Parameter estimation of a mathematical model using two distinct breast cancer cell lines under chemotherapy treatment

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Introduction

- Breast cancer is the most diagnosed cancer subtype in the world, with 2.3 million women diagnosed and 685,000 deaths only in 2020 (according to the World Health Organization).
- The systemic treatment of non-metastatic breast cancer consists of the use of neoadjuvant, adjuvant or combined chemotherapy.
- The cell culture technique is one of the tools that facilitates the study of the disease's dynamics and allows the discovery of new therapeutic targets.
- Triple negative breast cancer (TNBC): characterized by the non-expression of hormone receptors and it is asssociated with a poor prognosis and has an aggressive metastatic behavior.

Objective

In this work, we seek to fit a mathematical model of ordinary differential equations in to experimental data from two breast cancer cell lines, MCF-7 and MDAMB231, both under chemotherapy treatment with paclitaxel. Through this fit we aimed to find a set of values for the parameters that best represent the real system to be described.

Mathematical model

- The model considers the number of cancer cells, N, and the dose of the chemotherapeutic agent. The normal cell population is not taken into account as the experimental data used does not involve a co-culture of tumor and healthy cells.

$$\begin{cases} \dfrac{dN}{dt} = rN\left(1-\dfrac{N}{k}\right) - \mu(1-e^{-Q})N, \\ \dfrac{dQ}{dt} = q - \lambda Q. \end{cases} \tag{1}$$

- Experimental data provided by I. C. R. Silva, researcher from University of Brasília, and data avaliable in [2].
- For the parameter estimation process, the *lsqnonlin* available in MATLAB was used. The system 1 was inserted, along with its initial conditions and an objective function to be minimized, which in this case was the mean squared error (MSE).

Results and Discussion

The first set of experimental data used for parameter estimation are from the MCF-7 cell line.

Parameter	Value	Unity	Reference
r	0.08	day^{-1}	Estimated value
K	4×10^5	$(cell/cm^2)^{-1}$	Assumed value
μ	0.5	day^{-1}	Estimated value
q	50	$(\mu M)/day$	[2]
λ	20	day^{-1}	[3]

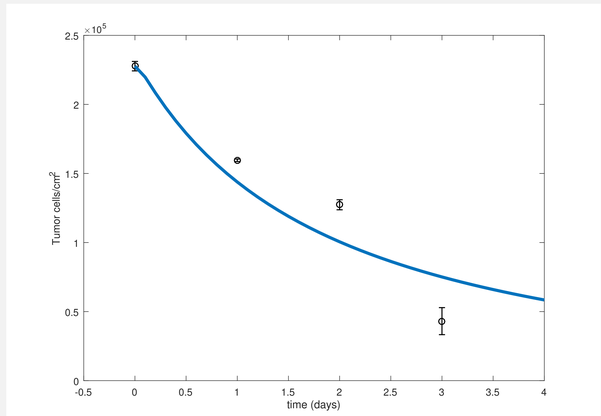

Figure: Curve fitting of population growth from MCF-7 cell line under treatment with 50μM paclitaxel and considering $N(0) = 227699.4$ cells/cm² and $Q(0) = 0$

The second set of experimental data used for parameter estimation are from the MDA-MB-231 cell line.

Parameter	Value	Unity	Reference
r	0.09	day^{-1}	Estimated value
K	1×10^5	$(cell/cm^2)^{-1}$	Assumed value
μ	7.85	day^{-1}	Estimated value
q	0.05	$(\mu M)/day$	Provided by I.C.R. Silva
λ	0.92	day^{-1}	Estimated value

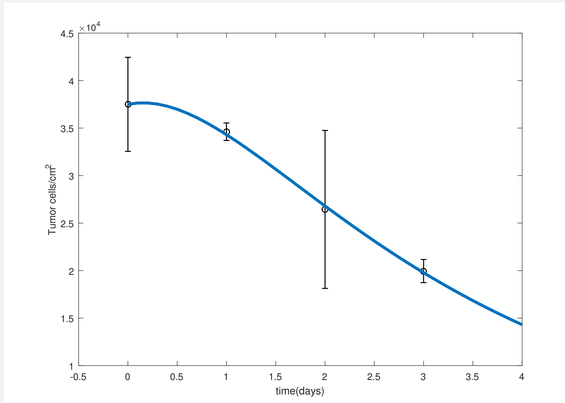

Figure: Curve fitting of population growth from MDA MB-231 cell line under treatment with 0.05μM paclitaxel and considering $N(0) = 37500$ cells/cm² and $Q(0) = 0$

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