Modeling Tumor Growth
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Introduction

Much progress has been made in finding treatments to reduce and clear malignant tumors. There are three main ways that tumors can be treated. These ways include traditional chemotherapy, radiation therapy and immunotherapy. Our job for this project is to reproduce the results of our selected paper on a certain immunotherapy treatment (siRNA), and to come up with our own change in our mathematical model to produce the best results.

The main goal of the treatment is to suppress the appropriate immune response to assist the body in combating the tumor, rather than affecting it directly.

Tumor cells form because normal cells undergo malignant transformations. IL-2’s are produced by T-helper cells when stimulated by an infection. Transforming Growth Factor-β (TGF-β) is another important factor in tumor growth. It is present in healthy cells to regulate cell growth but the process is mutated in tumor cells, and it actually allows tumor cells to keep producing. We need both cytokines and IL-2’s so that the cytokines can help the immune system and the IL-2’s are produced when stimulated by an infection.

Tumor-immune Interactions

This basic flowchart gives a visual on how the process of tumor cells are interacted in our body.

Differential Equations

A non-dimensionalization of the original model was necessary in order to reduce the stiffness of the differential equations for numerical simulations. Here are the non-dimensionalized differential equations with siRNA treatment, that were used in this project. Here w represents the effector cells, x represents the tumor cells, y represents the amount of IL-2, z represents TGF-β, and v represents siRNA.

\[
\begin{align*}
\frac{dw}{dt} &= \frac{a w}{1 + \frac{a}{b} w} + \frac{d w}{1 + \frac{d}{e} w}, \\
\frac{dx}{dt} &= \frac{e x}{1 + \frac{e}{f} x}, \\
\frac{dy}{dt} &= \frac{g y}{1 + \frac{g}{h} y}, \\
\frac{dz}{dt} &= \frac{h z}{1 + \frac{h}{i} z} - vi, \\
\frac{dv}{dt} &= D(t) - zv.
\end{align*}
\]

with initial conditions

\[
\begin{align*}
w(0) &= w_0, \\
x(0) &= x_0, \\
y(0) &= y_0, \\
z(0) &= z_0, \\
v(0) &= v_0.
\end{align*}
\]

Our Results

Here we considered a tumor where the dosage of siRNA was doubled (relative to the paper) and administered continuously for every other 1000 time steps (corresponding to 100 days). In other words, a constant dose of siRNA is administered for the first 1000 time steps, no siRNA is administered for the next 1000, and so forth.

Conclusions

• In the reference paper we saw that the tumor could be controlled with multiple injections of siRNA (rather than a continuous dosage, which is always controlled) with a high value of ‘a’.
• Since the given model was sensitive to the initial conditions (not provided) we were unable to get reliable data for multiple injection scenarios. For this reason we considered altering the continuous dosage model.
• In our simulation we saw that the tumor could also be controlled using a higher dosage of siRNA administrated continuously over set increments of time, rather than being continuous for all time (as in the reference paper).

Results from Paper

Here we consider an untreated tumor with a high immune response (c = 0.0035), where the survival of TGF-β production is close to zero the tumor experiences small oscillations with a small mass results. With a high β, however, an uncontrolled tumor mass results.

Here we consider the tumor with siRNA treatment. The first chart above represents a tumor with periodic injection of siRNA, which allows for supressed oscillations. The bottom group of charts shows the tumor’s behavior when periodic injections are administered.

References


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