Remodeling oncolytic virotherapy

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Abstract

some text

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1 Introduction

Viruses and cancer are both considered to be very destructive and harmful. But what if one of these could be used to combat the other? Viruses infect cells. These cells do not have to be healthy ones. By introduction of specific viruses into tumor affected tissue, the tumor may be repressed and eventually entirely eliminated. The field known as oncolytic virotherapy is still developing. There's still many uncertainties, but also possibilities. This paper aims to reproduce and possibly revise another paper published in the journal of theoretical biology. The paper demonstrated extensive modelling relevant to exploring the effects of varying amounts of normal and tumor cells.

Oncolytic virotherapy has a lot of potential. With that comes many things to consider. Before diving deeper and challenging some of these considerations in more mathematical detail, let's ask some general important questions. What is the desired balance of infection? Viruses used in these treatments don't exclusively infect tumor cells. This could either be beneficial or a hindrance. At which amount of infection does one group start to suffer? And what are the ideal ratios when it comes to tumor to normal cell infection? As the amount of tumor cells declines, it becomes harder for the virus in the system to find and infect tumor cells before the immune system eliminates the virus completely. This could result in stray tumor cells being left behind, only delaying the growth until it propagates significantly again. This is also only addressing the use of viruses which lyses the tumor cells. Some viral infections may cause the cells to be more susceptible to other forms of treatment, such as chemotherapy. This brings in a whole other amount of variables to consider.

In any case, the immune response is of great importance. The immune response may vary from person to person and tissue to tissue. Whether the person had been exposed to a virus before, or the immune system engages an unknown pathogen mediates different responses too. It's important to be aware of those factors in treatment. Time is of the essence in all instances of virotherapy. It usually takes 5 to 7 days for the immune response to completely halt production rate of the virus. As mentioned earlier, it's important that the treatment, in the case of the lysation approach, destroys all of the tumor cells. Having to accomplish this in the time frame of only 5 to 7 days is quite a feat. This swift approach is referred to as one shot virotherapy. This is why it's so important for the initial values to be right, further solidifying the significance of researching and being absolutely certain about the relevant mathematical models, due to there only being one shot at the initial treatment with a specific virus.

2 Methods

Since the ambition of this paper is to reproduce the results found in Okamoto et al. [2014], our objectives are the same as described in that article:
"We model the dynamics of an oncolytic virus within the context of its interactions with the populations of tumor cells and normal cells. We integrate key ecological processes, such as the growth of normal cells and tumor cells and an adaptive immune response, with an explicit treatment of how viruses differentially exploit the two cell types."

2.1 Variables

Variable	Explanation	Unit
t	Time	hr^{-1}
H	Normal (Healthy) cell type	-
C	Tumour (Cancerous) cell type	-
H_S	Normal cell that is susceptible	-
H_I	Normal cell that is infected	-
C_S	Tumour cell that is susceptible	-
C_I	Tumour cell that is infected	-
K_H	Carrying capacity of normal cells	cells
K_C	Carrying capacity of tumour cells	cells
β_H	Infection rate of normal cells	viruses $cell^{-1}$ hr^{-1}
β_C	Infection rate of tumour cells	viruses $cell^{-1}$ hr^{-1}
λ_H	Lysing rate of normal cells	$cell^{-1}$ hr^{-1}
λ_C	Lysing rate of tumour cells	$cell^{-1}$ hr^{-1}
b_H	Burst size of normal cells	-
b_C	Burst size of tumour cells	-
r_H	Per-capita growth rate of normal cells	hr^{-1}
r_C	Per-capita growth rate of tumour cells	hr^{-1}
ω	Rate of neutralisation by innate immune response	$virus^{-1}$ hr^{-1}
v	Virions	-

Table 1: All variables and their respective explanations

2.2 Equations

This model is a direct replica of the one presented in Okamoto et al. [2014], since that is the process we are trying to replicate. The model seeks to incorporate the effects of an oncolytic virus on the growth and maintenance of normal cells along with it's effects on tumour cells, thereby extending the work of Wu et al. [2004] which only aims to formulate the latter: characterising an oncolytic virus infecting a population of tumour cells. Wu et al. [2004] is itself an extension of previous models of virus-host interactions, further references to which van be found in Okamoto et al. [2014].

We start out with two separate cell populations both of which are divided into two sub populations: tumour cells (C) and normal cells (H), each having a susceptible (C_S & H_S) and an infected (C_I & H_I) sub population. All other parameter definitions can be found in table 1

2.2.1 Normal susceptible cell count

This first differential equation models the change in the number of normal cells that are still susceptible to an infection by virus particles.

$$\frac{dH_S}{dt} = r_H H_S(1 - \frac{(H_S + H_I)}{K_H}) - H_S \beta_H v \tag{1}$$

2.2.2 Tumour susceptible cell count

This second differential equation is very similar to equation (1), since it represents the same change in susceptible cells except it models tumour cells instead of normal ones.

$$\frac{dC_S}{dt} = r_C C_S(1 - \frac{(C_S + C_I)}{K_C}) - C_S \beta_C v \tag{2}$$

2.2.3 Normal infected cell count

This third differential equation is again similar to equation (1) in that it models normal cells, but in this case we're looking at the change in infected cells instead of susceptible ones.

$$\frac{dH_I}{dt} = \beta_H H_S v - \lambda_H H_I \tag{3}$$

2.2.4 Tumour infected cell count

This fourth differential equation relates to equation (3) in the same way as equation (2) relates to equation (1): This equation again models infected cells, but regards tumour cells instead of the normal cells found in equation (3)

$$\frac{dC_I}{dt} = \beta_C C_S v - \lambda_C C_I \tag{4}$$

2.2.5 Virion count

This fifth and final differential equation is a bit different from all of the other ones that came before, since it models virions instead of cell populations.

$$\frac{dv}{dt} = b_C \lambda_C C_I + b_H b_C \lambda_H H_I - \beta_H H_S v - \beta_C C_S - \omega v \tag{5}$$

3 Results

4 Discussion

5 Conclusion

6 Bibliography

References

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