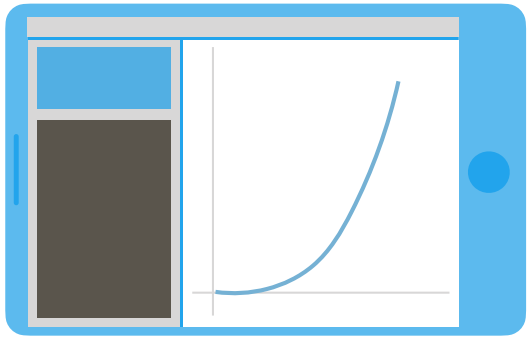

Slopes: A Free, Intuitive Mobile App to Enhance Learning in Differential Equations

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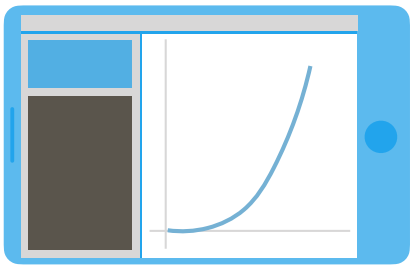
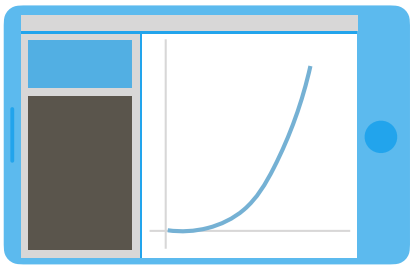
Check out the apps at
http://www.slopesapp.com
http://www.wavespdeapp.com



App Information

- Languages: **Swift and Kotlin**
- Platforms: **iOS and Android**
- http://slopesapp.com (ODE)
  - iPad Release: **Nov 2016**
  - iPhone Release: **July 2017**
  - Android Release: **Jan 2020**
  - Macs with M Chips: **Nov 2020**
- http://wavespdeapp.com (PDE)
  - iOS Release Date: **June 2019**

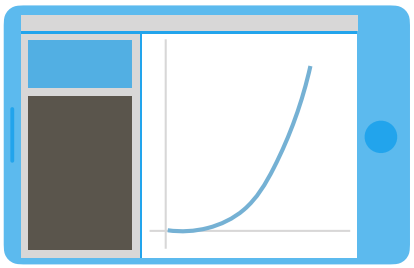


Why Mobile Devices?

* Portable
* Comparatively large screen
* Tactile interface

The Role of iPads in Constructing Collaborative Learning Spaces (Fisher, Lucas and Galstyan, 2013)

Using Slopes to Enhance Learning in Ordinary Differential Equations (K. Lucas and T. Lucas, 2022)



Class Approach

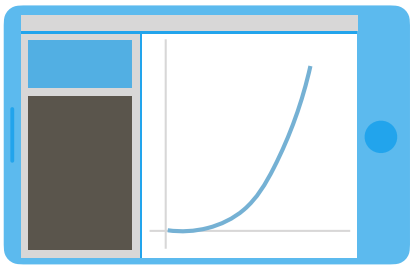
- Physical assumptions
- Mathematical expressions
- Think before you solve
  - Equilibrium solutions
  - Graphical analysis
    - Slopefields, Phase Planes, etc
- Analytical Solutions

Local Ecology

California Newt - *Taricha torosa*

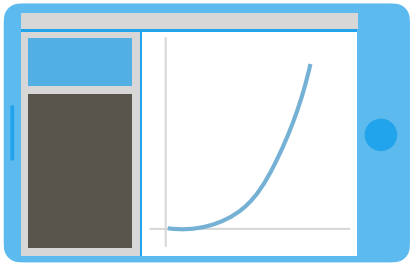
Population Models

Invasive Crayfish - *Procambarus clarkii*



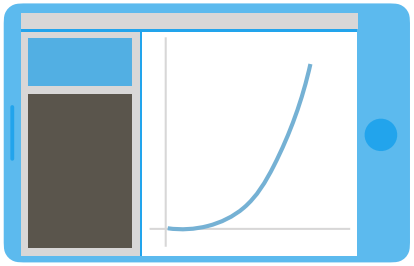
Crayfish Models

- Exponential Growth/Decay: **y' = ay**
- Exponential Growth with Constant Removal: **y' = ay - r**
- Logistic Growth: **y' = ay(1-y/b)**
- Logistic Growth with Constant Removal: **y' = ay(1-y/b) - r**
- Logistic Growth with Proportional Removal: **y' = ay(1-y/b) - ry**



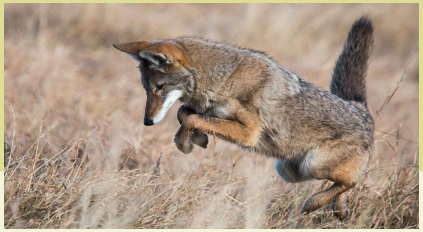
Bifurcation

A **bifurcation** occurs when a small change in a parameter value leads to a qualitative change in the long term behavior of the solution to a differential equation.



Semester Projects

- Main Goal: Understand and analyze a mathematical model using techniques learned in class
  - Slopefields/Phase Planes, Equilibrium Analysis, Numerical/Algebraic Solutions, ...
- Teams of 3-4 Students
- Final Poster Presentation
  - Judged by math and science faculty
- Images provided by Slopes



Mountain Lions vs. Deer
Three Models Examining Predator Prey Dynamics

Background

Over the last 16 months, Pepperdine has issued 17 warnings regarding mountain lions spotted on campus. In an effort to understand the dynamics behind this rise in sightings (and the Malibu ecosystem in general), we use predator/prey systems of differential equations. Within California, mountain lions feed primarily on deer, and deer are preyed on primarily by mountain lions. Given the omnipresent nature of deer on campus, this likely extends to our local ecosystem. We aim to better understand this relationship, we compare three predator/prey models with increasing complexity.

Basic Model and Coefficient Estimates

In its most nascent form, our model includes two species (mountain lions and deer), and models deer using exponential growth. The variables x and y represent deer (prey) and mountain lion (predator) populations, respectively. The equations are displayed below.

$$x' = ax - bxy$$
$$y' = -cy + dxy$$

Coefficients:

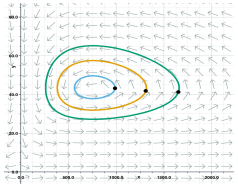
a	Rate of growth without predation.
b	Rate at which predation (interactions) decreases deer population.
c	Rate at which mountain lions die without prey.
d	Rate at which predation (interaction) increases mountain lion population.

While the true values of some parameters are unknown, zoological research can be used to guide many of these choices:

- Deer's maximum growth rate is estimated using reproduction statistics.
  - At any given time, 66% of female deer are pregnant. Deer have an average litter size of 1.9, are pregnant for about 203 days, and exhibit balanced sex ratios.
  - If we observed a deer population and returned 203 days later, we would therefore expect to see 62.7% more deer. Therefore, without external constraints the population will grow according to the equation $x = ce^{0.875t}$, with c denoting the starting population, and t denoting change in time (in years).
- The location of equilibriums is estimated using food intake requirements.
  - Should the growth in the deer population produce exactly the amount of meat required to sustain the mountain lion population, no change should occur in either.
  - The average mountain lion requires 6.57 pounds of meat per day to survive. As the average mule deer weighs 177 pounds, with at most 133 pounds being edible biomass, a mountain lion's survival requires 0.049 deer per day, which is 18.0 per year.

First Model Behavior

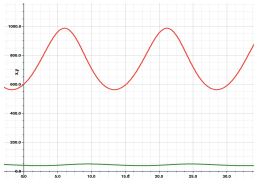
The phase plane has two equilibrium points: a saddle point at (0,0) and a center at (c/d, a/b). Only in cases of complete extinction and at (c/d, a/b) are both populations at rest. A phase plane is shown below, along with a graph of each population. Coefficients were informed by the research described above. Except in the case when an initial value is zero, populations continuously orbit around the center.



a = 0.875, b = 0.02, c = 0.2, d = 0.000265

Initial Conditions: Deer = 600, Mountain Lion = 40

Equilibrium points: (755, 44), (0,0)



Jacobian at (0,0): $\begin{bmatrix} 0.87 & 0 \\ 0 & -0.2 \end{bmatrix}$, *$\lambda_1$= 0.87, λ_2= -0.2 (unstable, saddle)*

Jacobian at (755,44): $\begin{bmatrix} 0 & -15.1 \\ -0.012 & 0 \end{bmatrix}$, *$\lambda_1$= 0.417i, λ_2= −0.417i (unstable, non−generic, confirmed as center using numerical methods.)*

Logistic Growth and Ratio Dependence

Our second model introduces the concepts of logistic growth and density dependence. The equations are displayed below.

$$x' = ax\left(1 - \frac{x}{k}\right) - \frac{bxy}{(1 + fx + y)}$$
$$y' = -cy + \frac{dxy}{(1 + fx + y)}$$

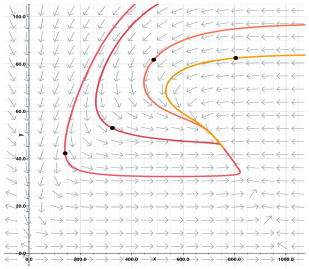
Logistic growth is introduced by the addition of (1-x/k) to the part of the equation controlling deer growth. This takes resource scarcity into account, and ensures that the deer population do not expand beyond its carrying capacity (k). The importance of this feature is highlighted by a potential behavior observable in the first model: without mountain lions the deer population will expand infinitely. While California's natural carrying capacity for deer is an unexpectedly contentious topic, the deer population peaked at approximately 2 million before declining substantially to its current level of 540,000.

Density dependence is introduced by the denominator now beneath both interaction terms. The effect of this change is best explained by an example. Say that an environment has 100 deer and 1 mountain lion. Say that a second environment has 10 deer and 10 mountain lions. Under our first model, both interaction terms end up the same: 100 times some interaction coefficient. This is obviously a departure from how deer and mountain lions interact in reality. Thus, the new model makes the effectiveness of predation dependent on this ratio between species. The most effective ratio can be determined using the value the coefficients (in this case just f, as one can always be omitted). For example, if f = 1, the second environment would yield a larger interaction term under the new model.

To ensure comparability between models, values of coefficients representing biological constants (a, c) remain unchanged from the previous model, and interaction coefficients (b, d) are appropriately scaled to adjust for the new terms.

Second Model Behavior

The phase plane of the second model is shown below. As the model is not linear, the Jacobian (matrix below) serves as a useful linear approximation.



Parameters:

a = 0.875, b = 1.8, c = 0.2, d = 0.1, f = 0.44, k = 1000

Equilibrium points: (757, 44), (0,0), (1000, 0)

Jacobian:

$$\begin{bmatrix} a - \frac{2ax}{k} - \frac{by(y+1)}{(fx+y+1)^2} & \frac{-bx(fx+1)}{(fx+y+1)^2} \\ \frac{dy(y+1)}{(fx+y+1)^2} & -c + \frac{dx(fx+1)}{(fx+y+1)^2} \end{bmatrix}$$

Using this Jacobian, the equilibrium points can be categorized. The Jacobian for the only equilibrium where both species survive is shown below, along with the useful indicators it provides.

$$J = \begin{bmatrix} -0.45896 & -3.1775 \\ 0.0014 & -0.2347 \end{bmatrix} \quad \lambda_1 = -0.257 \quad tr(J) = -0.694$$
$$\lambda_2 = -0.437 \quad det(J) = 0.112$$

This makes (757, 44) a nodal sink (stable). Using the same techniques, (0,0) and (1000, 0) can both be categorized as saddle points.

When initial populations are non-zero, they will eventually sink into a single equilibrium of 757 deer and 44 mountain lions. Unlike the previous model, the equilibrium is always approached (nodal sink) rather than circled around (center).

Adding a Third Species

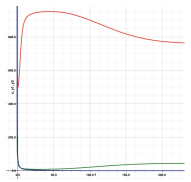
When compared to empirical data, it becomes clear that both models discussed though this point are incomplete. Just 5,000 wild mountain lions roam California—well below what our two-species model predicts. While a wildlife policy of suppressing dangerous mountain lions while protecting deer from predation is likely the largest culprit, it is also worth considering other interactions within our ecosystem. Our third and final model maintains the concepts discussed in its antecedent while adding a third species: coyotes. The equations are displayed below, with y_1 denoting mountain lions and y_2 denoting coyotes.

$$x' = ax\left(1 - \frac{x}{k}\right) - \frac{b_1xy_1}{(1 + fx + y_1 + gy_2)} - \frac{b_2xy_2}{1 + fx + y_1 + gy_2}$$
$$y_1' = -c_1y_1 - my_1y_2 + \frac{d_1xy_1}{(1 + fx + y_1 + gy_2)}$$
$$y_2' = -c_2y_2 - ny_1y_2 + \frac{d_2xy_2}{(1 + fx + y_1 + gy_2)}$$

Most new parameters are direct extensions of the previous model (b_2, c_2, d_2). The new term gy_2 in each denominator generalizes the ratio to consider all three species. New interaction terms between mountain lions and coyotes are also included (my_1y_2, ny_1y_2). Coyotes live in the same environments as mountain lions, and consume the same prey (deer). As mountain lions and coyotes are directly antagonistic to each other (beyond the indirect effects of consuming deer), both coefficients are negative. As mountain lions are far larger predators than coyotes (137 pounds vs 31 pounds), it can be assumed that n is the larger coefficient.

Third Model Behavior

A plot of all three populations is shown below. Using our starting conditions and parameters (as well as reasonable variations thereof), the mountain lions (green) and coyotes (blue) engage in conflict, suppressing the population of each. The mountain lions eventually win, sending the coyotes into extinction. A numeric solver was used to find the equilibrium that all three species approach.



Parameters:

a = 0.875, b_1 = 1.8, b_2 = 1.8, c_1 = 0.2, c_2 = 0.1, f = 0.44, k = 1000, m = 0.007, n = 0.017, d_1 = 0.1, d_2 = 0.092, g = 2

Equilibrium: The deer population approaches 759.7, the mountain lion population approaches 44.5, and the coyote population approaches extinction.

Conclusion, Sources

While all three models share similar equilibrium points (between mountain lions and deer), behavior around these points differs substantially between models. Furthermore, each addition of complexity made our models more fragile. While both species refused to die in the first model, far more scenarios involved extinction in the third model. This could be due to the nature of natural ecosystems, or the nature of mathematical models.

Dubey, B., and Upadhyay, R.K. *Persistence and Extinction of One-Prey and Two-Predators System.* Nonlinear Analysis: Modeling and Control. 2004, Vol 9, No. 4.

Green et. al., *Reproductive Characteristics of Female White-Tailed Deer*, Theriogenology, Volume 94, 2017.

Longhurst et. al., *The California Deer Decline and Possibilities for Restoration*, California Nevada Wildlife Transactions, Wildlife Society, 1976.

Pettorelli et. al., *Predation, Individual Variability and Vertebrate Population Dynamics*, Oecologia, 2011.

Pierce, Becky et. al. *Selection of Mule Deer by Mountain Lions and Coyotes: Effects of Hunting Style, Body Size, and Reproductive Status.* " 2000. Journal of Mammalogy, Volume 81, Issue 2.

Xiao, Dongmei and Ruan, Shigui. *Global dynamics of a ratio-dependent predator-prey system.* Journal of Mathematical Biology. 2000.

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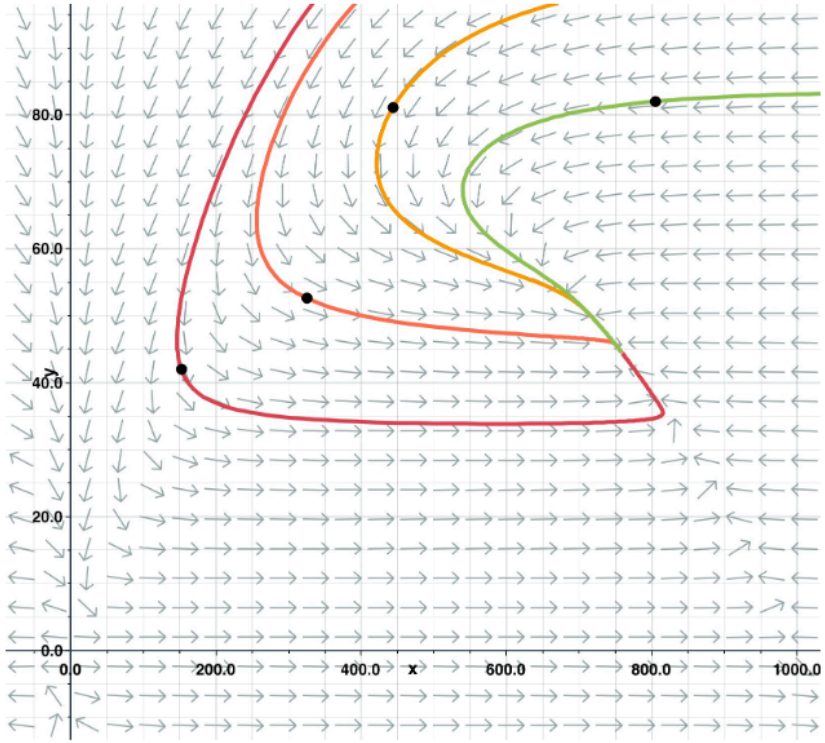

Parameters:

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$d = 0.1$, $f = 0.44$, $k = 1000$

Equilibrium points: (757, 44), (0,0), (1000, 0)

Jacobian:

$$\begin{bmatrix} a - \frac{2ax}{k} - \frac{by(y+1)}{(fx+y+1)^2} & \frac{-bx(fx+1)}{(fx+y+1)^2} \\ \frac{dy(y+1)}{(fx+y+1)^2} & -c + \frac{dx(fx+1)}{(fx+y+1)^2} \end{bmatrix}$$

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Tumor Growth Effects on Healthy and Immune Cells

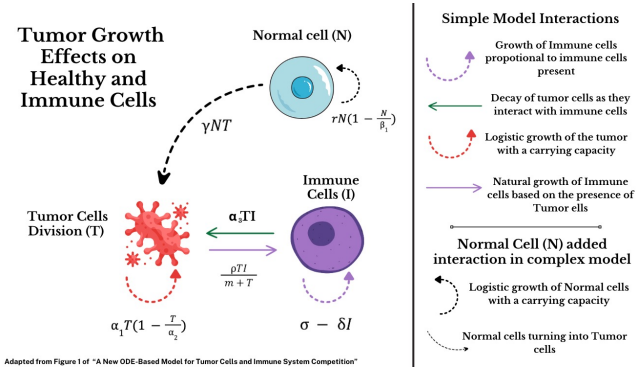
Pepperdine University

Introduction

When cells divide, there is a small chance that mutations occur and that these mutations will create tumor cells. However, the body has many ways of protecting itself and preventing tumor cells from continuing to divide. One of the mechanisms the body employs is the destruction of tumor cells with immune cells. If the body doesn't destroy tumor cells, they will compete with healthy cells for resources, potentially endangering the healthy cells. The rate of growth of tumor cells, combined with the strength of the immune system, informs cancer treatment options.

We adapted our model from Alharbi et al. [1] We assumed that normal cells turn immediately into tumor cells and that the immune cells modeled are killer T cells. The equilibria are measured in concentration of cells; for example, the concentration of tumor cells at equilibrium equals the number of tumor cells at equilibrium divided by the initial number of tumor cells.

Diagram



Adapted from Figure 1 of "A New ODE-Based Model for Tumor Cells and Immune System Competition"

Simple Model: Tumor Cells vs Immune Cells

$$\frac{dT}{dt} = \alpha_1 T\left(1 - \frac{T}{\alpha_2}\right) - \alpha_3 TI$$
$$\frac{dI}{dt} = \sigma - \delta I + \frac{\rho TI}{m+T}$$

Assumptions:

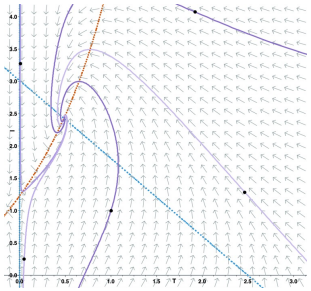
1. Immune cells are killer T cells
2. Immune cells naturally die
3. In the absence of tumor cells, immune cells are created at a constant rate
4. A tumor already exists

Term	Description	Value
T	**Amount of tumor cells**	**Concentration of Cells***
α_1	Growth of tumor cells proportional to existing tumor cells	0.4426
α_2	Carrying capacity for tumor cells	2.5
α_3	Eradication of tumor cells proportional to number of immune cells	0.1469
I	**Amount of immune cells**	**Concentration of Cells***
σ	Immune cells generated at a constant rate	0.7
δ	The natural death of immune cells, proportional to the existing number of immune cells	0.57
ρ	The immune cells' response rate proportional to the interaction of tumor and immune cells	0.7829
m	The immune system's threshold of production ("half saturation")	0.8620

*Concentration of cells refers to the number of current cells of type (T/I/N) / number of initial cells (T/I/N)

Simple Model Graphs

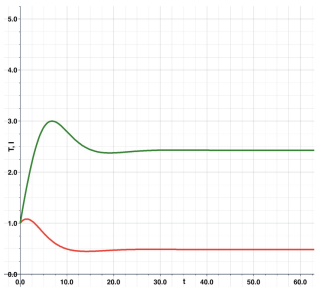
Simple Model Phase Plane



T-nullclines (blue) and I-nullcline (orange) intersect at the equilibrium points:

- (0, 1.2281) which is a saddle upon appearance
- (0.4847, 2.4288) which is a spiral sink upon appearance

Simple Model Systems Graph



Stable Equilibrium Values (for $T_0 = I_0 = 1.0$)

- T = 0.4847
- I = 2.4288

These equilibrium values coincide with the stable equilibrium we found through the nullclines of the phase plane

Equilibrium Analysis

The Jacobian of the simple system is:

$$J = \begin{bmatrix} \alpha_1 - \frac{2\alpha_1}{\alpha_2}T - \alpha_3 I & -\alpha_3 T \\ \frac{\rho m I}{(m+T)^2} & -\delta + \frac{\rho T}{m+T} \end{bmatrix}$$

At the equilibrium point (0, 1.2281) the eigenvalues of the Jacobian are

$$\lambda_1 = -0.57,$$
$$\lambda_2 = 0.2622.$$

Since there is one positive and one negative eigenvalue, we classify this point as a saddle

At the equilibrium point (0.4847, 2.4288) the eigenvalues of the Jacobian are

$$\lambda_1 = -0.1870 + 0.2326i,$$
$$\lambda_2 = -0.1870 - 0.2326i.$$

Since there are two negative and complex eigenvalues, we classify this point as a spiral sink

Simple Model Analysis

According to our model, if we do not begin with the presence of at least one tumor, there will be no recorded tumor growth and the immune cells will stabilize at an equilibrium concentration of 1.2281 cells per initial cell count. Assuming the presence of at least one tumor, both tumor and immune cells will initially grow before entering competition and eventually leveling off to an equilibrium concentration of 0.4847 tumor cells per initial cell count and 2.4288 immune cells per initial cell count. In this scenario, immune cells successfully repress tumor growth. By assumption 4, we will not be considering the unstable equilibrium.

Sources

[1] Alharbi, S.A.; Rambely, A.S. A New ODE-Based Model for Tumor Cells and Immune System Competition. Mathematics 2020, 8, 1285.

[2] Unni, Pranav, and Padmanabhan Seshaiyer. "Mathematical Modeling, Analysis, and Simulation of Tumor Dynamics with Drug Interventions." Computational and mathematical methods in medicine vol. 2019 4079298. 8 Oct. 2019, doi:10.1155/2019/4079298

[3] Yin A, Moes DJAR, van Hasselt JGC, Swen JJ, Guchelaar HJ. A Review of Mathematical Models for Tumor Dynamics and Treatment Resistance Evolution of Solid Tumors. CPT Pharmacometrics Syst Pharmacol. 2019 Oct;8(10):720-737. doi: 10.1002/psp4.12450. Epub 2019 Aug 9. PMID: 31250989; PMCID: PMC6813171.

Complex Model: Involving Normal Cells

$$\frac{dT}{dt} = \alpha_1 T\left(1 - \frac{T}{\alpha_2}\right) - \alpha_3 TI + \gamma NT$$
$$\frac{dI}{dt} = \sigma - \delta I + \frac{\rho TI}{m+T}$$
$$\frac{dN}{dt} = rN\left(1 - \frac{N}{\beta}\right) - \gamma NT$$

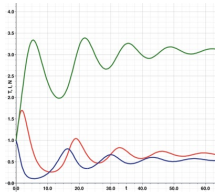
Term	Description	Value
N	**Amount of normal cells**	**Concentration***
r	Logistic growth of normal cells	0.4312
γ	The rate at which tumor cells crowd out normal cells	0.64
β	The carrying capacity of normal cells	3.34×10^5

Additional Assumption:

5. Normal cells immediately turn into tumor cells, rather than first turning into abnormal cells

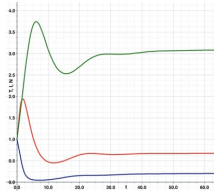
Complex Model Graphs

(a) Less Aggressive $\alpha_1 = 0.1426$



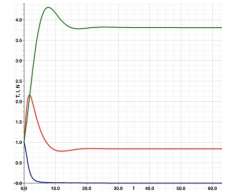
Stable Equilibrium**: T = 0.6737; I = 3.0900; N = 0.5469

(b) Unchanged $\alpha_1 = 0.4426$



Stable Equilibrium**: T = 0.6737; I = 3.0900; N = 0.2041

(c) More Aggressive $\alpha_1 = 0.8426$



Stable Equilibrium **: T = 0.8396; I = 3.8098; N = 0.0000

**for $T_0 = I_0 = N_0 = 1.0$

As we increase tumor growth rate aggression, cell concentrations reach equilibrium more quickly.

Equilibrium Analysis

The Jacobian of the complex system is:

$$J = \begin{bmatrix} \alpha_1 - \frac{2\alpha_1}{\alpha_2}T - \alpha_3 I + \gamma N & -\alpha_3 T & \gamma T \\ \frac{\rho m I}{(m+T)^2} & -\delta + \frac{\rho T}{m+T} & 0 \\ -\gamma N & 0 & r - \frac{2r}{\beta}N - \gamma T \end{bmatrix}$$

J(0, 1.2281, 0) has the eigenvalues:

$\lambda_1 = -0.57$
$\lambda_2 = 0.4312$
$\lambda_3 = 0.2622$

This represents a saddle

J(0.6737, 3.0900, 0.2041) has the eigenvalues:

$\lambda_1 = -0.1299 + 0.3628i$
$\lambda_2 = -0.1299 - 0.3628i$
$\lambda_3 = -0.0859$

This represents a spiral sink

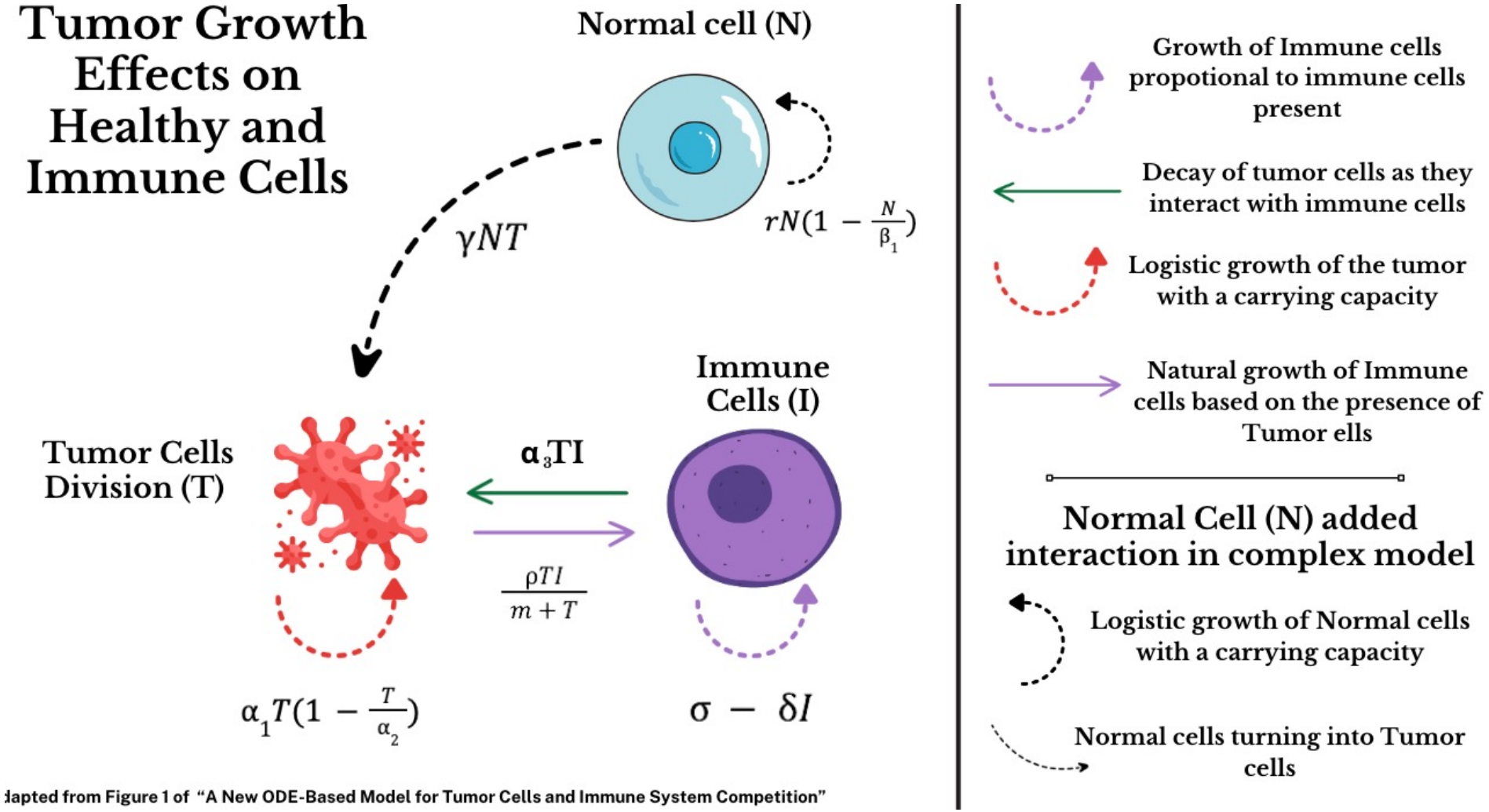
J(0, 1.2281, 3.34×10^5) has the eigenvalues:

$\lambda_1 = 213760$
$\lambda_2 = -0.57$
$\lambda_3 = -0.4312$

This represents a saddle

Complex Model Analysis

Based on our unchanged complex model (b), involving the presence of normal cells mildly increases tumor cell concentration, while normal cells are severely impacted by their interaction with tumor cells. When evaluating our complex model with a less aggressive tumor growth rate (a), all the cell's concentrations take longer to reach equilibrium as they are interacting more competitively. The normal cell concentration is less affected by tumor presence and ultimately reaches a higher equilibrium concentration. When evaluating our complex model with a more aggressive tumor growth rate (c), all cell concentrations reach equilibrium more quickly than the unchanged complex model (b). In this case, normal cells are severely impacted and completely die out, whereas tumor cells reach a higher equilibrium than in all other cases. Immune cells also reach a higher equilibrium, indicating a healthy immune response from our host. By assumption 4, we will not be considering the unstable equilibria.



dapted from Figure 1 of "A New ODE-Based Model for Tumor Cells and Immune System Competition"

Simple Model: Tumor Cells vs Immune Cells

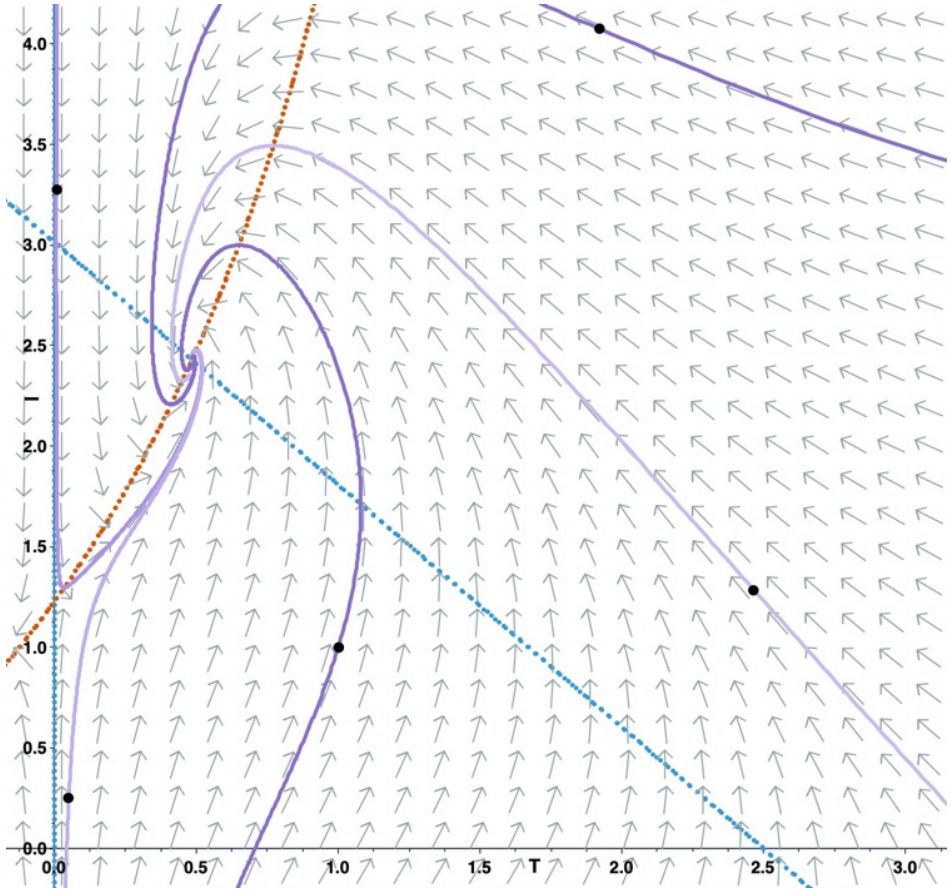
$$\frac{dT}{dt} = \alpha_1 T\left(1 - \frac{T}{\alpha_2}\right) - \alpha_3 TI$$

$$\frac{dI}{dt} = \sigma - \delta I + \frac{\rho TI}{m+T}$$

Assumptions:

1. Immune cells are killer T cells
2. Immune cells naturally die
3. In the absence of tumor cells, immune cells are created at a constant rate
4. A tumor already exists

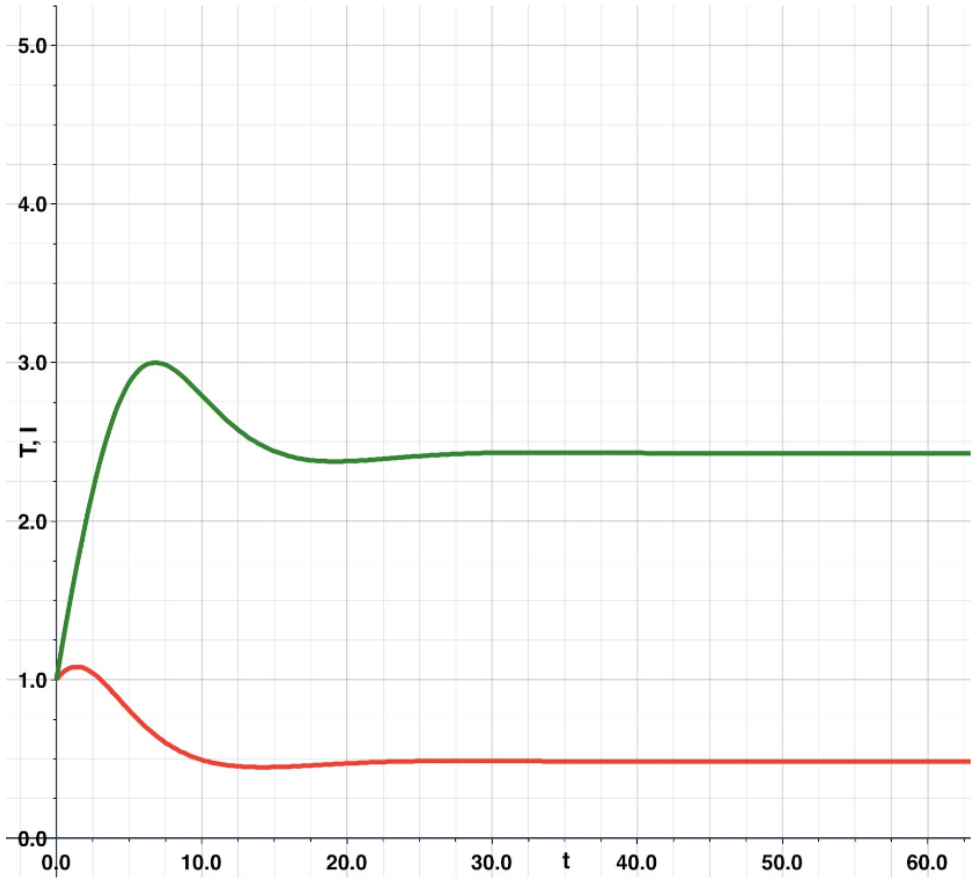
Simple Model Phase Plane



T-nullclines (blue) and I-nullcline (orange) intersect at the equilibrium points:

- (0, 1.2281) which is a saddle upon appearance
- (0.4847, 2.4288) which is a spiral sink upon appearance

Simple Model Systems Graph



Stable Equilibrium Values (for $T_0 = I_0 = 1.0$)

- T = 0.4847
- I = 2.4288

These equilibrium values coincide with the stable equilibrium we found through the nullclines of the phase plane

$$\frac{dT}{dt} = \alpha_1 T\left(1 - \frac{T}{\alpha_2}\right) - \alpha_3 TI + \gamma NT$$

$$\frac{dI}{dt} = \sigma - \delta I + \frac{\rho TI}{m + T}$$

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{\beta}\right) - \gamma NT$$

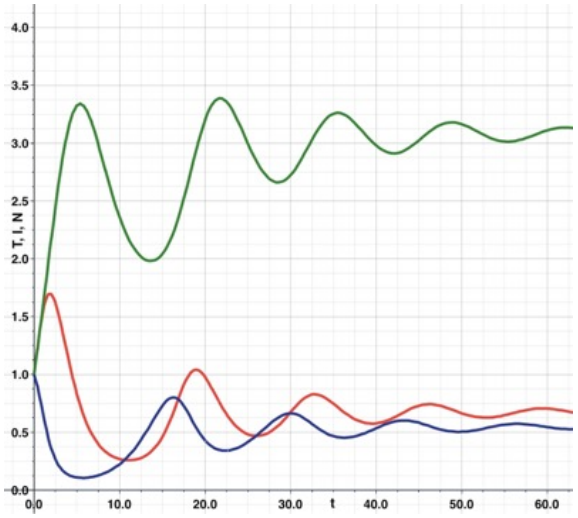
Term	Description	Value
N	**Amount of normal cells**	**Concentration***
r	Logistic growth of normal cells	0.4312
γ	The rate at which tumor cells crowd out normal cells	0.64
β	The carrying capacity of normal cells	3.34×10^5

Additional Assumption:

5. Normal cells immediately turn into tumor cells, rather than first turning into abnormal cells

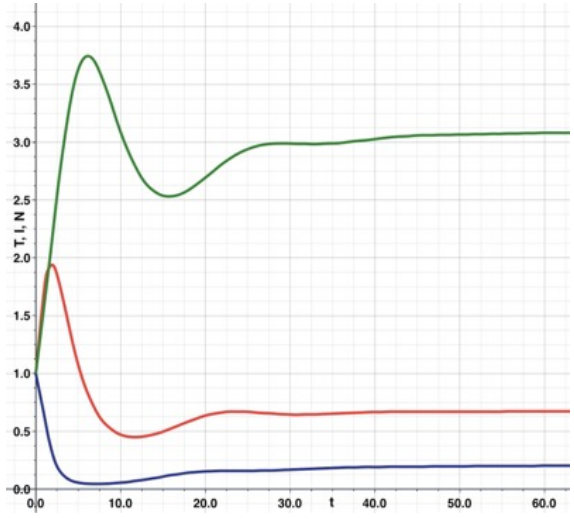
Complex Model Graphs

(a) Less Aggressive
$\alpha_1 = 0.1426$



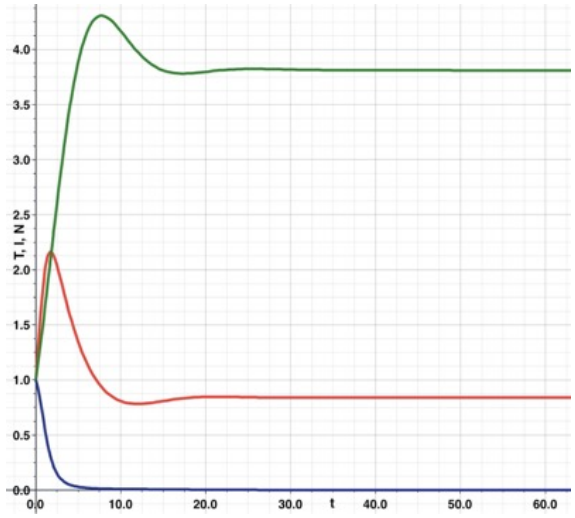
Stable Equilibrium**:
T = 0.6737; I = 3.0900;
N = 0.5469

(b) Unchanged
$\alpha_1 = 0.4426$



Stable Equilibrium**:
T = 0.6737; I = 3.0900;
N = 0.2041

(c) More Aggressive
$\alpha_1 = 0.8426$

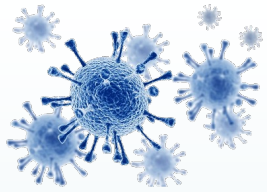


Stable Equilibrium **:
T = 0.8396; I = 3.8098;
N = 0.0000

**for $T_0 = I_0 = N_0 = 1.0$

As we increase tumor growth rate aggression, cell concentrations reach equilibrium more quickly.

2 Models Examining SIR Dynamics Infection of T-Cells by HIV



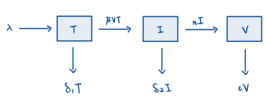
Background

Since the first reported cases of HIV in the 1980s, this infectious disease has skyrocketed in cases as well as deaths resulting from the virus. In an effort to better understand the innerworkings of the disease from a viral level, we will use an SIR model that closely examines the infection of CD4+ T-cells by the HIV virus. Within the body, when the HIV virus is introduced, T-cells become susceptible to infection by the virus. Once a virus comes in contact with a T-cell, that T-cell becomes infected. After a certain amount of time, the T-cell bursts, leaving more viruses. To represent this, we will utilize 2 models in increasing complexity.

Basic Model and Coefficient Estimates

In its most nascent form, our model includes three populations (Helper T-Cells, Infected T-Cells, and Free Virus) and models virus growth and infection rate. The variables T, I, and V represent Helper T-Cells (Susceptible), Infected T-Cells (Infected), and Viruses (Recovered), respectively. This model deviates from the standard SIR model by introducing a free virus population that grows proportionally to the death of infected cells. That constant of proportionality n is the burst coefficient from when infected cells die and release the virus. The equations are displayed below and represent a mm of an infected body at any given place.

$$\frac{dT}{dt} = \lambda - \delta_1 T - \beta VT$$
$$\frac{dI}{dt} = \beta VT - \delta_2 I$$
$$\frac{dV}{dt} = nI - cV$$



Parameter	Description	Value	Reference
λ	Rate of production of new T-Cells	100 $day^{-1}mm^{-3}$	[4]
δ_1	Rate of death of uninfected cells	0.02 day^{-1}	[4]
β	Infection coefficient	2.4×10^{-5} mm^3 day^{-1}	[4]
δ_2	Rate of death of infected cells	0.24 day^{-1}	[4]
n	Burst coefficient of the virus	*varies*	[4]
c	Rate of clearance of free virus	2.4 day^{-1}	[4]
T_0	Initial T-cell population	1000 cells mm^{-3}	[4]
I_0	Initial infected cell population	0 cells mm^{-3}	[4]
V_0	Initial virus population	0.001 cells mm^{-3}	[4]

λ is scaled to match [2]. The burst coefficient varies in the literature. For both our complex model and basic model we will explore n=100 and n=500, with the addition of n=10 for the basic model.

Sources

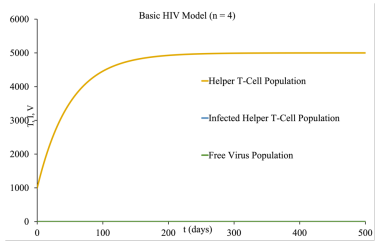
[1] Bagnoli, F., Lio, P., & Sguanci, L. (2006). Modeling viral coevolution: HIV multi-clonal persistence and competition dynamics. Physica A: Statistical Mechanics and its Applications, 366, 333-346.
[2] Chao, D. L., Davenport, M. P., Forrest, S., & Perelson, A. S. (2004). A stochastic model of cytotoxic T cell responses. Journal of Theoretical Biology, 228(2), 227-240.
[3] Luo, J., Wang, W., Chen, H., & Fu, R. (2016). Bifurcations of a mathematical model for HIV dynamics. Journal of Mathematical Analysis and Applications, 434(1), 837-857.
[4] Perelson, A. S., Kirschner, D. E., & De Boer, R. (1993). Dynamics of HIV infection of CD4+ T cells. Mathematical biosciences, 114(1), 81-125.

First Model Behavior

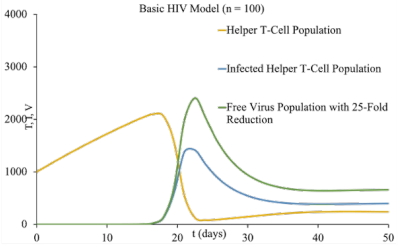
The equilibrium points are $\left(\frac{\lambda}{\delta_1}, 0, 0\right)$ & $\left(\frac{c\delta_2}{n\beta}, \frac{c}{n}\left(\frac{\lambda n}{c\delta_2} - \frac{\delta_1}{\beta}\right), \frac{\lambda n}{c\delta_2} - \frac{\delta_1}{\beta}\right)$, for our parameters (5000,0,0) & (24000/n, 416.7-2000/n, 173.6n-833.3). The Jacobian for the system is:

$$\begin{bmatrix} -\delta_1 - \beta V & 0 & -\beta T \\ \beta V & -\delta_2 & \beta T \\ 0 & n & -c \end{bmatrix}$$

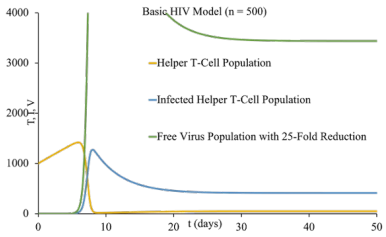
For n=4 the equilibrium (5000,0,0) is a sink with eigenvalues (-0.02,-0.037, -2.60) and the other equilibrium is not positive for I and V. Below is a plot that shows the stable equilibrium.



For n=100, (5000,0,0) is a saddle with eigenvalues -0.02, 2.31, and -4.95. The equilibrium (240, 396.7, 16527.8) is a spiral sink with eigenvalues are −2.68, −0.189±0.223i. The virus population grows and solutions tend toward the second equilibrium.

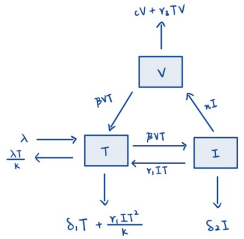


For n=500, (5000,0,0) is a saddle with eigenvalues 5.56, -0.004, and -9.89. The equilibrium (48, 412.7, 85972.2) is a spiral sink with eigenvalues−2.73, −0.06±0.187i. The virus population grows and solutions tend toward the second equilibrium.



Logistic Growth and Clonal Amplification

Our second model introduces logistic growth of T-cells, the clonal amplification rate of T-cells after simulation by infected T-cells, and the removal rate of infected T-cells and virus by CTL responses and antibodies, respectively.



$$\frac{dT}{dt} = (\lambda + \gamma_1 IT)\left(1 - \frac{T}{k}\right) - \delta_1 T - \beta VT$$
$$\frac{dI}{dt} = \beta VT - (\delta_2 + \gamma_2 T)I$$
$$\frac{dV}{dt} = nI - (c + \gamma_3 T)V - \beta VT$$

Parameter	Description	Value	Reference
γ_1	Clonal amplification rate of T-cells after stimulation by infected cells	0.001 day^{-1}	[1]
γ_2	Removal rate of infected cells by CTL responses	0.001 day^{-1}	[1]
γ_3	Removal rate of free virus by antibodies	0.005 day^{-1}	[1]
k	Carrying capacity of Helper T-cells	1500 mm^{-3}	[4]

The parameters γ_1, γ_2, and γ_3 are scaled to match [4]

Clonal Amplification

Clonal amplification is introduced with the addition of the term $\gamma_1 IT$ to λ,, which is the part of the equation that controls the production of new T-cells. This takes into account the cloning of healthy T-cells when healthy T-cells interact with infected T-cells. This is very similar to the term in the basic model βVT where the creation of infected T-cells is proportional to interaction with T-cells with a coefficient of infection. This is an important addition because one of the tell-tale signs of an infection is a large increase in the white blood cell count which will affect the population of healthy T-Cells and in turn, the rest of the populations. This clonal amplification is carried into the rest of the populations.

Logistic Growth

Logistic growth is introduced with the addition of $(1-T/K)$ multiplied by $(\lambda+\gamma_1 IT)$ which was added with the clonal amplification. This is an important addition because without it as $t\to\infty$ the population of T-cells could also go to infinity which as we know, is impossible in the body. This allows for a more grounded and accurate model to real life.

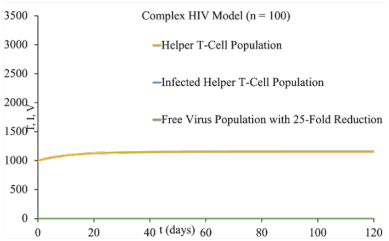
This model has a lower T-cell equilibrium than the first model due to the addition of a carrying capacity.

Second Model Behavior

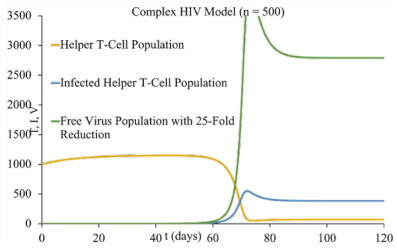
The points (1153, 0, 0) is an equilibrium for all n. We suspect this is the only positive equilibrium n=100. There is a second equilibrium (71, 385, 69791) for n=500. The Jacobian is

$$\begin{bmatrix} -\frac{\lambda}{k} + \gamma_1 I - \frac{2\gamma_1 IT}{k} - \delta_1 - \beta V & \gamma_1 T - \frac{\gamma_1 T^2}{k} & -\beta T \\ \beta V - \gamma_2 I & -\delta_2 - \gamma_2 T & \beta T \\ -\gamma_3 V - \beta V & n & -c - \gamma_3 T - \beta T \end{bmatrix}$$

For n=100 the eigenvalues of (1153, 0, 0) are −0.087, -8.578, and -1.008. All eigenvalues are negative. The equilibrium is a nodal sink and is stable for its long-term behavior.



For n=500, (1153, 0, 0) is a saddle because the eigenvalues a −0.087, 0.25, and -9.83. The equilibrium (71, 385, 69791) is a nodal sink because the eigenvalues are -3.493, -0.687, -0.3 Solutions tend toward this stable equilibrium.



Conclusions

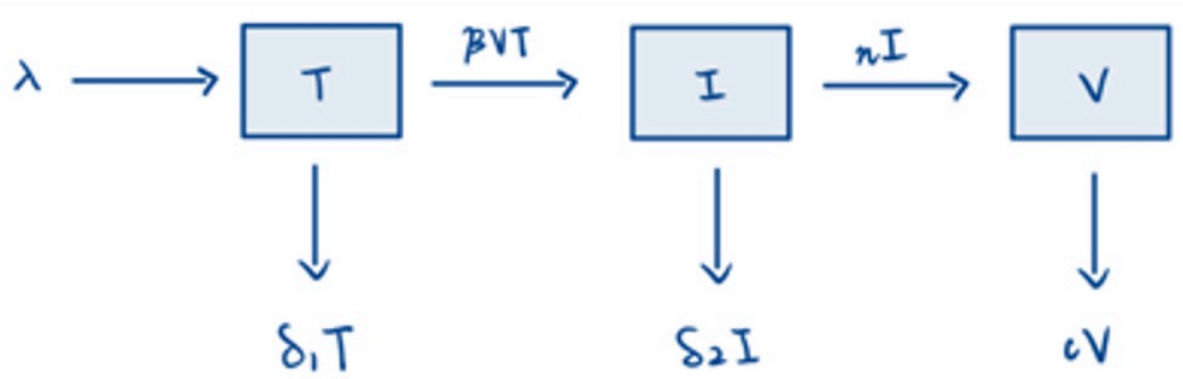
Both models had a change in stability for the first equilibriu as n varies . That equilibrium shifted from unstable to stable n=4.8 in the first model. In the second model that equilibriu shifted from stable to unstable when n is between 412-413. When n is below the critical value, the virus population doe not grow and cells do not become infected.

The virus in the second equilibrium increased as we increas n. When n is above the critical value, the virus equilibrium increases significantly due to the increased bursting of virus after an infected T-cell dies.

$$\frac{dT}{dt} = \lambda - \delta_1 T - \beta VT$$

$$\frac{dI}{dt} = \beta VT - \delta_2 I$$

$$\frac{dV}{dt} = nI - cV$$



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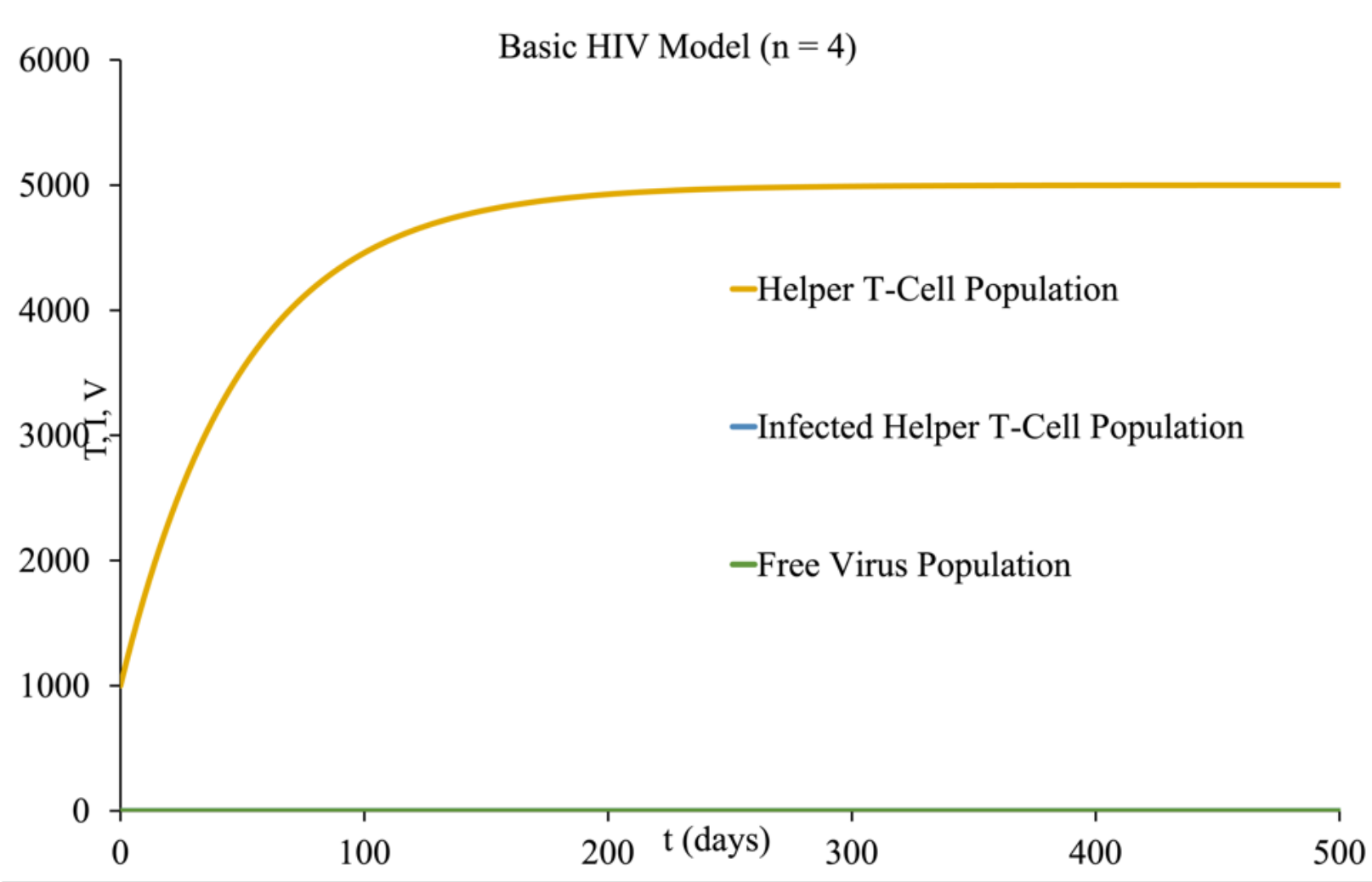
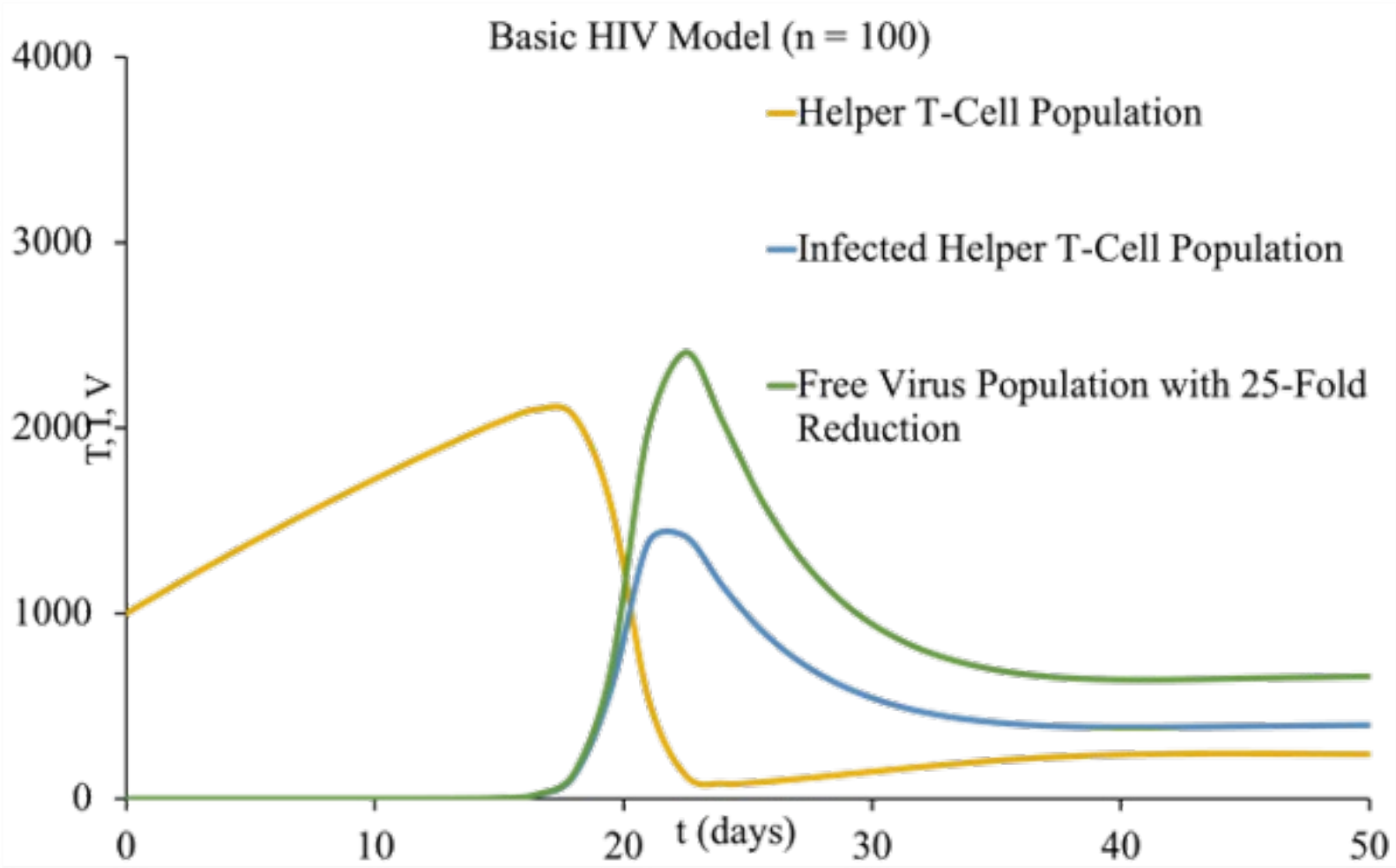


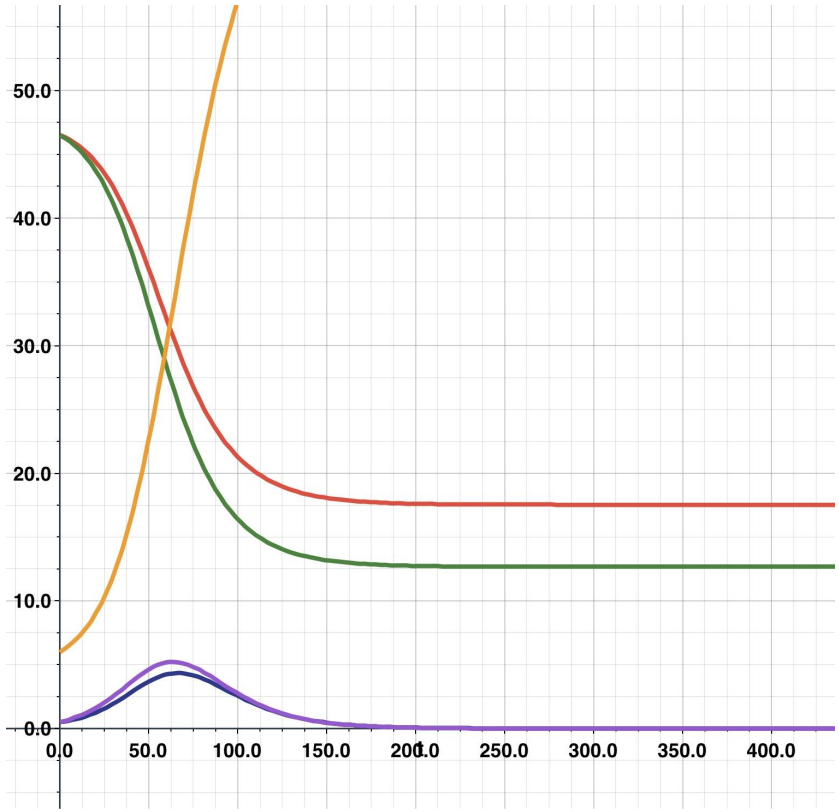
For n=100, (5000,0,0) is a saddle with eigenvalues -0.02, 2.31, and -4.95. The equilibrium (240, 396.7, 16527.8) is a spiral sink with eigenvalues are $-2.68, -0.189 \pm 0.223i$. The virus population grows and solutions tend toward the second equilibrium.



Masked and Unmasked SIR Model

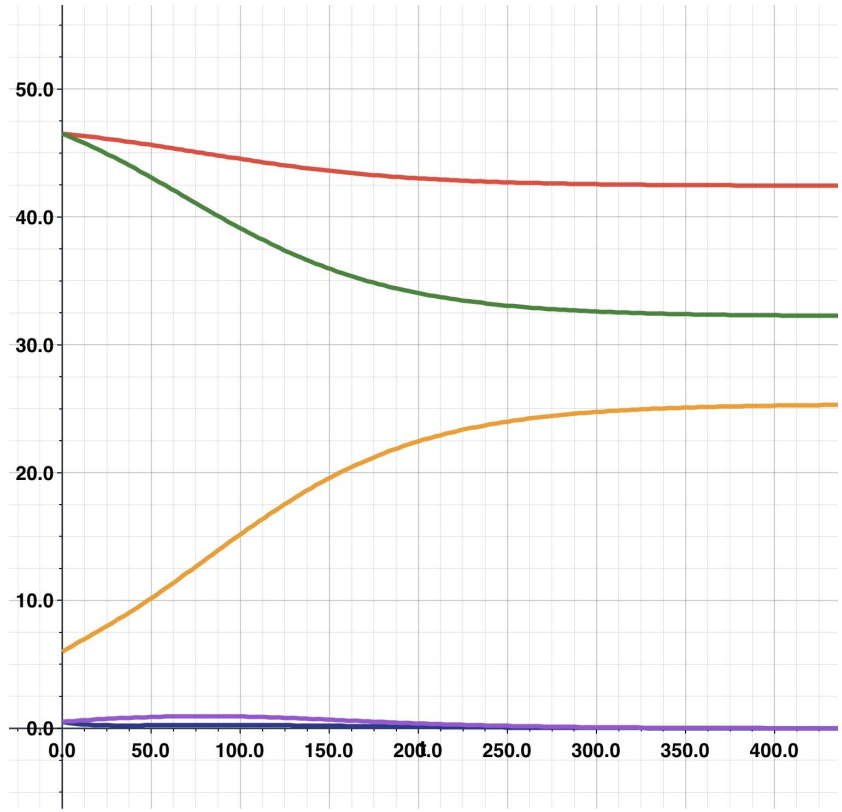
dS_M/dt	$= -a(1-b)^2 S_M I_M - a(1-b) S_M I_U$	
dS_U/dt	$= -a(1-b) S_U I_M - a S_U I_U$	
dI_M/dt	$= a(1-b)^2 S_M I_M + a(1-b) S_M I_U - c I_M$	
dI_U/dt	$= a(1-b) S_U I_M + a S_U I_U - c I_U$	
dR/dt	$= c(I_M + I_U)$	

Analysis of Varying Effectiveness



Time (days)

25% Mask Effectiveness



Time (days)

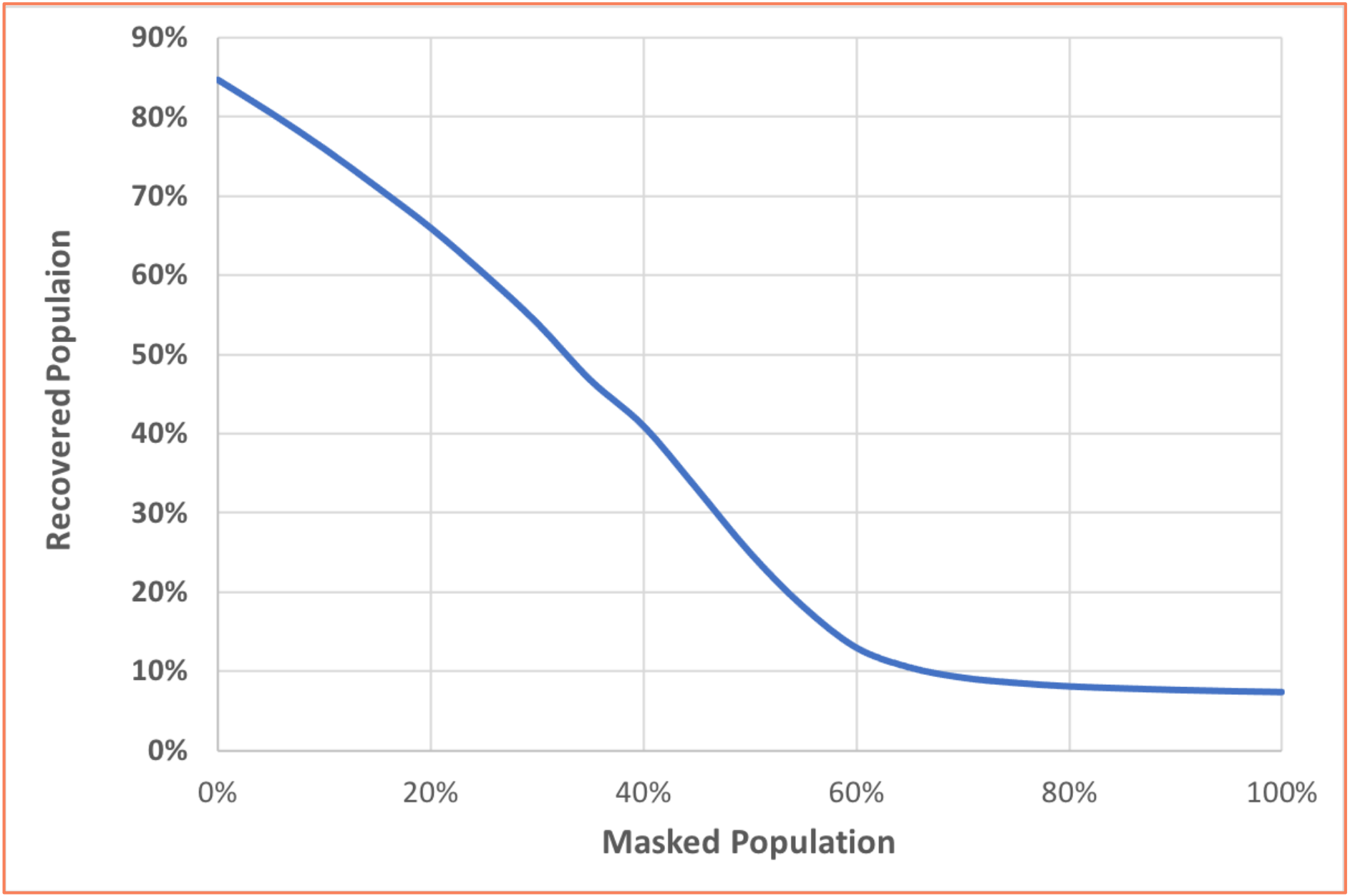
75% Mask Effectiveness

Red = S_M
Green = S_U
Blue = I_M
Purple = I_U
Yellow = R

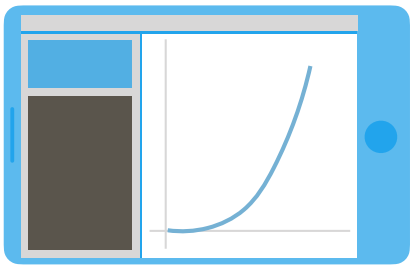
Masked 50%
Unmasked 50%

Key observation: Wearing masks reduces infections in both the masked and unmasked populations.

% Recovered vs % Masked Population

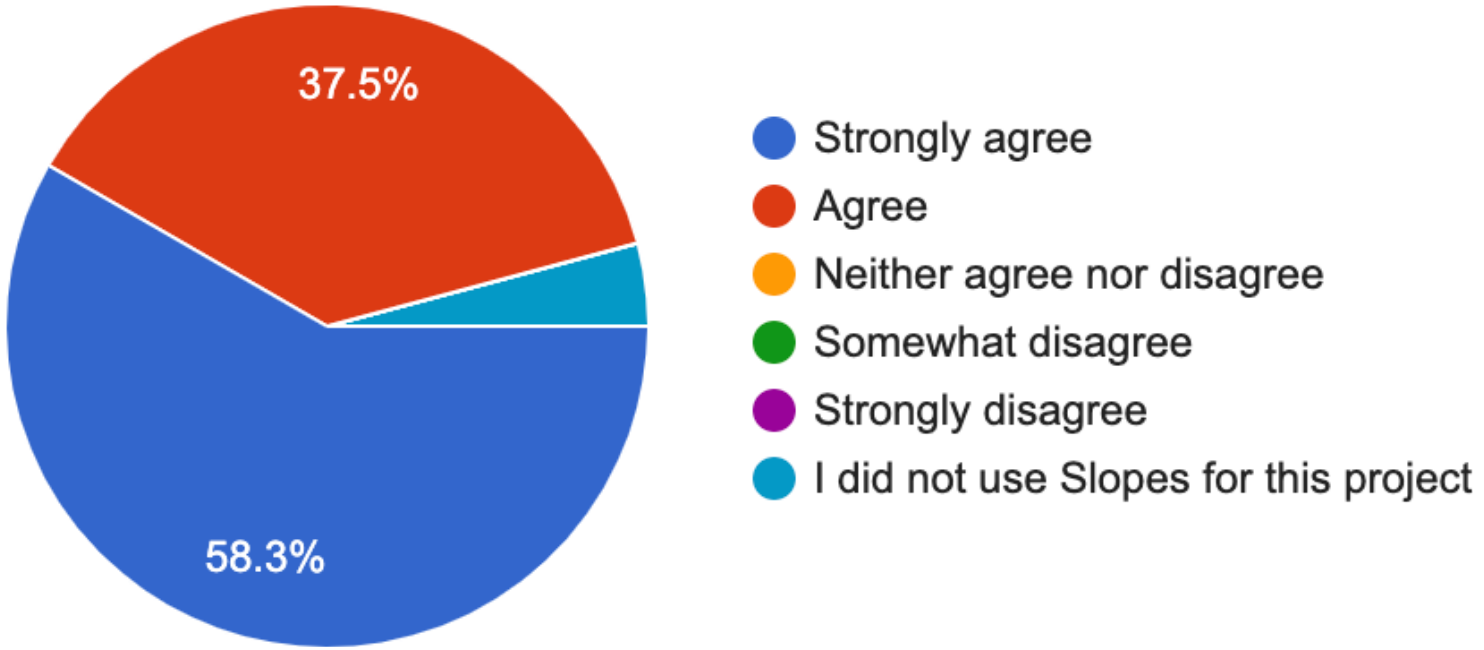


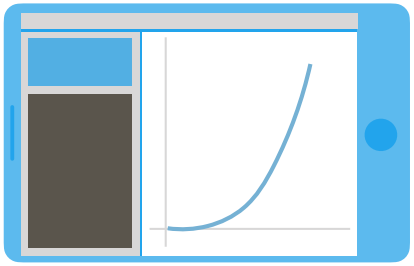
Mask effectiveness = 0.75



Student Feedback

To what extent do you agree with the following statement: “I feel that using Slopes increased my understanding of the mathematical models in my project.”

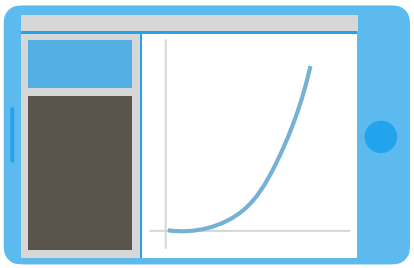




Student Feedback

“It's good just because visualizing helps a lot to be able to understand, especially when you get to higher levels of math and things get kind of hard to understand sometimes.”

“I really love how interactive it is …You can move it around and manipulate it. I like being able to click to see, okay, what does the solution with this initial condition look like?”



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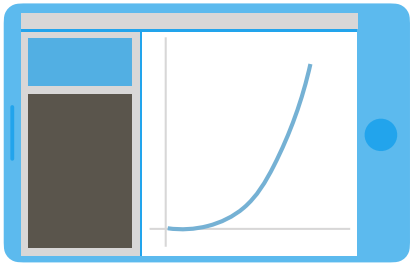
* Comp Sci: Stan Warford



Questions?

Check out the apps at

http://www.slopesapp.com

http://www.wavespdeapp.com