Remodeling oncolytic virotherapy

Orfeas Gkourlias & Dennis Wiersma

2022-06-17

Contents

1 Abstract **2**

2 Introduction **3**

3 Methods **4**
3.1 Variable explanations 4
3.2 Formulas 4
3.3 Parameter definitions 4

4 Results **5**

5 Discussion **6**

6 Conclusion **7**

1 Abstract

[1]

2 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 eleminated. 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 exstensive 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 hinderance. 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 adressing the use of viruses which lysates 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 intial values to be right, further solidying 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.

3 Methods

3.1 Variable explanations

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

3.2 Formulas

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

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

$$\frac{dC_I}{dt} = \beta_C C_S v - \lambda_C C_I \tag{3}$$

$$\frac{dH_I}{dt} = \beta_H H_S v - \lambda_H H_I \tag{4}$$

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

Referentie naar eq1: (1)

3.3 Parameter definitions

4 Results

5 Discussion

6 Conclusion

Bibliography

[1] jlmelville. *Google's Turbo colormap as an R palette*. 2019. URL: https://gist.github.com/jlmelville/be981e2f36485d8ef9616aef60fd52ab.