Customized cancer therapy based on the dynamic analysis of the Tumor-Immune-Drug System interaction

PROBLEM STATEMENT: Chemotherapy is vital to cancer therapy but leading to serious side effects. The problem of optimizing an individual's appropriate schedule and drug dosage remains unresolved.

DESCRIPTION: I have settled a master mathematical model for the Tumor-Immune-Drug System Interaction, developed a matrix for deciding the treatment plan is effective and painless for patient.

NAME: Xin Chen
AFFILIATION: Princeton High School

WORKSHOP THEME(S): This project intends to focus on mathematical modeling on tumor and individualized immune status, using the parameters fitting and optimization of the mathematical model to make the model more accurately reflect the actual situation, providing theoretical guidance for the customization and optimization of tumor treatment.

KEYWORDS: Customized cancer therapy; dynamic analysis; Tumor-Immune-Drug System interaction.

ADDITIONAL DETAILS

- I analyzed the dynamic scenarios of the 5 distinct models in the publications, then built the master model covering the dynamic characters of the 5 models.
- To better understand the dynamic of master TID model, I studied the temporal evolution and phase plot of the model.
- The master model is numerically verified. It showed how the master model can be applied to design optimal drug treatment.

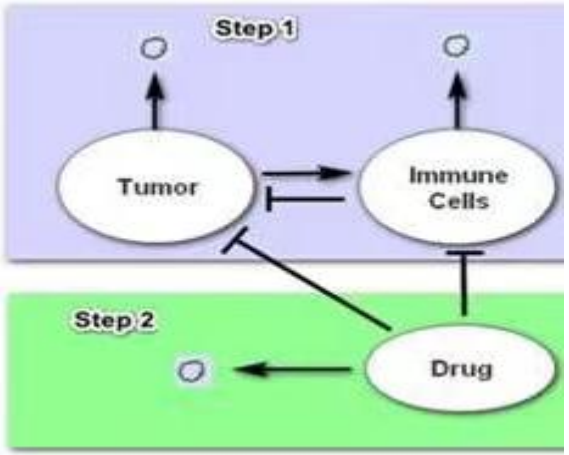

Figure 1. Illustration of Tumor-Immune-Drug network

I summarized 5 distinctive models from recent publications, Based on the above five model assumptions, their applicable scenarios, and their dynamics, we concatenate all five distinct equations into a master equation sets to capture all possible tumor-immune-drug relationship.

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The master equations:

The assumption of the master equation is the combination of all five model assumptions.

$$\frac{dT}{dt} = \underbrace{r_1 T(1-p_1 T)}_{growth} - \underbrace{\mu_1 IT \frac{I^{n1}}{g+I^{n1}} \frac{T^{n0}}{g12+T^{n0}}}_{repression\ term} - \underbrace{d_{11} TD}_{drug\ effect}$$

$$\frac{dI}{dt} = v_2 + \rho_2 T + \underbrace{r_2 I(1-p_2 I)}_{growth} + \underbrace{\mu_2 \frac{IT^n}{h+T^n}}_{promotion} + \mu_{22} T(1-\beta T)I - d_{22} TI - \underbrace{d_2 I}_{death} - d_{21} ID$$

$$\frac{dD}{dt} = v(t) - d_3 D$$

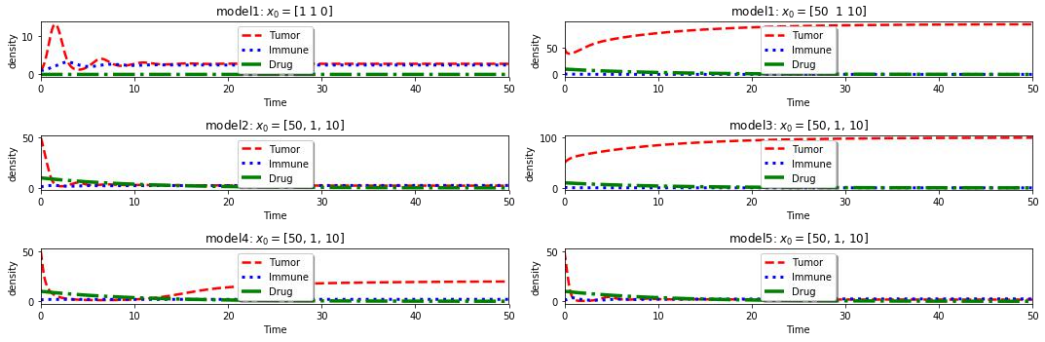

Figure 2. Master equation to capture dynamics in five distinctive published TID models.

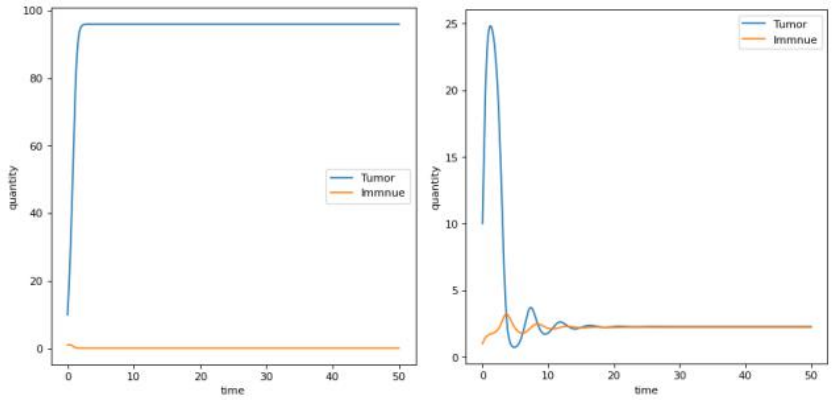

Figure 3 (left) time series of tumor and immune cell at μ1=1.5, μ2=3.5; (right) time series of tumor and immune cell at μ1=2.2, μ2=4.2

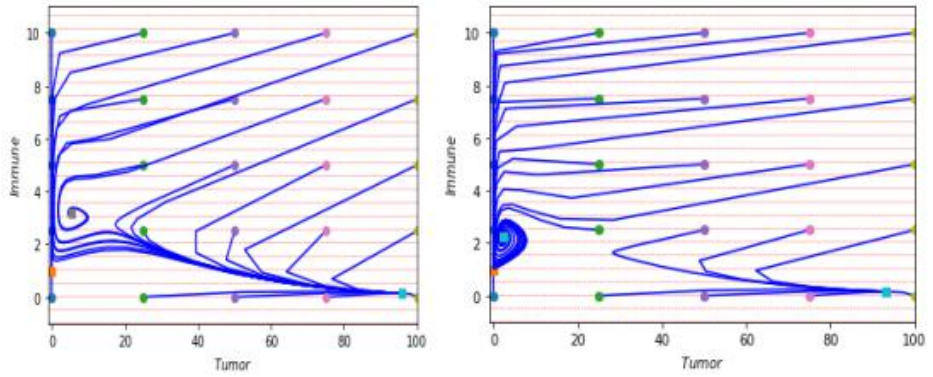

Figure 4 (left) phase portrait of network at μ1=1.5, μ2= 3.5; (right) phase portrait of network at μ1=2.2, μ2=4.2

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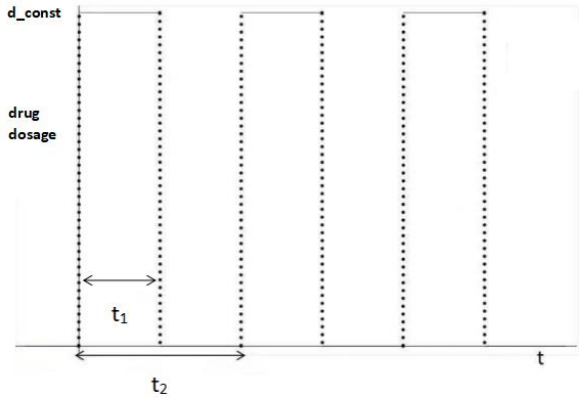

Figure 5. taking drug effect function

After establishing the master equation, we can investigate how to design the best drug treatment to eliminate the tumor in the shortest timeframe.As figure 5 illustrates,we assume that the chemotherapeutic drug is given to the patient as a continuous Dirac Delta Function.

In order to conduct a more precise search, we searched thousands of different combinations of t_1,t_2 and D_{const} . As illustrated in Figure 7, despite the drug influx parameters in Figure 7, first row can all eliminate the tumor, last subfigure of the second row (red boxed image) is preferred treatment. Because t_2 is long, while D_{const} is relatively smaller in dosage

It shows the situation when the initial condition of TID is fixed at T=50, I=1, D=10 while t_1,t_2 and D_{const} are being varied. Interestingly, it is observed that when the drug influx rate is too small, the tumor growth would slow down, but remain increasing. When t_1=1,D_{const} =10, the tumor growth is significantly slowed down, but occurs as an oscillation. While when t_1=2, D_{const} =10, the tumor cell can be eliminated from the system within 3 drug cycles.

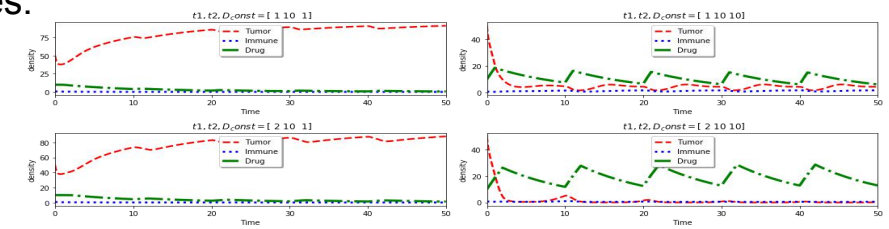

Fig 6. Effect from Drug influx rate to TID dynamic

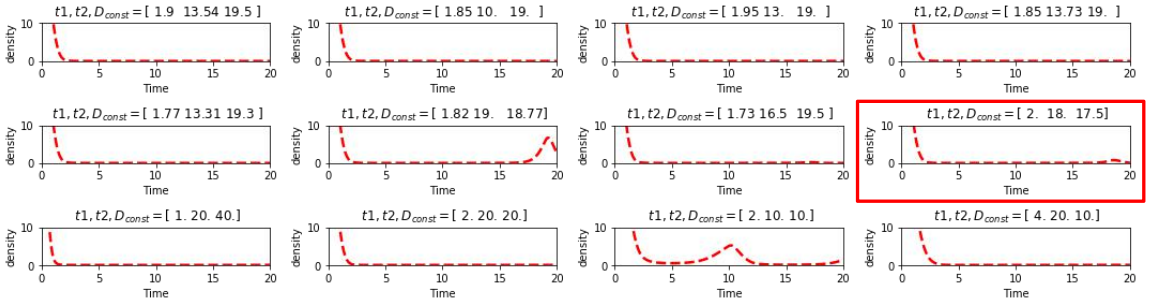

Figure 7. TID system dynamic under various drug treatment (selected 16 representative)