Effectiveness of antibodies in syncytia-forming viruses

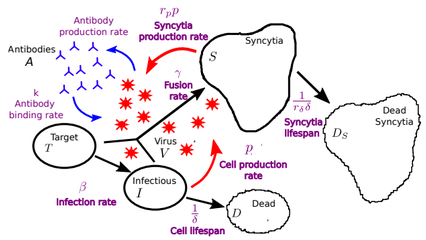
Isabelle Beach and Hana M. Dobrovolny

Department of Physics and Astronomy, Texas Christian University, Fort Worth, USA

Background

- Viral infections result from viruses invading normal cells to produce more virus, resulting in damage or death of the cells.
- Sometimes, the virus will fuse cells together to create multi-nucleated cells called syncytia. Not only does it give the virus more resources, it also provides a larger space for the virus to hide from antibodies in the extracellular environment.
- Syncytia formation is linked to enhanced progression of variants of viruses, indicating that formation of syncytia may aid in a virus's evasion of immune factors.[1]
- In this study, the effects of syncytia formation on cell characteristics were explored in order to determine why a virus would engage in syncytia formation.

Mathematical model



We examine an extension of the syncytia formation model proposed by Jessie and Dobrovolny (JTB, 2021),

$$\begin{aligned}
\frac{\mathrm{d}T}{\mathrm{d}t} &= -\beta TV - \gamma T(I+S)\\
\frac{\mathrm{d}I}{\mathrm{d}t} &= \beta TV - \gamma I(T+2I+S) - \delta I\\
\frac{\mathrm{d}S}{\mathrm{d}t} &= \gamma T(2I+S) + \gamma I(2I+S) - r_\delta \delta S\\
\frac{\mathrm{d}V}{\mathrm{d}t} &= pI + r_p pS - cV - k_V AV\\
\frac{\mathrm{d}A}{\mathrm{d}t} &= \lambda V - \delta_A A - k_A AV.
\end{aligned}$$

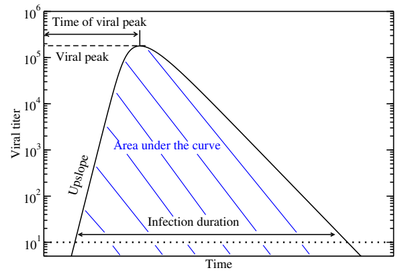
- Virus, V, infects healthy target cells, T, at a rate β.
- Infected cells, I, produce virus at rate p or fuse with other cells to create syncytia, S, at rate γ. Infected cells die at rate δ.
- Syncytia produce virus at rate $r_p p$ and die at rate $r_\delta \delta$.
- Virus is cleared from the system at a rate of c.
- Antibodies, A, are produced at rate λ, proportional to V, and remove free virus at rate k_v. They are naturally cleared at rate δ_A or bind with the virus at rate k_A.

Measurements

We use parameters that simulate an infection with respiratory syncytial virus (Gonzalez-Parra et al. JTB (2018)).

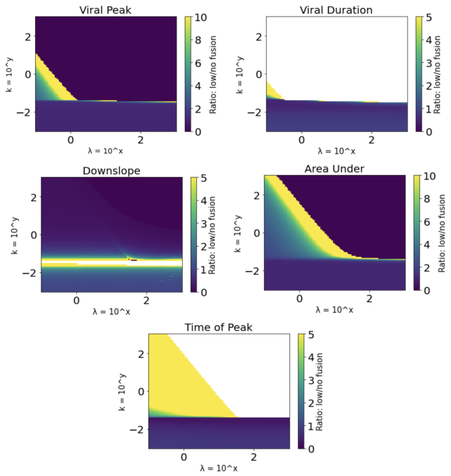
Parameter	Value
p	4.66×10^6 RNA/mL $\cdot$ h^{-1}
β	2.04×10^{-8} (RNA/mL)$^{-1} \cdot$ h^{-1}
c	0.0763 /h
δ	0.0735 /h
γ	[0.01,1 /h]
r_δ	[1×10^{-3}, 1×10^3]
r_p	[1×10^{-3}, 1×10^3]

We used the following measurements to assess changes in the viral dynamics.



Low/no syncytia formation

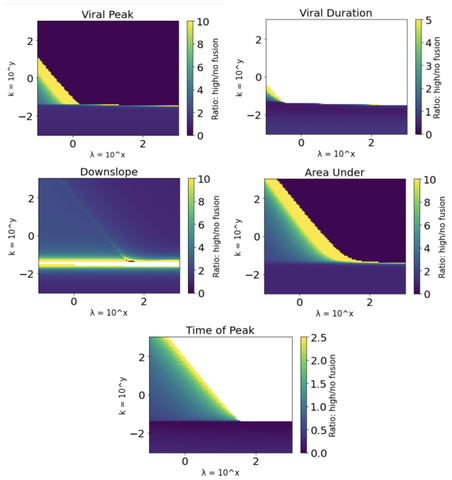
We examine the ratio of viral characteristics when the syncytia formation rate (SFR) is low ($\gamma = 0.1$) to no syncytia formation ($\gamma = 0$).



When SFR is low, the viral peak and duration are only altered/increased in small ranges: low antibody production (λ) and mid/low antibody binding (k). The decay rate (downslope) only peaks when k is in the lower range (across all values of λ). AUC and time of peak increases slightly as λ increases and k decreases.

High/no syncytia formation

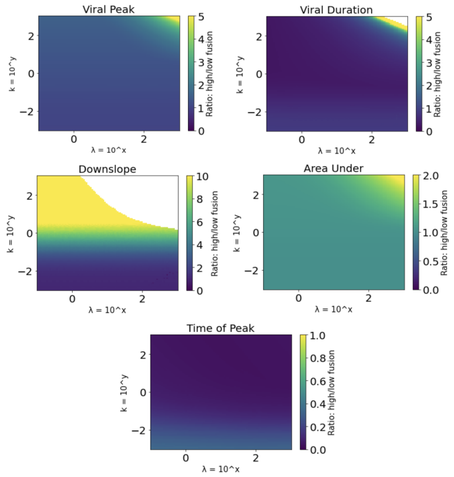
The high/no graphs display the ratio of viral characteristics when SFR is high ($\gamma = 1$) to no syncytia formation ($\gamma = 0$).



High SFR only impacts the viral peak and duration at low antibody production and low to mid ranges of binding rate. AUC can be greatly increased as λ increases while k decreases. Time of peak is slightly altered as λ increases and k decreases. Decay rate (downslope) peaks when k is lower through all values of λ.

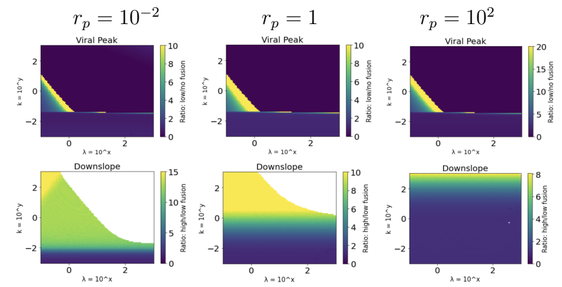
High/low syncytia formation rate

The high/low graphs display the ratio of viral characteristics when SFR is high to low.



High SFR does not change the viral peak, duration, AUC, or time of peak, except when antibody production and binding rates are high. The decay rate is higher for low syncytia formation when λ is high and k is low.

Effect of syncytia production rate



Increasing the syncytia production rate (r_p) can almost double the height of the viral peak, even at a low fusion rate. It can also change the parameter range - antibody production (λ) and antibody-viral binding rate (k) and speed at which the virus decays. As the syncytia production rate increases, the graphs seem to show a move from fastest decay at low λ and high k to all λ and high k. r_p seems to have an inverse relationship with decay rate, as the ratio of decay in high fusion to low fusion declines as r_p increases.

Conclusions

- Syncytia formation can have a protective effect against antibodies for some values of λ and k.
- Syncytia formation rates can greatly change the characteristics of viral titer by up to factors of 10.
- The biggest difference that syncytia formation rate makes is in the decay rate of the virus, since the syncytia protect the virus from antibodies.
- Changes in the syncytia production rate can also change

Future directions

- Examining the effect of syncytia lifespan (r_δ) on viral characteristics like viral peak, decay rate, or infection duration can be done in future studies.
- Sensitivity analysis can be run to determine which parameters have the strongest effect on the various viral characteristics.

SciCom Let's Talk Science

This study looked at the effects of a virus fusing (healthy) cells together on the virus's longevity, strength, and decay. Fusion allows the virus to avoid antibodies, potentially lengthening the infection.