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PARAMETER ESTIMATION OF AGE-STRUCTURED MODEL OF CELL CYCLE USING ADJOINT SENSITIVITY ANALYSIS

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ABSTRACT

Age-structured models describe heterogeneous populations of individuals. Life of the individual consist of a finite number of phases, which differ in properties such as the ability to reproduce. There is the age-structure of a subpopulation in each phase, i.e. individuals in the subpopulation differ in the dwell time in the phase. In every moment of time the individual can go to the beginning of a next phase, become older in a current phase or die - these events depends on a transition functions, which determines their probability. This approach allows more realistic modeling of the population growth than using models assuming homogeneity of the population, which is especially important for complex organisms with long reproduction time.

The main aim of this study was to develop a methodology for parameter estimation of the age-structured models using adjoint sensitivity analysis. A basic model of the cell cycle was used as a simple example of the age-structured model. The model consists of three phases: G_0/G_1, S and G_2/M. Parameters in this case were transition functions values and initial cells distributions in each phase. Parametric and nonparametric estimation approaches were used.

The main source of the experimental data was the flow cytometry. Results were obtained for artificially generated input data and experimental measurements of the cell number of HCT-116 cell line. Our results show that using a combined estimation approach gives the best adjustment of the model to the experimental data. Real average durations of the cell cycle phases were achieved.

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REFERENCES

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