Treatment of Viral Coinfections

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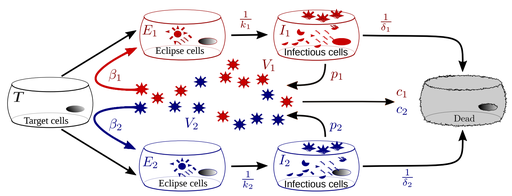
Abstract

Previous reports show that it is not uncommon for patients to have two viruses at the same time. At the current time, we do not know how to treat co-infections. In order to test the effects of having these concurrent infections, we simulate the two infections using a mathematical model. We use our model to simulate influenza A virus (IAV) coinfected with respiratory syncytial virus (RSV) and parainfluenza virus (PIV) coinfected with human rhinovirus (hRV). Using the model, we can estimate the co-duration of the viruses, the individual duration, and the peak virus amount for both viruses, both with and without drug treatment of the infections to figure out the best treatment strategies for co-infections. We find that sometimes treating one infection can lead to the lengthening of the other infection.

Coinfection Model



The two viruses compete for the target cells. They both continue to follow the infection cycle until they both die. Using models of different infections, we can simulate this process with drugs added.

Coinfection Equations

$$\text{Target cells}: \quad \frac{T}{t} = -\beta_1 T V_1 - \beta_2 T V_2$$

$$\text{Eclipse cells}: \quad \frac{E_1}{t} = \beta_1 T V_1 - k_1 E_1 \qquad \frac{E_2}{t} = \beta_2 T V_2 - k_2 E_2$$

$$\text{Infected cells}: \quad \frac{I_1}{t} = k_1 E_1 - \delta_1 I_1 \qquad \frac{I_2}{t} = k_2 E_2 - \delta_2 I_2$$

$$\text{Virus}: \quad \frac{V_1}{t} = p_1 I_1 - c_1 V_1 \qquad \frac{V_2}{t} = p_2 I_2 - c_2 V_2.$$

In the model, target cells are infected by either virus at rate β_i. The cells then enter the eclipse phase (E_i) where the virus is replicating inside the cells, but not yet producing virus. The cells move from the eclipse phase to the infectious phase (I_i) at rate k_i and die at rate δ_i. Virus is produced at rate p_i by infectious cells and virus is cleared at rate c_i.

Modeling Drug Effect

We model the effect of a drug using the drug efficacy, a number between 0 and 1, that is related to the drug concentration,

$$\varepsilon = \frac{\varepsilon_{\max} D}{D + \mathrm{IC}_{50}}$$

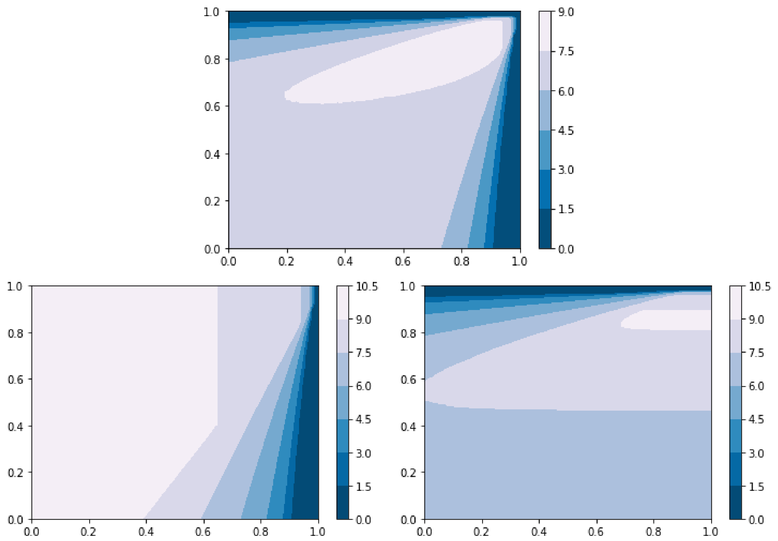
where D is the drug concentration, $\varepsilon_{\max}$ is the maximum effect of the drug, and IC_{50} is the concentration at which half the maximum effect is achieved. We model a drug that blocks infection by multiplying β by $(1-\varepsilon)$. We model a drug that blocks viral release by multiplying p by $(1-\varepsilon)$.

Methods

- We study two different pairs of viruses.
- IAV and RSV are paired together because their growth rates are similar.
- PIV and hRV are paired together because PIV's growth rate is much slower than hRV.
- The affect of coinfection might vary drastically for the different pairs.
- The parameter values for all four viruses are taken from Pinky and Dobrovolny (2016) PloS One.

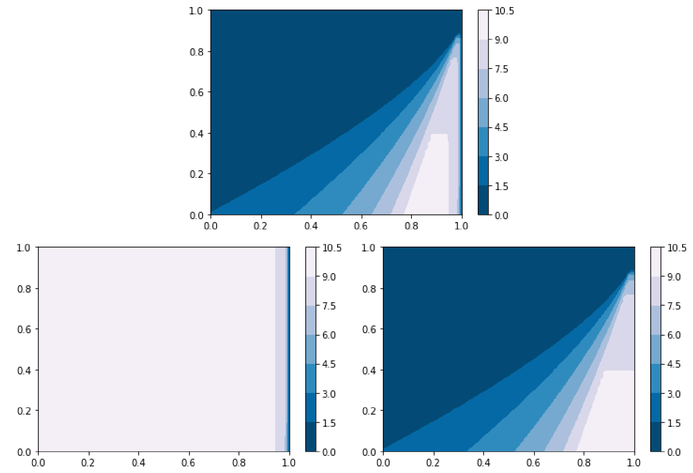
Similar Growth Rates

We applied drugs that block infection to both viruses, varying the efficacy from 0 (no drug) to 1 (fully blocking infection). The contour plots below show the effect of treatment on the coinfection duration (top) and the duration of infection of each virus individually (bottom).



Different Growth Rates

We used the same drugs on the two viruses with different growth rates. The top contour plot shows the effect of treatment on coinfection duration and the bottom plots show the effect on the duration of infection of each virus individually.



Conclusion

- For similar viruses near a drug efficacy of 0.8, for both viruses, the coinfection duration is at its longest.
- Unless we are certain efficacy is very high, treating these coinfections may lead to longer durations.
- Even with only one drug working on only a virus with an efficacy of 0.8, the co-infection is not much shorter.
- For viruses with different growth rates, drug treatment helps if the faster-growing virus is treated.

Overview

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The effects of coinfections are still relatively unknown. In order to further our understanding of coinfections, we analyzed how drugs and the infection rates of the viruses affect the coinfection. We used two pairs of viruses: IAV and RSV because of their similar infection rates, and PIV and hRV because they have very different infection rates. We found that treatment affects the two pairs of viruses differently, and might increase the coinfection duration if the viruses have similar growth rates.