

Supplementary Material S2

Description of the Modeling Program Flow

Present version of simulator deals with three pools of elements: 'stem cells', first generation of 'daughters' ('multipotent cells'), somatic cells and regulating molecules ('Regulator'). Each of the pools (**Cells1**: 'stem cells'; **Cells2**: multipotent cells; **Cells3**: somatic cells; **Regulator**) is represented by the array of elements, each of the array entries ($C1_k$, $C2_k$, $C3_k$, R_k) represents number of elements having corresponding age $k\Delta t$. To account for the sleeping stem cells their formal 'age' is set to negative values, reflecting the time they are 'asleep'. Simulation program contains a 'while' cycle with a number of sequential events in it. Current number of cycles k is a number of elemental time steps and defines the time elapsed from the start of simulation. Initial conditions are given by four initial age distributions (four arrays: $C1_i[]$, $C2_i[]$, $C3_i[]$, $R_i[]$), equivalent representation of probability functions (e.g. probability of the regulator synthesis in one division act for each cell type), lifetimes (for the cell types and the regulator molecule) and initial values of control parameters. Corresponding initial distributions are generated separately prior to the main simulation cycle. Functions cannot be changed during the simulations, but few parameters of these functions can be changed. Contemporary values of the critical control parameters can be changed at any moment during the simulation. Simulator continuously displays current values of all critical and support parameters, and graphs representing the history of their changes from the start of the simulation.

Corresponding simulation program was realized using LabVIEW platform by National Instruments [S2.1]. One of the main advantages of this platform is a possibility of good mnemonic representation of the simulator functionality, and this was quite useful for constructive discussions with biologists and biochemists. Simulator runs on the personal computer with average computing capacity under Windows 10. Currently it cannot handle very large numbers of the elements in the arrays (at the moment up to 10^5 elements). Corresponding 'flow chart' of the simulator presented below is copied from so-called 'Block Diagram Window'. Virtual 'control panel' of the simulator presented in Supplementary Material S3 copied from the 'Front Panel Window' is used to control initial conditions and the process of simulation.

Flow Diagram of the Simulator Software Code

Full simulation cycle (elementary time step) contains a number of elementary 'events' related to different aspects of simulation, and numbered in the following diagram as steps №1 to №9 (Figures S2.1 to S2.3). Four sets of age distributions (stem cells, multipotent cells, somatic cells and regulator substance) undergo stepwise changes in each simulation cycle influencing each other. Four horizontal colored lines represent data changes and manipulations in corresponding distributions (Red for stem cells, green for somatic cells and blue for regulatory molecules). Symbol 'i' in the blue square indicates that corresponding task is executed not every cycle, allowing for the 'elementary reaction rate' variations. Dice symbol indicates that small random variations could be introduced in corresponding values. Green 'buttons' indicate that corresponding step can be engaged by choice.

Full cycle of simulation is broken into three consecutive images represented in the following Figures S2.1 to S2.3 below.

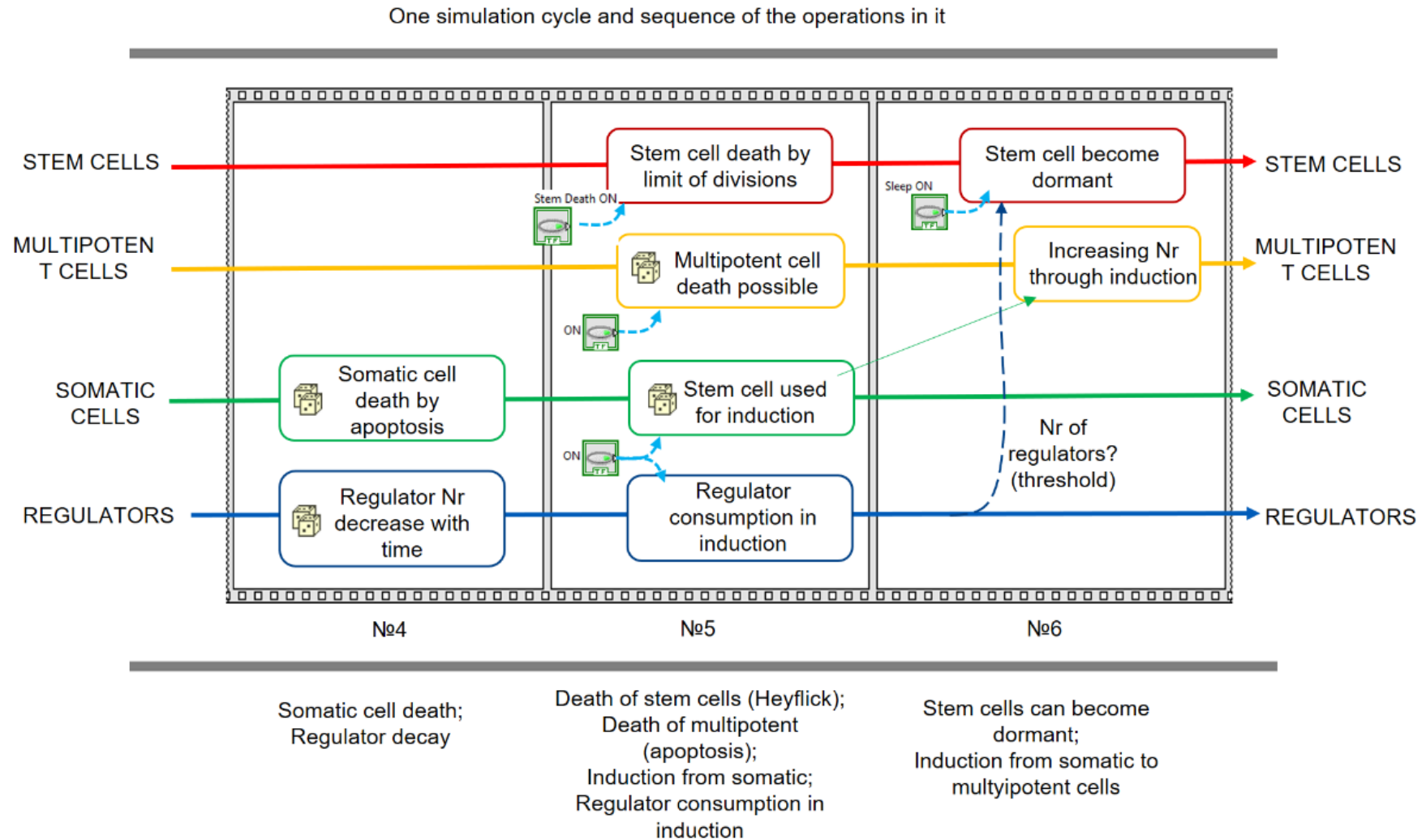


Figure S2.2 Second part of the simulation cycle.

One simulation cycle and sequence of the operations in it

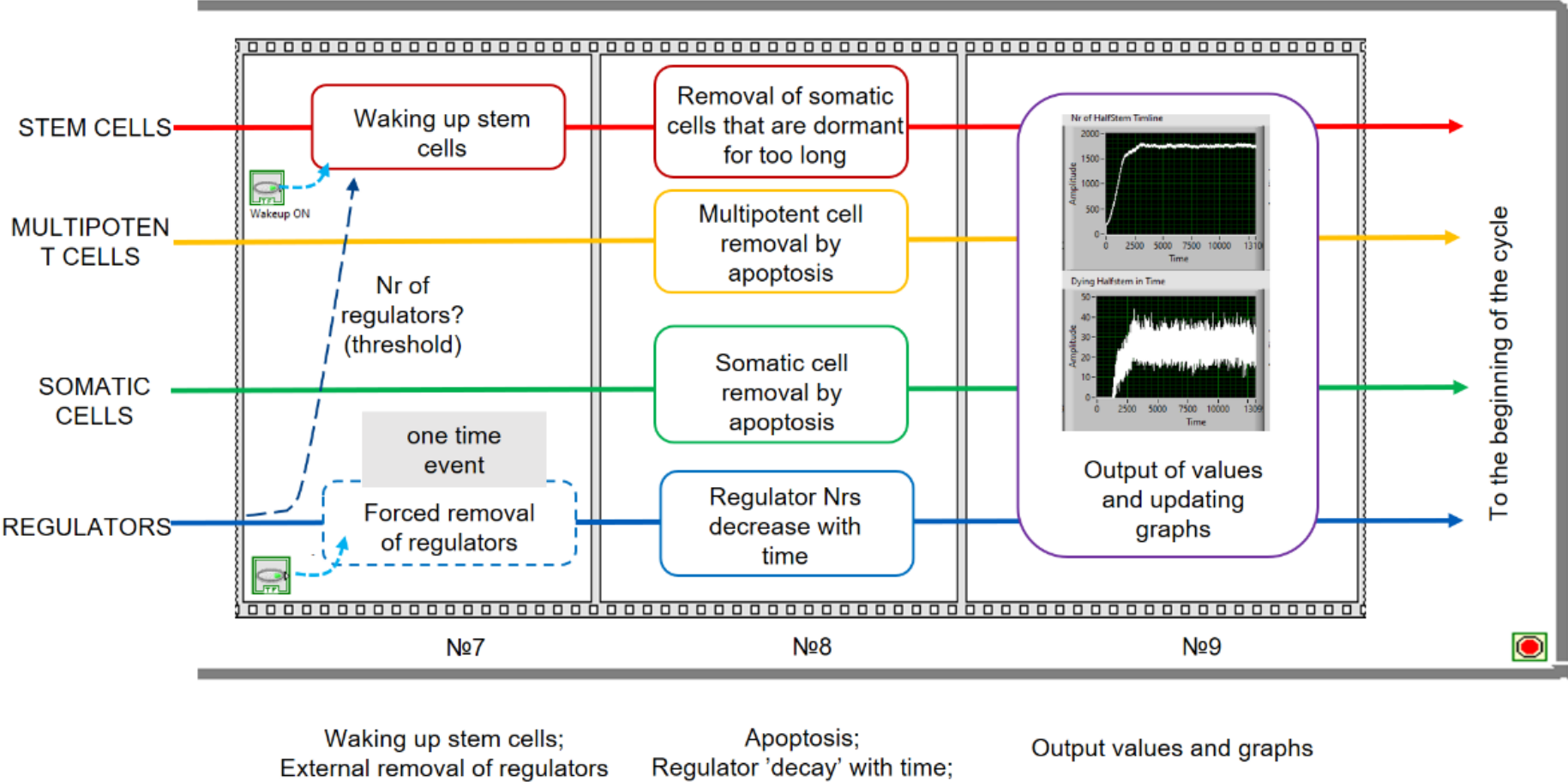


Figure S2.3 Third part of the simulation cycle.