Optimal Control Applied to Cancer Vaccine Protocols

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Summary

- Our objective was to approximate optimal solutions to a cancer vaccine protocol
- The mathematical model we are using involves time delays which makes it more difficult to find solutions
- We used the Sparse Optimization Suite which is implemented through FORTRAN to solve the optimal control problem
- Our output indicated a booster shot should be given around 1.5 days in from the initial immunization in order to optimize the therapy

Important Terminology

- Time Delay: A delay in a state based on previous events within the system
- Performance Measure: A measurement of how well your system is meeting its defined goal
- Control and State Trajectories: Predicted path of control variables and the state of the system
- Dynamical System: Body or system which changes over time
- Mathematical Model: A representation of real life scenarios using equations, graphs, diagrams, etc.

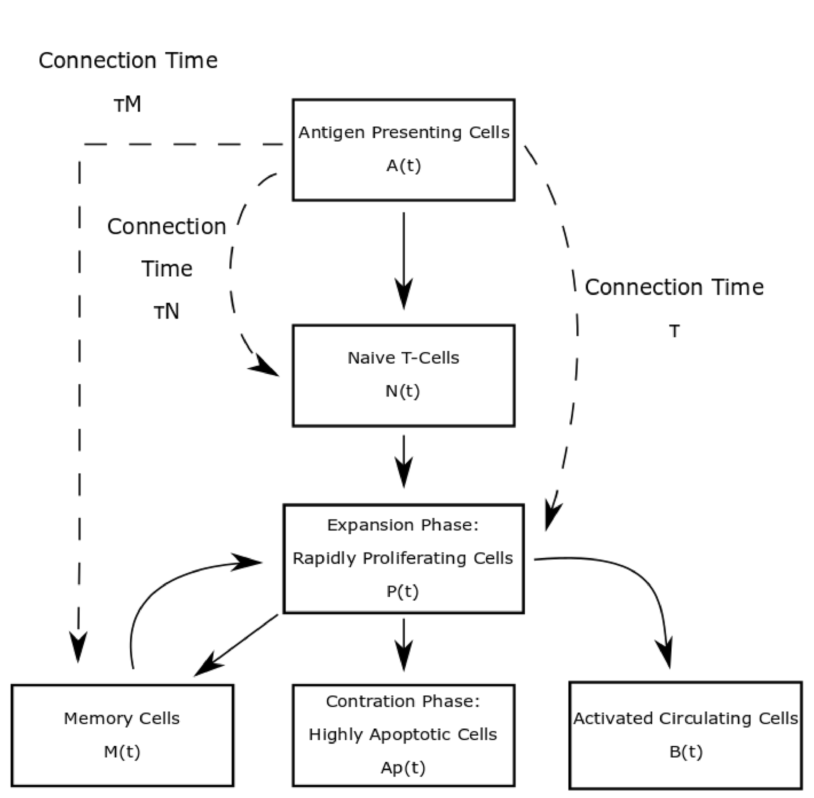

Figure 1: Immune Cell Flow Diagram

Biological Background

- The mathematical model we are using was developed by Dr. Ami Radunskaya and Dr. Sarah Hook in 2012
- The mathematical model describes the growth and death of cell populations after given a cancer vaccine
- After injection, there is a sharp incline in antigen presenting cells, which activates the immune cells
- This starts the immune cell flow from naive t-cells to rapidly proliferating cells
- From there, the proliferating cells flow to memory cells, highly apoptotic cells, and activated circulating cells
- *In Figure 1, dashed arrows represent cell flows involving time delays*

Optimal Control Problem

$$\max_{\mathbf{u}} \; aM(T) - b\int_0^T u^2(t)\,dt \text{ s.t.}$$

$$\frac{dA}{dt} = \mu_{BS}e^{-\mu_D(t-PL)}u(t)^2 - \delta_D A(t)$$

$$\frac{dP}{dt} = gA(t-\tau_N) + \rho\frac{A(t-\tau)P(t-\tau)}{\theta + A(t-\tau)}A(t) + wA(t-\tau_M)M(t-\tau_M) - (\delta_A + \frac{1}{T})P(t)$$

$$\frac{dN}{dt} = -\delta_N N(t) - gN(t-\tau_N)A(t-\tau_N)$$

$$\frac{dM}{dt} = \frac{r}{T}P(t) - wA(t-\tau_M)M(t-\tau_M)$$

$$\frac{dB}{dt} = \frac{1}{T}(\mu^*_{SB} + P(t) + \frac{\Delta\theta_{shut}}{\theta_{shut} + A(t)}) - \delta\tau B(t)$$

Important Math Definitions

- A(t) = Antigen Presenting Cells
- N(t) = Naive T-Cells
- M(t) = Memory Cells
- P(t) = Rapidly Proliferating Cells
- B(t) = Activated Circulating Cells
- τ = APC-Proliferating T-cell Synaptic Time
- τ_N = APC-Naive T-cell Synaptic Time
- τ_M = APC-Memory T-cell Synaptic Time

Results

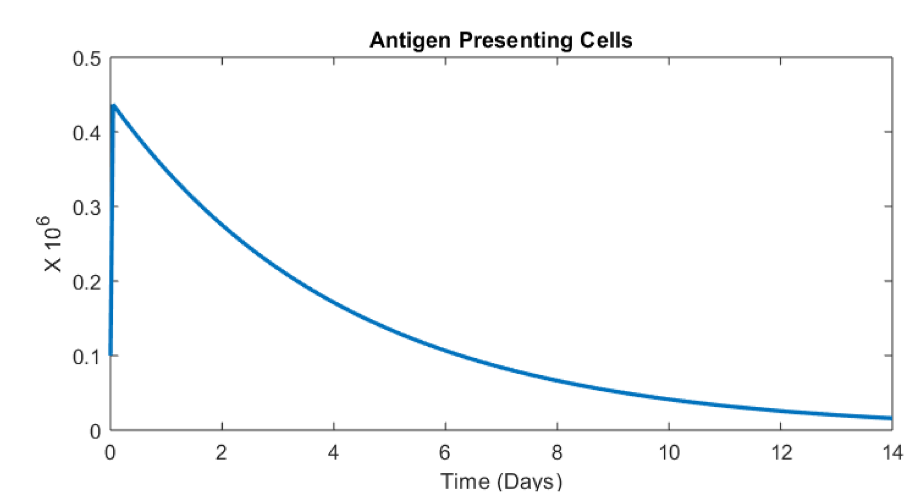

Figure 2: Antigen Presenting Cell Population

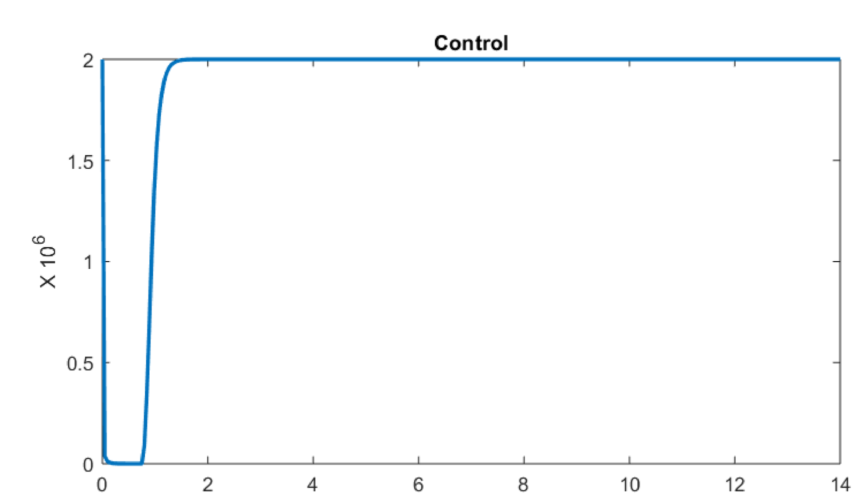

Figure 3: Control (Vaccine Administered)

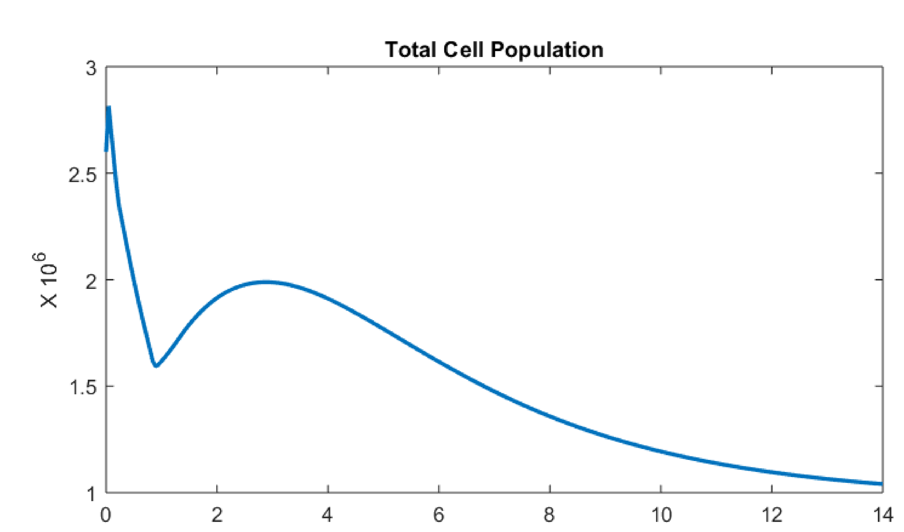

Figure 4: Total Cell Population

Conclusion

- After utilizing the Sparse Optimization Suite, we can see that in order to optimize the vaccine efficiency, a booster shot should be given around 1.5 to 1.8 days after the initial injection
- While a booster shot is expected for optimization, using genetic algorithms, Ami Radunskaya and Sarah Hook found that it should be given around day 3 instead
- This difference could be explained as we were assuming some initial conditions of certain parameters. In order for us to be more confident on the output of the Sparse Optimization Suite, we would need these initial parameters from a biologist

References

[1] Hook, S., Radunskaya, A., Modeling the kinetics of the immune response, New Challenges for Cancer Systems Biomedicine, SIMAI Springer Series, Italia, 2012.

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