lw=Aw=1

for each survived cell in the cell population vector:

M-phase reached?

no

yes — make a copy of the cell and all its attributes

for each daughter cell:

reset cell-cycle timer

add random xyz displacement

stop proliferating?

no — modify inherited cell cycle length making it virtually infinite

yes — modify inherited cell cycle length by adding a random value

Each newborn cell inherits attributes form its mother cell. Some attributes may undergo changes depending from simulation parameters. Cell cycle lenght changes by a Gaussian value. If the variation is negative, it is scaled to prevent cell cycle length to shorten below LOW_CYCLE_LIMIT parameter.
This mechanism allows for a balance between lineage-specific cycle lengths, introducing fluctuations while ensuring no unrealistically short cycle durations.
If the parameter governing the Gaussian variation is set to 0, it leads to fixed cell cycle lengths within each lineage.

Write hourly population statistics in *TrackByHours.txt* file

Write daily population statistics in the console
Each 10 days:
Write clonal aboundances in *CloneTableBy10dd.txt* file

Write all attributes of all cells in *FinalPopulation.txt* file

End