

S5 Text

Value range of spontaneous apoptosis rate

Based on Eq. (8) in Kolokotroni *et al.* (2011), the apoptosis rate of stem and LIMP cells, R_A , must satisfy the following inequality in order to have a stable or growing tumor:

$$e^{R_A T_c} \leq (1 + P_{sym})(1 - P_{sleep} + P_{sleep} \frac{P_{G_0 \rightarrow G_1} / T_{G_0}}{R_A + 1 / T_{G_0}}) \quad (1)$$

The second term of the above inequality is maximized for the maximum value of P_{sym} , i.e. 0.4 (the upper bound of this parameter considered in the present work) and the minimum value of P_{sleep} , i.e. 0. By substituting the above values in Eq (1), and after performing some derivations, the upper bound of R_A for a given cell cycle duration, T_c , can be derived, above which no solution, i.e. set of parameter values that gives a stable or growing tumor, exists:

$$R_A \leq \frac{\ln 1.4}{T_c} \quad (2)$$

Let [18, 134] be the considered value range of T_c . When R_A is below the lower bound of the second term in Eq (2), i.e. $\ln 1.4 / 134 \approx 0.0025 \text{h}^{-1}$, a solution exists for all values of T_c considered. In the present work R_A has been assumed to vary between 0 and 0.001h^{-1} .

References

Kolokotroni EA, Dionysiou DD, Uzunoglu NK, Stamatakos GS. Studying the growth kinetics of untreated clinical tumors by using an advanced discrete simulation model. *Math Comput Model.* 2011;54:1989-2006. doi:10.1016/j.mcm.2011.05.007