Optimal Bang-Bang Control in Coupled Dynamical Systems

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Introduction:

We investigate the coupled dynamics of cancer cells and healthy cells during fractionated cancer therapy. The problem is solved using optimization methods. The model achieves a state with efficient reduction of cancer cells and minimum damage to healthy cells surrounding the tumor.

Computational Methods:

The model is based on coupled rate equations taking into account

- partial recovery of cells (γ),
- different radiation sensitivity of tumor and healthy cells to radiation (*a*),
- growth rates (c) and death rates (b).

We use the optimization module of COMSOL MULTIPHYSICS®. The control parameter is represented by the dosis rate u(t) which can be switched on (corresponding to a maximum dose) and off (treatment free period)

$$
\begin{aligned}
\dot{x}_1^H(t) &= -a^H \cdot u(t) \cdot x_1^H(t) + c^H \cdot x_1^H(t) + \gamma^H \cdot x_2^H(t) \\
\dot{x}_2^H(t) &= a^H \cdot u(t) \cdot x_1^H(t) - b^H \cdot u(t) \cdot x_2^H(t) - \gamma^H \cdot x_2^H(t) \\
\dot{x}_1^T(t) &= -a^T \cdot u(t) \cdot x_1^T(t) + c^T \cdot x_1^T(t) + \gamma^T \cdot x_1^T(t) \\
\dot{x}_2^T(t) &= a^T \cdot u(t) \cdot x_2^T(t) - b^T \cdot u(t) \cdot x_2^T(t) - \gamma^T \cdot x_2^T(t)
\end{aligned}
$$

The functional depending on the state vector (including all cell cell types, time, and dosis rate) is (α_1 = 0,3, α_2 = 0,7),

$$F(T, x, u) := -\alpha_1 x_1^H(T_{final}) + \alpha_2 x_1^T(T_{final})$$

Results:

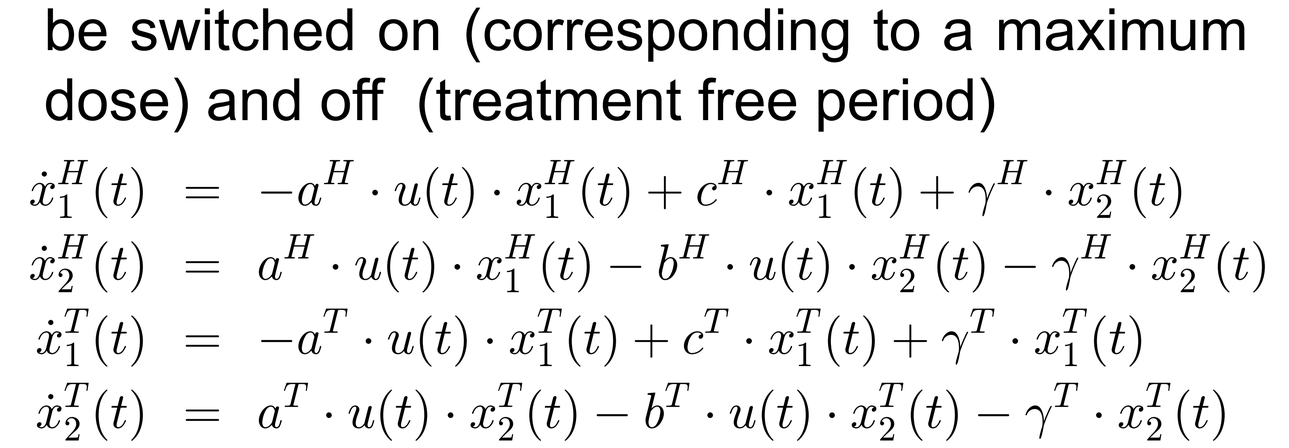

Figure 1. dynamics of cancer cells and healthy cells in dependence on initial value for the cancer cells for optimized u(t)

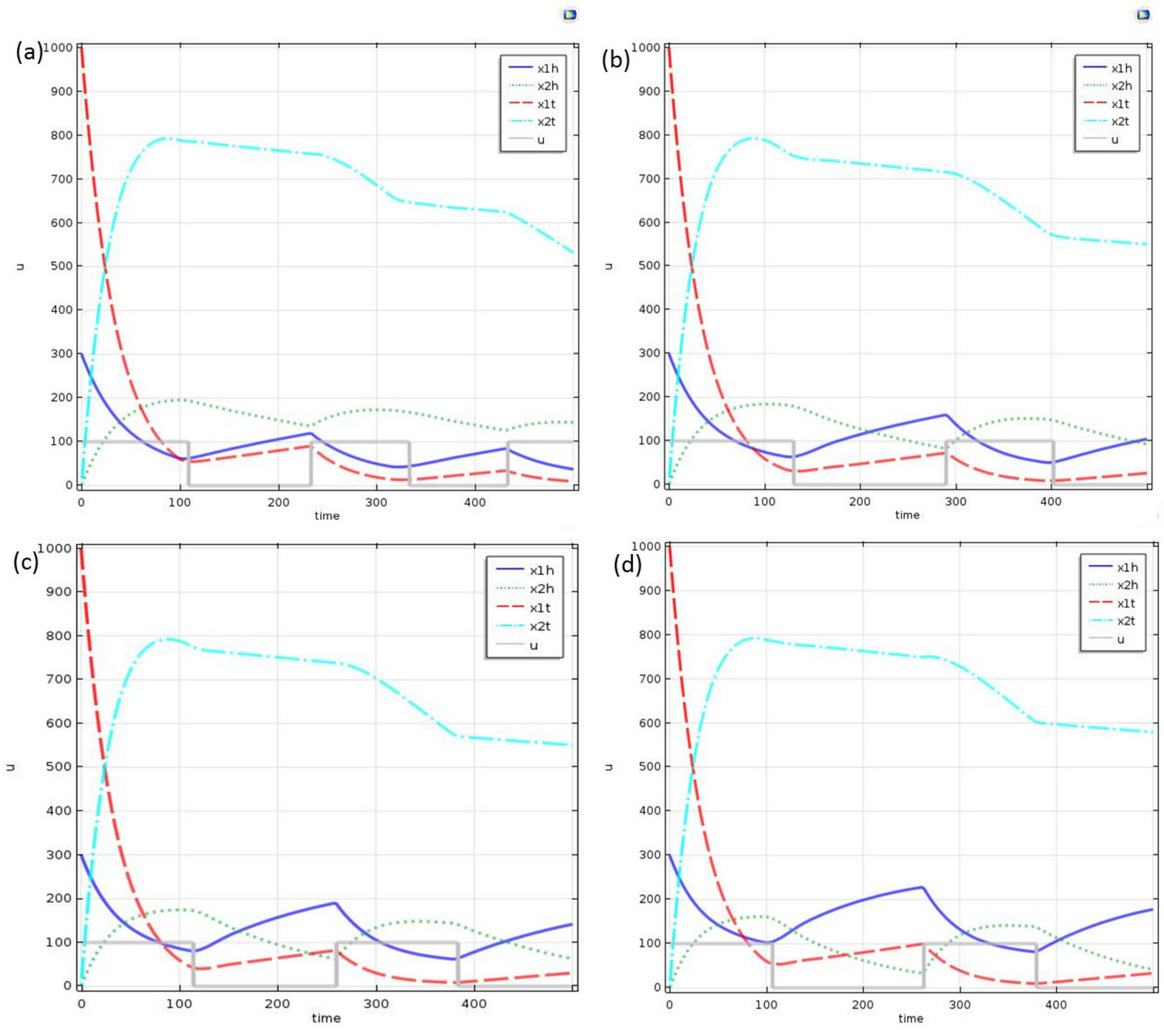

Figure 2. dynamics of cancer cells and healthy cells in dependence on recovery rate for the healthy cells for optimized u(t): a) $3 \cdot 10^{-3}$, b) $5 \cdot 10^{-3}$, c) $7 \cdot 10^{-3}$, d) $1 \cdot 10^{-2}$

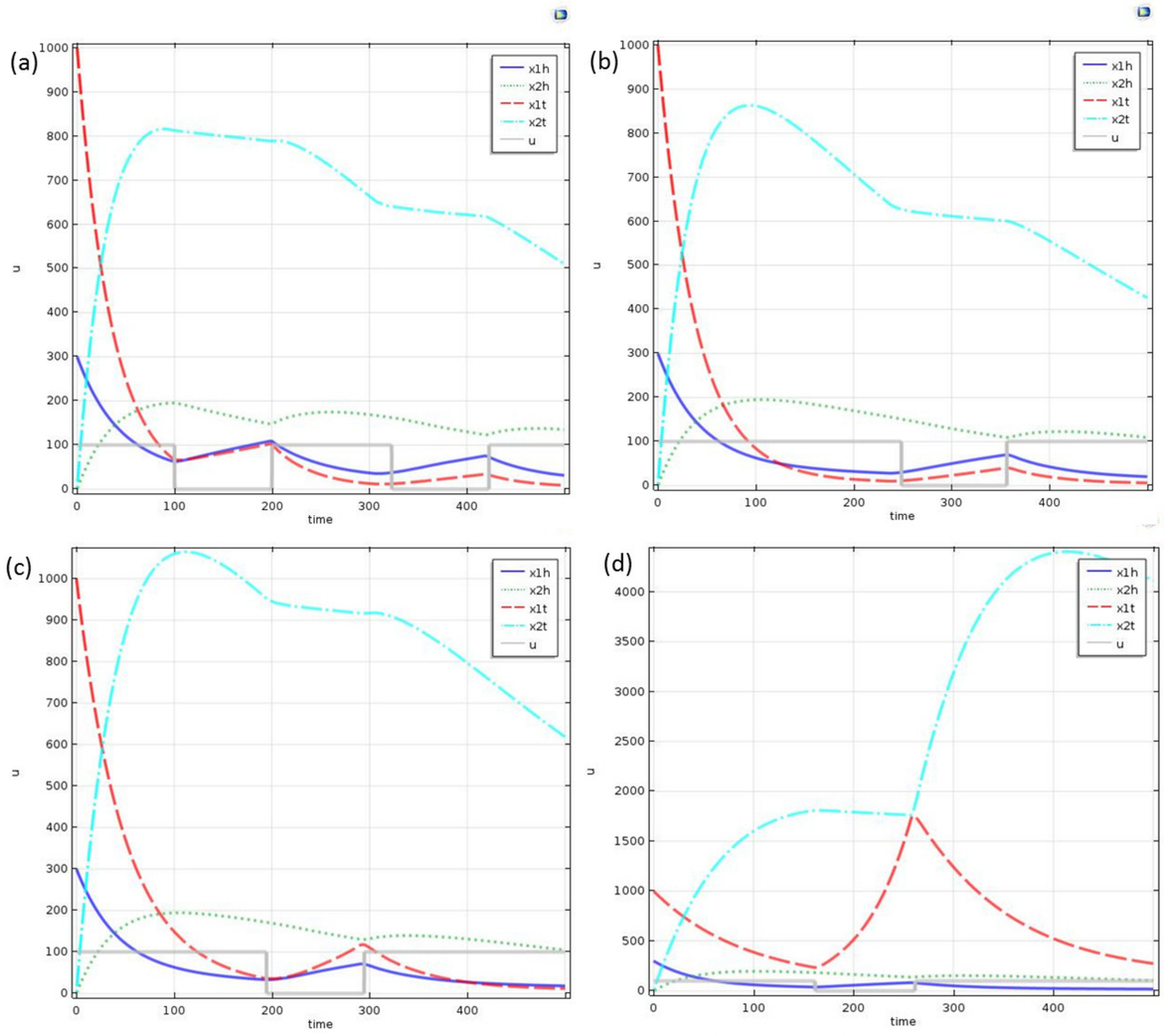

Figure 3. dynamics of cancer cells and healthy cells in dependence on growth rate for optimized u(t):
a) $2 \cdot 10^{-3}$, b) $4 \cdot 10^{-3}$, c) $1 \cdot 10^{-2}$, d) $2 \cdot 10^{-3}$

Conclusions Simulations on the basis of coupled differential equations allows, for a given parameter system, the optimization of fractionated radiative treatment.

References:

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