Syncytia Virus Characteristics

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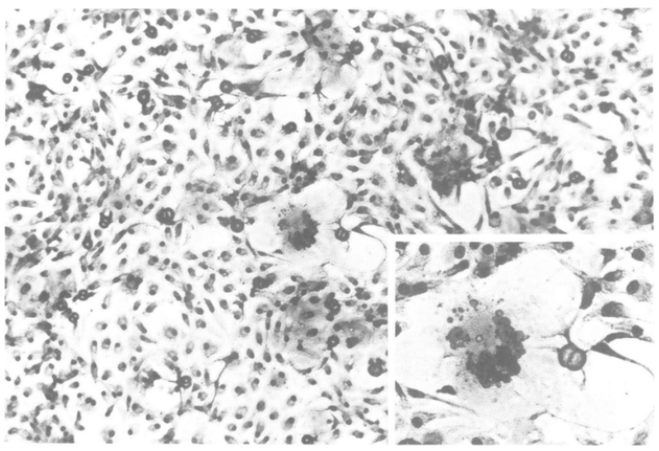
Background

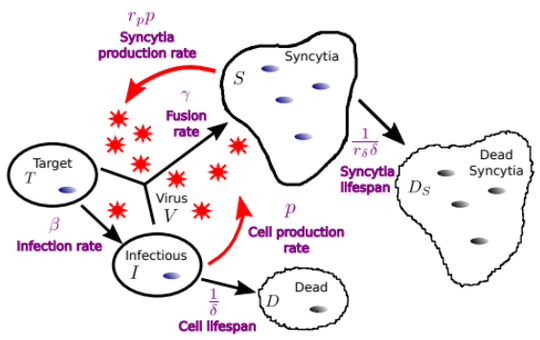
- Respiratory Syncytial Virus (RSV) is a common, contagious infection of the lungs and the respiratory tract
- RSV is characterized by the formation of syncytia — fusion of single cells into a large multinucleated cell
- Experimental limitations make it difficult to measure characteristics such as production and lifespan of the virus
- It is not clear how syncytia viral production and lifespan alter the course of RSV infection
- Mathematical modeling can help predict and measure syncytia viral characteristics

Syncytia



- Syncytia are multinuclear cells that have formed as a result of RSV
- Syncytia can produce virus just as a single nuclear infected cell, but the production rate is unknown
- Syncytia viral characteristics can vary from that of a uninuclear infected cell

Viral Characteristics



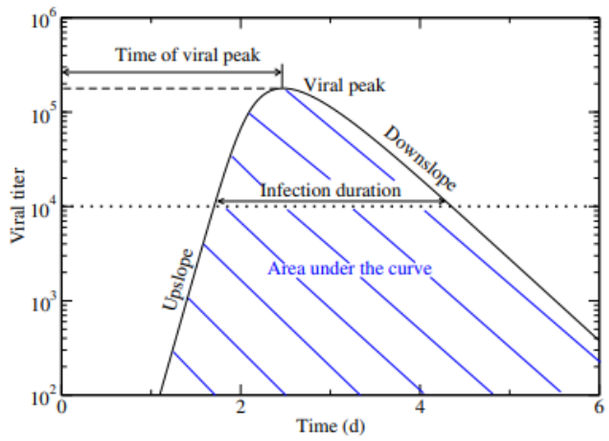
- A target cell can either become infected or fuse with an already infected cell into syncytia
- Infected cells and syncytia cells produce virus until they are dead
- The virus infects new target cells and the process starts over
- The infected cells and the syncytia cells have different viral production rates and lifespans

ODE model

$$
\begin{aligned}
\dot{T} &= -(\beta T V) - \gamma T(I+S) \\
\dot{I} &= (\beta T V) - \gamma I(I+S) - \delta I \\
\dot{D} &= \delta I \\
\dot{S} &= \gamma T(I+S) + \gamma I(I+S) - R_\delta \delta S \\
\dot{D}_s &= R_\delta \delta S \\
\dot{V} &= \rho I + R_\rho \rho(S) - cV
\end{aligned}
$$

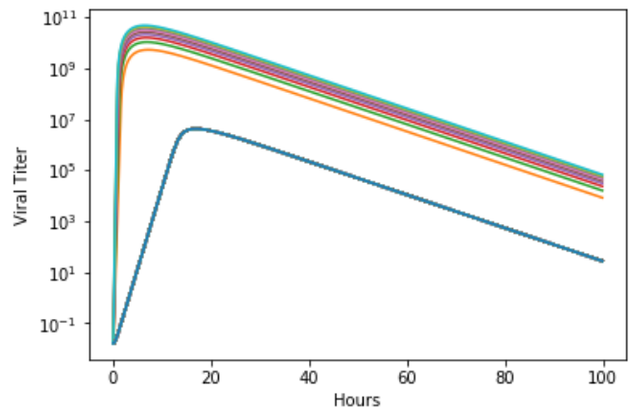
- T - Single nucleated target cells
- V - Virus
- I - Infected cells
- S - Syncytia
- c - Clearance rate
- β - The rate target cells become infected
- γ - The rate target cells fuse into syncytia
- ρ - The rate infected cells produce virus
- R_ρ - The ratio of syncytia cell and infected cell viral production rate
- δ - The average lifespan of infected cells
- R_δ - The ratio of syncytia cell and infected cell average lifespan

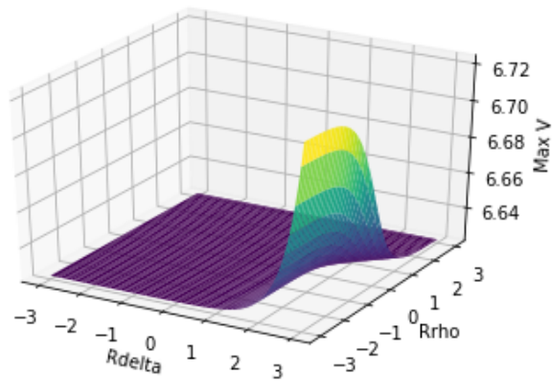
Viral Titer Curve



- The system of differential equations will produce a viral titer curve that will be used to assess the role of syncytia
- The peak viral load is the maximum amount of virus and is commonly used as an indicator of the transmissibility of an infection
- The time of viral peak is the time between the start of the infection and the peak of the virus
- The viral upslope is the exponential growth rate of the viral titer during the first day of infection
- The viral downslope is the exponential decay rate of the viral titer and is linked to both the lifespan of infectious cells and the clearance rate of virus
- The area under the curve (AUC) is often used to assess the severity of an infection
- The infection duration is defined as the duration of time the viral titer is over 10^4 and is indicative of how long an infected patient might experience symptoms

Model Simulations





- Changing values of syncytia lifespan and production rate affect viral titer characteristics, particularly the maximum viral load
- Changes in the syncytia fusion rate also affect viral titer characteristics
- Changes in other viral titer characteristics as a function of syncytia properties were minimal

Conclusions

- Just as predicted, the syncytia production rates and lifespans did have effects on the syncytia viral characteristics
- The varying syncytia lifespan and production rate had a direct correlation on the max viral load and could possibly be used to estimate relative syncytia lifespan and production rate.
- The varying syncytia formation rate had an effect on the range of the max and min viral load

Future directions

- Our next model should include the immune response of the host
- Probability and randomness should also be included in our next model
- Since RSV takes place in the respiratory tract where cells and virus are not well-mixed, models other than ODE models should be considered

Acknowledgements

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