Supplementary File S2

Ghadiri et al., "A multiscale agent-based framework integrated with a constraint-based metabolic network model of cancer for simulating avascular tumor growth"

File S2: A pseudo-code representing the whole simulation procedure:

Implementation of the simulation is expressed by the pseudo-code presented in Procedure 1. Lines 6 to 9 are corresponded to ABM part of the simulation in which the states and actions of cells would be determined. Lines 10 to 12 are corresponded to CBM part of the simulation in which the amount of metabolite consumption and biomass production of cells would be determined.

Procedure 1: *simulation*

1 **Input:** simulation parameters (from Table 1), number of simulation steps: N
2 **Output:** L_i, $C_{m,xyz}$ //L_i: the location of cancerous cell i, $C_{m,xyz}$: the concentration of //metabolite m at position x,y and z in 3D simulation space

3 *Initialize* $biomass_1$ *and* $C_{m,xyz}$ *for all values of m, x, y and z* //$biomass_i$: *biomass of cell i*
4 SET s to zero //s = step

5 REPEAT

6 **for** all cells

7 $state_i$ = STATE_TRANSITION ($state_i$, $biomass_i$, $neighbor_i$, $C_{m,Li}$)

//Determine the state of cells according to their current state, microenvironment, //neighbors and biomass (based on transition diagram in Figure 2)

8 **for** all cells

9 ACTION ($state_i$)

//Cells do actions according to their states (based on transition diagram in Figure 2)

10 **for** all cells

11 $C_{m,Li} = C_{m,Li}$ – FBA.consumption (m, L_i)

12 $biomass_i = biomass_i$ + FBA.biomass (L_i)

13 $C_{m,xyz}$ = DIFFUSE ()

14 $s = s + 1$

15 UNTIL $s < N$