Assumptions:

• Glucose supply is constant and evenly distributed across the grid.

• At equilibrium, GSoa equals the sum of all normal cells’ glucose uptake when grid is fully occupied by normal cells.

• Glucose uptake reflects energy efficiency → higher uptake → higher proliferation → higher fitness.

• Normal cells have constant glucose uptake; tumor cell glucose uptake is positively correlated with karyotype fitness.

Distinction Between Frontal and Temporal Lobe:

• The only difference between the two simulations is glucose supply level (GSoa).

Overall Model Description:

The program will simulate tumor and normal cell growth on a two-dimensional grid. There is competitive interaction between tumor and normal cells, described by a Lotka-Volterra (LV) competition model. Intra-species competition (tumor-tumor and normal-normal) is also included.

Program Logic:

1. Configuration:

• Read the configuration file (Config) in YAML format, which includes known parameters:

• Grid size (N × N),

• Initial normal cell proliferation rate Rc,

• Initial tumor cell proliferation rate Rt,

• Normal cell glucose uptake Cg,

• Initial proportion of the grid occupied by normal cells m%,

• Mis-segregation rate MSR.

2. Karyotype Library:

• Read the pre-defined karyotype file KaryoLib, a data.frame:

• First column: karyotype string (e.g., “1.2.3”)

• Second column: fitness value

• Diploid karyotype has all 22 chromosomes with copy number = 2

3. Initialization:

• Build a N × N growth grid. Each grid cell can hold one biological cell.

• Place a tumor cell with diploid karyotype at the center of the grid.

• Randomly distribute normal cells according to m% on remaining grid space.

• Create a Cells data.frame with 31 columns to store cell state:

1. $X: x-coordinate

2. $Y: y-coordinate

3-24: karyotype (22 columns)

25. $f: fitness

26. $r: proliferation rate

27. $G: glucose uptake

28. $Label: 0 = normal, 1 = tumor

29. $DivisionTime: estimated division time

30. $Time: time elapsed since last division

31. $Status: 0 = dead, 1 = alive

4. Parameters Calculation:

• Total glucose supply GSoa = N \* N.

• For each normal cell, assign a proliferation rate Rci drawn from Rc ± 5%.

• Estimate division time: DNt = 24 \* Rci, DTt = 24 \* Rt for tumor cells.

• For each cell, calculate growth rate r within a 5 × 5 local neighborhood:

• Tumor cell:

DTti = (Rt \* (Fk / Fd)) \* (1 - ((Nt + a \* Nn) / K))

• Normal cell:

DNtj = Rc \* (1 - ((b \* Nt + Nn) / K))

Where:

• K = N \* N,

• a = Cg / Tgk,

• b = 1 / a,

• Tgk = (Fk / Fd) \* Tg,

• Tg = 1.2 \* Cg,

• Fk: fitness of current cell karyotype,

• Fd: fitness of diploid karyotype.

If on the edge of the grid, use a virtual border filled with normal cells.

5. Time-based Simulation:

• Use time step deltaT = 1 hour, 24 steps = 1 day.

• Sort Cells by $DivisionTime.

• If $DivisionTime <= $Time, proceed with division (see section 6).

• Check for cell death (see section 7).

• Remove dead cells ($Status == 0).

• At each loop, increment $Time by deltaT.

• Save Cells as CSV every 24 steps (1 day).

• Stop simulation when all grid cells are occupied.

6. Cell Division:

• A cell divides when $DivisionTime <= $Time.

• Compute new $DivisionTime as:

• Tumor: DTti = 24 \* Rti

• Normal: DNtj = 24 \* Rcj

• Check for neighboring empty grid to allow division.

• Create a temporary data.frame Temp (2 rows × 31 columns) by copying the dividing cell’s data, with $Time reset to 0.

• Mis-segregation (MS) Event:

• Only tumor cells undergo MS events.

• MS occurs with probability MSR (i.e., runif(1) < MSR).

• If MS occurs: randomly change copy number in one of columns 3–24 (increase or decrease by 1, keeping values between 0–10).

• Update $f by looking up KaryoLib.

• Recalculate $r, using same formulas as in section 4.

• Recompute $DivisionTime = 24 \* r.

• Replace original cell row with two rows in Cells.

7. Cell Death:

• A cell dies if its glucose supply G is ≤ 20% of its uptake.

• Total available glucose is the sum of all $G values in Cells.

• If G ≤ 0.2 \* sum($G), set $Status = 0.