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Machine Learning Cancer Immunotherapy

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MACHINE LEARNING CANCER IMMUNOTHERAPY

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PROJECT DESRCIPTION

The aim of our research is to establish the viability of machine learning in relation to the prediction of TGF-B cancer treatment success. Our method begins by analying the dynamical system model of cancer invasion with subsequent immune system response. Important model parameters are identified. Numerical solutions are then run with suitably randomly chosen parameters to create a stimulated dataset that is used to train different predictive machine learning models. When presented with, new data the classifiers accuracy is reported. In the future we look forward to applying real world data to our system.

OVERVIEW

We worked to create a set of numerical simulations for a cancer immune model. This was accomplished with the help of a diagnostic classifier which we accurately predicts if cancer is present sixty days after discovery.

IMPORTANT TERMS

- exponential growth & decay
  - y'=ry, y(0)=y0
- logistic equation
  - y'=ry(1-(1/B)y), y(0)=y0
- predator-prey system
  - x'=ax(1-(b/a)y), y'=-cy(1-(d/c)x), x(0)=x0, y(0)=y0

EQUILIBRIUM AND EIGENVALUES FOR EACH MODEL

- Exponential growth/decay, y=0 is a fixed point equilibriu. Attracting when r<0 and repelling when r>0.
- logistic equation, y=0 and y=B are fixed points. When r>0 and 0<|y0|<B, y' is increasing and y=B. In this case y=0 is repelling and y=B is attracting. When r<0, these roles are reversed.
- Predator-prey system, there are two fixed points (x=0, y=0) and (x=c/d, y=a/b). For (0,0), the eigenvalues of the Jacobian {-c,a}

MATHEMATICAL MODEL

2. The unknowns are, as functions of time,

C	Cancer cells
M_1	Pro-inflammatory macrophages
M_2	Anti-inflammatory macrophages
T	T cells
I_{10}	Interleukin, inhibits T cells, we assume $I_{10} = constant * M_2$
I_{12}	Interleukin, activates T cells, we assume $I_{12} = constant * M_1$
T_β	Changes the phenotype of M_1 to M_2, we assume $T_\beta = constant * C$

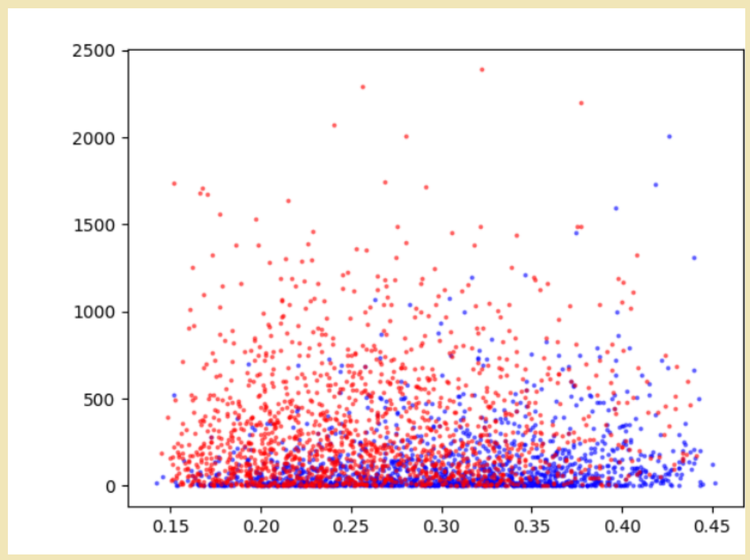
3. The parameters used in the model equations are,

$\mu_C \in (0.00007,\ 0.00010)$	In death rate of C
$\gamma \in (5.0,\ 190.0)$	In death rate of M_1 and in replacement rate of M_2 by M_1
$\lambda_c \in (0.003,\ 0.013)$	Logistic proportionality factor
$C_0 \in (500,000,\ 1,200,000)$	Logistic carrying capacity
$\mu \in (0.25,\ 0.35)$	In death rate of M_1 and M_2
$k_1 \in (1500,\ 5000)$	Production rate of M_1
$\mu_T \in (0.01,\ 0.39)$	Death rate of T
$k_T \in (2000,\ 4600)$	In growth rate of T
$K_1 \in (0.01 * C_0, 0.07 * C_0)$	In decay rate of M_2
$K_2 \in (70,000,\ 130,000)$	In growth rate of T

MACHINE LEARNING RESULTS

- We produced different datasets to match classifier to train. Datasets include 3000 to 8000 numerical solutions. In each simulation the parameter is changed slightly, while the initial conditions remain the same. The intervals produce 50% cancer and 50% no cancer over the course of 60 days

MACHINE LEARNING RESULTS



IMPROVEMENTS

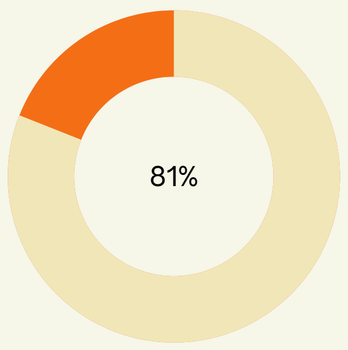
- Introducing real-world data
  - Do we have the ability to make real-world predictions using real data?
- Expand the models real-world data
  - this could be accomplished by using the equations found in the article "TFG-B inhibition can overcome cancer primary resistance to PD-1 blockade: a mathematical model."
- Try other classification algorithms (example: regression tree)
  - How does the accuracy of this algorithm compare to the other algorithms that have been applied

1. References
   a. Ching Shan Chou and Avner Friedman, Introduction to Mathematical Biology: Modeling, Analysis, and Simulations, Springer Undergraduate Texts in Mathematics and Technology, 1st Edition (2016), Springer
   b. Steven H. Strogatz, Nonlinear Dynamics and Chaos: With Applications to Physics, Biology, Chemistry, and Engineering, Studies in Nonlinearity, 2nd Edition (2015), CRC Press
   c. James D. Murray, Mathematical Biology: I. An Introduction, Interdisciplinary Applied Mathematics 17, 3rd Edition (2002), Springer
   d. N. Siewe and A Friedman, TGF-β inhibition can overcome cancer primary resistance to PD-1 blockade: A mathematical model. PLoS ONE 16(6): e0252620 (2021)

CONCLUSION

We studied a simple differential systems model for cancer immune system dynamics. From this model, we proceeded to run a series of simulations using suitably randomly chosen parameters. Based on our simulations it is apparent that the sufficient condition is rather strict. We used two two different machine learning classifiers that are 'trained' on our stimulated data. A kNN (k Nearest Neighbor) algorithm and a Keras classifier. The kNN algrothim reports an accuracy of only 81% whereas the Keras classifier reported 98.65% accuracy. Therefore, we concluded that machine learning is a viable tool for the prediction of cancer states. The TGF-B inhibitor therapy can be learned by a machine in order to find an accurate diagnosis.

KNN ALGORITHM



KERAS CLASSIFIER