Taran Srikonda Mathematical Modeling Research Plan

- TITLE

Mathematical Modeling of Integrated Approaches for Treating Leukemia

- INTRODUCTION/RATIONALE (PROBLEM) - The introduction includes a brief review of current and related literature with an explanation of the writer's interest in the subject

Leukemia, also referred to as the cancer of blood cells, has proven to be one of the most harmful forms of cancer, with nearly 60,000 new cases and 24,000 deaths per year. Acute lymphocytic leukemia is one type of leukemia that is most apparent in younger children, while Acute Myeloid Leukemia is apparent in older individuals. All subtypes of Leukemia have a five-year survival of 65.7%. Recent research on Acute Myeloid Leukemia cancer cells shows that the search for more effective cancer treatments is necessary. Beyond traditional treatments, such as radiotherapy and chemotherapy, combination therapies should be introduced. The importance of further understanding the efficacy of combination therapies has proven to be critical and with mathematical modeling, the optimal dosages and treatment strategies can be studied. Through our analysis, we will have a better understanding of specific dosages and times between treatment installations that are optimal, and we can predict which combination of therapies will be most efficient. We will explore parameter values and combinations thereof in our model to study how treatment strategies vary in different scenarios, and we will discuss reasonable treatment strategies that can be implemented when two or more therapies are combined suitably.

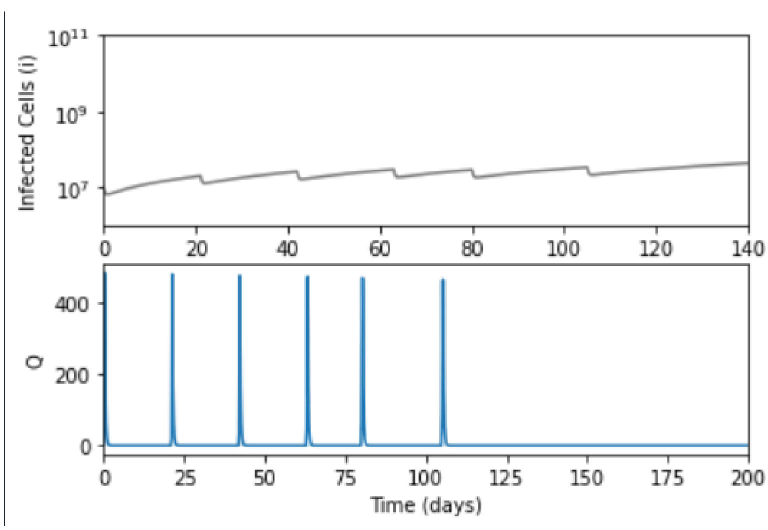
- ➔ Concise Objectives:
  - Develop a mathematical model that integrates different treatment strategies for Acute Myeloid Leukemia
  - Model Development: derive equations that describe leukemia growth and control
  - Analyze the model using numerical methods
  - Optimizing therapies to minimize costs and burden of side effects)
- ➔ Important Variables
  - Concentration of drug dosages
  - Timing and frequency of treatment(s)
  - Number of treatments

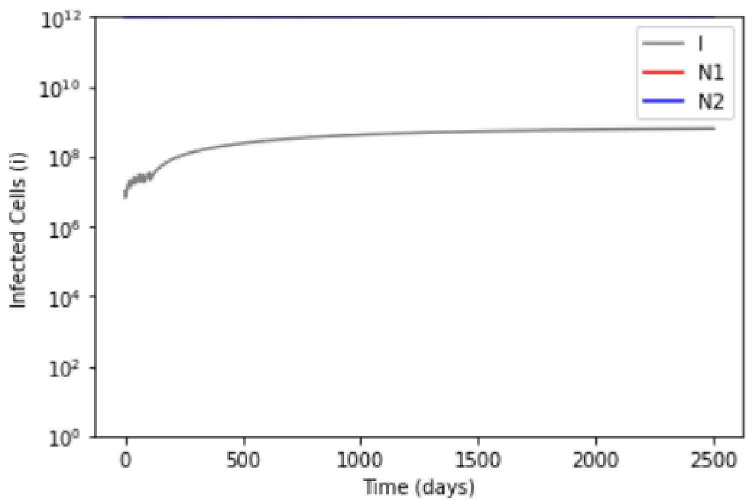
- EXPERIMENTAL PROCEDURE - This section explains the equipment and supplies used and the methods employed.

To begin, we will develop differential equations that represent leukemia growth and progression as well as different combination therapies, including radiotherapy + chemotherapy and immunotherapy + chemotherapy. Once these differential equations are developed, we will simulate them using numerical methods in Python (through the Spyder Integrated Development Environment). Once modeled, we will adjust certain parameters that control leukemia growth and treatment, and observe effects on the infected cell growth progression. Through repeated trials, we will come to a conclusion on which combination therapies are most effective, and how they should be implemented. Utilizing differential equations that are modeled based on certain parameters, we will be able to better understand the most efficient and cost-effective treatment routines for combination therapies. We anticipate the progress of the project to follow these steps:

1. Review of literature on leukemia, leukemia treatment strategies, recent advances in treatment, and approaches to model leukemia and leukemia treatment
2. Development of a mathematical model that incorporates treatment by immunotherapy, chemotherapy, and radiation
3. Mathematical analysis of equilibrium model behavior
4. Sensitivity analysis of the effects of parameters on important metrics
5. Numerical simulation of the mathematical model
6. Implementing optimization routines to maximize treatment efficacy while minimizing financial and physiological costs associated with treatment
7. Programming will occur in Python using the Spyder IDE. Numerical simulation will be conducted with standard techniques such as Runge-Kutta algorithms. Optimization routines will be drawn from Optimal Control Theory

Images/Diagrams of Prior Models:





*The following images are models of infected cell growth rate based on adjusting different parameters in chemotherapy.

- BIBLIOGRAPHY - List major references (e.g. science journal articles, books, internet sites) from your Introduction.

- ❖ Khatun, M.S.; Biswas, M.H. Modeling the effect of adoptive T cell therapy for the treatment of leukemia. *Comput. Math. Methods* 2020, *2*, e1069.
- ❖ Gil, W.f.f.m., et al. “A Mathematical Model on the Immune System Role in Achieving Better Outcomes of Cancer Chemotherapy.” *TEMA (São Carlos)*, Sociedade Brasileira de Matemática Aplicada e Computacional, 16 Sept. 2019, www.scielo.br/j/tema/a/n8PP5qY3Vfns9Rhjzf3YR3r/.