The role of growth models in oncolytic virus therapy

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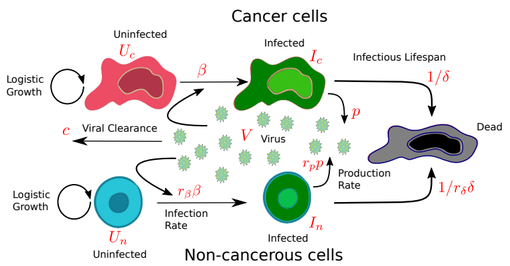
Background

- Cancer is a leading cause of death worldwide causing around one in every six deaths.
- Most standard treatments have serious side effects, so new treatments are being studied.
- One such treatment is the use of oncolytic (cancer-killing) viruses.
- Mathematical models of cancer cells can be used by researchers to study the use of oncolytic viruses to treat tumors, however, there are several different models that describe how cancer cells grow.
- We study how the choice of a particular model affects the predicted outcome of treatment.

Mathematical model



- In this model, both cancerous (U_c) and non-cancerous (U_n) replicate.
- Both types of cells can be infected by virus (V), but at different rates (β or $r_\beta\beta$).
- Once infected (I_c and I_n), both types of cells produce a virus, yet again at different rates (p and $r_p p$).
- Infected cells eventually die at different rates based primarily on the cell type (δ and $r_\delta\delta$).
- Lastly, the virus is cleared from the system at a clearance rate (c).

$$\begin{aligned}
\frac{\mathrm{d}U_c}{\mathrm{d}t} &= \lambda U_c\left(1-\frac{U_c+I_c}{K}\right)-\beta U_c V\\
\frac{\mathrm{d}I_c}{\mathrm{d}t} &= \beta U_c V-\delta I_c\\
\frac{\mathrm{d}U_n}{\mathrm{d}t} &= r_\lambda\lambda U_n\left(1-\frac{U_n+I_n}{r_K K}\right)-r_\beta\beta U_n V\\
\frac{\mathrm{d}I_n}{\mathrm{d}t} &= r_\beta\beta U_n V-r_\delta\delta I_n\\
\frac{\mathrm{d}V}{\mathrm{d}t} &= pI_c+r_p pI_n-cV.
\end{aligned}$$

Our goal is to find parameter combinations that cure the cancer without killing all the noncancerous cells.

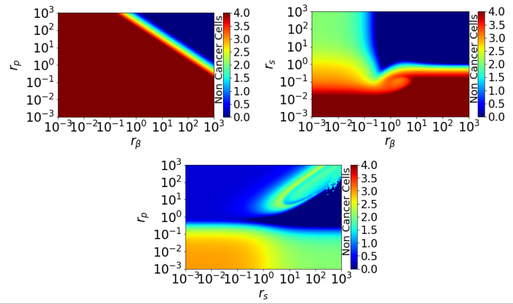
Methods

- We used Python's `odeint` to simulate the system of ordinary differential equations.
- We assumed that the virus was selective for cancer cells based on differences in β, p, and δ.
- We assumed that in the absence of noncancerous cells, the virus cures the cancer
- We found the number of noncancerous cells after 100 days.
- We substituted different growth models to see if there were any differences in the predicted outcomes.

Exponential

The exponential model assumes that all cells divide regularly,

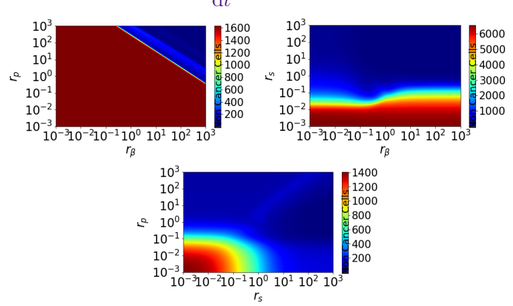
$$\frac{\mathrm{d}N}{\mathrm{d}t}=aN.$$



Mendelsohn

The Mendelsohn model assumes that some cells divide regularly while others are in a dormant state,

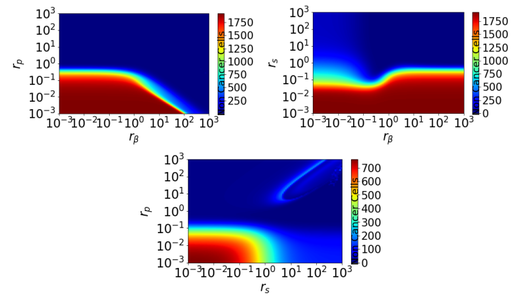
$$\frac{\mathrm{d}N}{\mathrm{d}t}=aN^b.$$



Logistic

The logistic model assumes that all cells regularly divide until resources such as space or nutrients become limited,

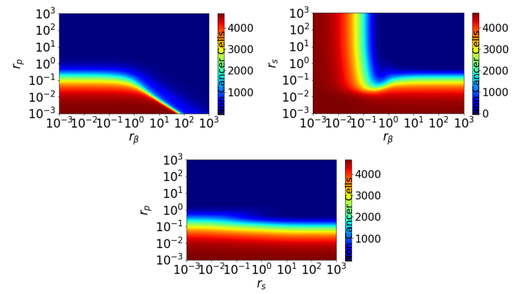
$$\frac{\mathrm{d}N}{\mathrm{d}t}=aN\left(1-\frac{N}{b}\right).$$



Linear

The linear model assumes that the number of new cells added remains constant at all times,

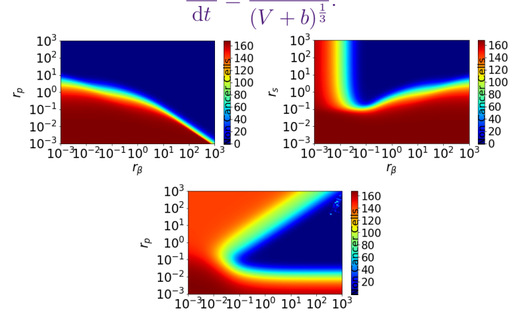
$$\frac{\mathrm{d}N}{\mathrm{d}t}=\frac{aV}{V+b}.$$



Surface

The surface model assumes that only the cells on the surface of a spherical tumor divide,

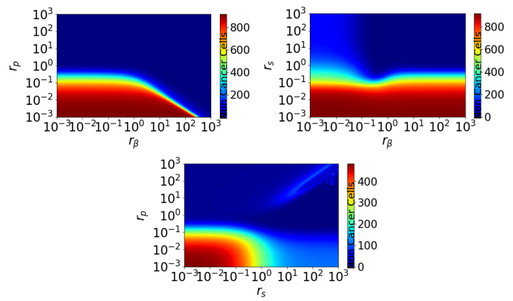
$$\frac{\mathrm{d}N}{\mathrm{d}t}=\frac{aV}{(V+b)^{\frac{1}{3}}}.$$



Gompertz

The Gompertz model assumes that cells are less likely to divide as they age,

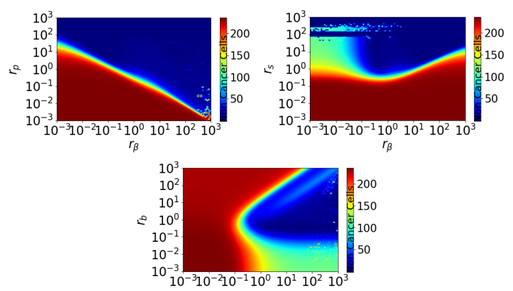
$$\frac{\mathrm{d}N}{\mathrm{d}t}=aN\ln\left(\frac{b}{V+c}\right).$$



Bertalanffy

The Bertalanffy model assumes that cells near the surface of a spherical tumor divide and cells in the interior die,

$$\frac{\mathrm{d}N}{\mathrm{d}t}=aN^{\frac{2}{3}}-bN.$$



Conclusions

- The choice of growth model changes the number of noncancerous cells at the end of 100 days, although there are some parameter regions that leave noncancerous cells unharmed for all models.

Future Work

- Stochastic simulations that take into account the fact that cells and virus are discrete objects will provide more realistic predictions.
- The model can be extended to include combination therapy.