Using a Mathematical Model to Compare Infection Parameters in Cotton Rats by Age

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Background

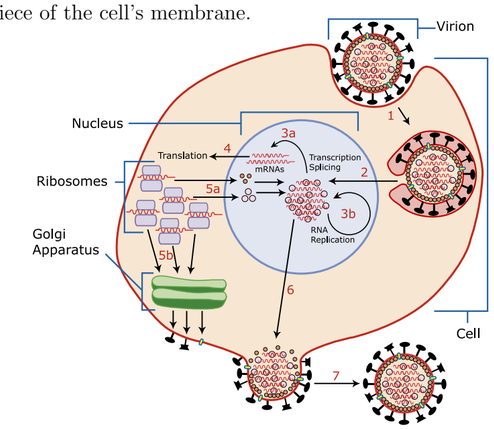
- Viral kinetics can be quantified using mathematical models of viral infections.
- Parameter values that describe different virus characteristics can be obtained by fitting experimental data to the model.
- These parameter values can then be used to quantify parts of the virus's life cycle.
- Immune system responses in both humans and rats vary in their susceptibility to diseases across different age groups.
- Comparing the different parameter values across across age groups yields insight into how RSV affects different age groups.

RSV

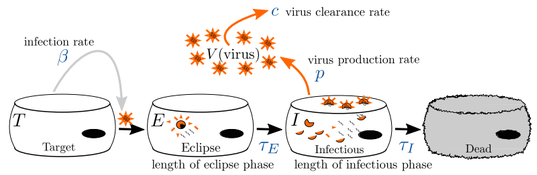
- Respiratory syncytial virus is a viral respiratory infection that has infected 100% of people by the time they are 2 years old.
- While often very mild in adults, it can be deadly in infants and the elderly.
- There is currently no vaccine and no treatment for RSV.
- Improving our understanding of disease dynamics will help develop appropriate treatment and vaccines.

Viral replication

Viruses enter cells by binding to receptors on the cell surface. Once inside the cell, they use the cell's replication machinery to make copies of their own RNA. Viral RNA collects near the surface and is packaged into new virions by stealing a piece of the cell's membrane.



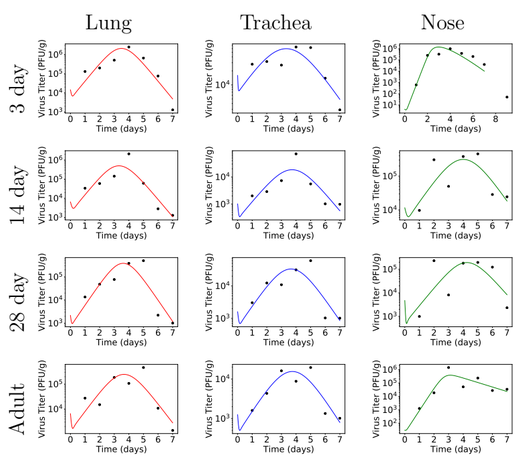
Mathematical model



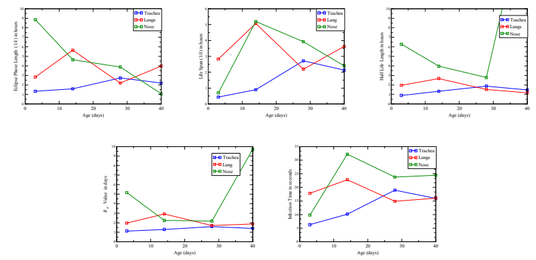
$$\begin{aligned}\dot{T} &= -\beta TV\\ \dot{E} &= \beta TV - kE\\ \dot{I} &= kE - \delta I\\ \dot{V} &= pI - cV\end{aligned}$$

- Target cells are infected with virus at rate β.
- Eclipse cells are infected, but not yet producing virus and transition to infectious at rate k.
- Infectious cells actively produce virus, and die at rate δ.
- Infectious cells produce virus at rate p.
- Virus is cleared at rate c.
- The infecting time $t_{\text{inf}} = \sqrt{2/p\beta}$ is the average time between release of virus and infection of the next cell.
- The basic reproductive number $R_0 = p\beta/c\delta$ is the average number of secondary infections from a single infected cell.
- Experimental data was taken from a previously published studies on RSV infection of cotton rats and ferrets.

Results: Cotton rats fits to data



Results: Cotton rat viral kinetics



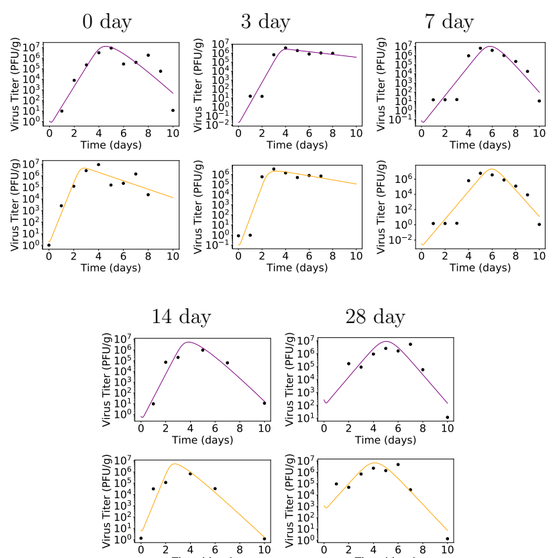
- Nose parameter values tend to be higher than either lung or trachea values.
- There are no clear consistent trends with age for any parameter.

Results: Cotton rat statistics

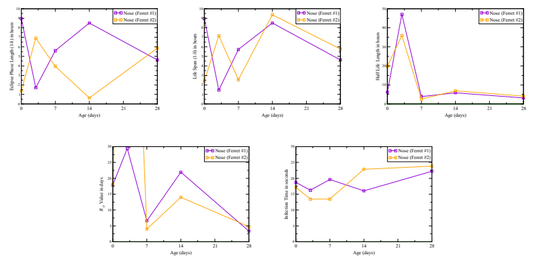
We use ANOVA to test for statistically significant difference between parameter values based on location or age.

Parameter	k	δ	c	R_0	t_{inf}
p-value (location)	0.256	0.569	0.536	0.571	0.573
p-value (age)	0.060	0.387	0.416	0.391	0.391

Results: Ferret fits to data



Results: Ferret viral kinetics



Both ferret nose half life values are similar.

Conclusions

- There do not seem to be clear trends in parameter variation with age.
- We have also not found any statistically significant differences in the parameters measured from different locations in the respiratory tract.

References

- G.A. Prince and D.D. Porter, (1976) Am. J. Pathol. 82(2):339–352
- G.A. Prince, A.B. Jenson, R.L. Horswood, E. Camargo, and R.M. Chanock, (1978) Am. J. Pathol. 93(3):771–791

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Respiratory syncytial virus (RSV) is an extremely common viral respiratory infection that currently has no vaccine or treatment. The changing immune system according to age is an obstacle to developing treatment as different age groups have different levels of susceptibility to RSV. One way to approach this problem is by using a mathematical model to quantify different viral values. After obtaining these values, it was found that there was no major trend across age or location. To see if this lack of a trend holds, this same method can be applied to calculate the viral values in a different species.