The effect of multipartite viruses on infection duration

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Background

- Some viruses consist of several separate strands of RNA or DNA, rather than a single long strand.
- Multipartite viruses package the individual RNA/DNA strands in separate viral particles, which are released from the infected cell.
- For a new cell to become infected, it must receive at least one copy of each strand of the virus.
- This process seems inefficient, as it requires multiple viral particles to infect a single host cell.

Single Particle Virus

We examine three types of models depicting virus infection:

$$\begin{aligned}\frac{dT}{dt} &= -\beta VT\\ \frac{dI}{dt} &= \beta VT - \delta I\\ \frac{dV}{dt} &= pI - cV.\end{aligned}$$

In this model, healthy target cells, T, are infected by virus, V, at rate β. Once infected, the target cells enter the infectious state, I, and produce virus at rate p. Virus is cleared from the system at rate c and infectious cells die after time $1/delta$.

Two Particle Virus

$$\begin{aligned}\frac{dT}{dt} &= -\beta_1 V_1 T - \beta_2 V_2 T + k_1 I_1 + k_2 I_2\\ \frac{dI_1}{dt} &= \beta_1 V_1 T - k_1 I_1 - \beta_2 V_2 I_1\\ \frac{dI_2}{dt} &= \beta_2 V_2 T - k_2 I_2 - \beta_1 V_1 I_2\\ \frac{dI}{dt} &= \beta_2 V_2 I_1 + \beta_1 V_1 I_2 - \delta I\\ \frac{dV_1}{dt} &= p_1 I - c_1 V_1\\ \frac{dV_2}{dt} &= p_2 I - c_2 V_2\end{aligned}$$

The two pieces of the viral genome are denoted by V_1 and V_2. They can each separately infect target cells, T, with their own rates β_1 and β_2. Once the viral pieces enter the target cells, we have partially infected cells I_1 and I_2 that can be further infected by the other piece of the viral genome. The fully infected virus, I, releases both particles. Partially infected cells can also revert back to uninfected cells at rates k_1 and k_2.

Three Particle Virus

$$\begin{aligned}\frac{dT}{dt} &= -\beta_1 V_1 T - \beta_2 V_2 T - \beta_3 V_3 T + k_1 I_1 + k_2 I_2 + k_3 I_3\\ \frac{dI_1}{dt} &= \beta_1 V_1 T - \beta_2 V_2 I_1 - \beta_3 V_3 I_1 - k_1 I_1 + k_2 I_{12} + k_3 I_{13}\\ \frac{dI_2}{dt} &= \beta_2 V_2 T - \beta_1 V_1 I_2 - \beta_3 V_3 I_2 - k_2 I_2 + k_1 I_{12} + k_3 I_{23}\\ \frac{dI_3}{dt} &= \beta_3 V_3 T - \beta_1 V_1 I_3 - \beta_2 V_2 I_2 - k_3 I_3 + k_1 I_{13} + k_2 I_{23}\\ \frac{dI_{12}}{dt} &= \beta_2 V_2 I_1 + \beta_1 V_1 I_2 - \beta_3 V_3 I_{12} - k_2 I_{12} - k_1 I_{12}\\ \frac{dI_{13}}{dt} &= \beta_1 V_1 I_3 + \beta_3 V_3 I_1 - \beta_2 V_2 I_{13} - k_1 I_{13} - k_3 I_{13}\\ \frac{dI_{23}}{dt} &= \beta_2 V_2 I_3 + \beta_3 V_3 I_2 - \beta_1 V_1 I_{23} - k_3 I_{23} - k_2 I_{23}\\ \frac{dI}{dt} &= \beta_3 V_3 I_{12} + \beta_2 V_2 I_{13} + \beta_1 V_1 I_{23} - \delta I\\ \frac{dV_1}{dt} &= p_1 I - c_1 V_1\\ \frac{dV_2}{dt} &= p_2 I - c_2 V_2\\ \frac{dV_3}{dt} &= p_3 I - c_3 V_3.\end{aligned}$$

This model describes a virus with three particles, V_1, V_2, and V_3. Cells can be partially infected, at rates β_1, β_2, and β_3, with one particle (I_1, I_2, and I_3) or with two particles (I_{12}, I_{13}, and I_{23}). Partially infected cells can revert back to uninfected or, if they had two particles, back to infection with only one particle. Only fully infected particles, those with all three components, can produce new virus particles.

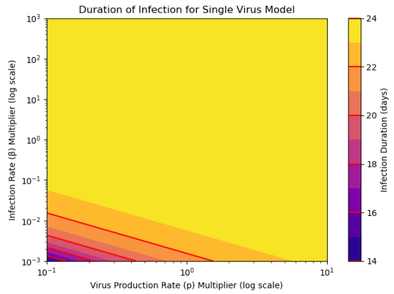
Parameter Values for Simulation

We ran simulations of the model to see how having multiple particles changed the outcome of the infection.

Model	Equation
β	3.2×10^{-5} $(\mathrm{TCID}_{50}/\mathrm{mL}\cdot\mathrm{d})^{-1}$
p	4.6×10^{-2} $\mathrm{TCID}_{50}/\mathrm{mL}/\mathrm{d}$
k	0
δ	5.2 /d
c	5.2 /d
V_0	7.5×10^{-2} $\mathrm{TCID}_{50}/\mathrm{mL}$
T_0	4×10^{8} cells

Infection rate and production rate were varied for one of the particles were systematically varied to see how these changes alter the course of the infection. We measured the duration of the infection as these parameters changed.

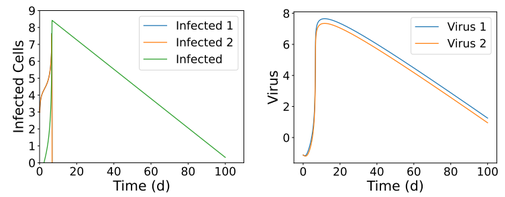
Single Virus Model



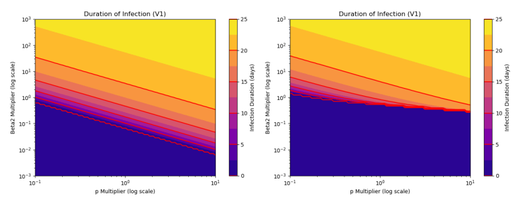
The figure shows that infections last longest when both β and p are high (yellow region). In contrast, low values of β and p result in shorter infections (blue and purple shades), as virus spreads quickly and is cleared more efficiently.

Two Particle Virus Model

The two particle model has a bit of a delay since both particles need to enter cells in order to cause an infection.



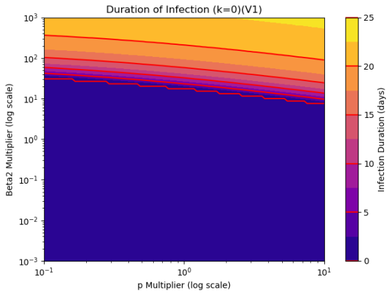
Two Particle Virus Model



Without Reversion(left): The two-virus particle graph shows that without viral reversion ($k = 0$), infection duration depends strongly on the infection rate (β): high β prolongs infection, while low β leads to quick clearance.
With Reversion(right): increasing the k value to 0.4 raises the threshold for the β multiplier, meaning a higher infection rate is needed for the virus to persist.

Three Particle Virus

This model supports the idea that three particles require a high infection rate to compensate for their structural disadvantage



The three-particle model shows that infections are generally shorter compared to single- or two-particle viruses, with most conditions leading to rapid clearance. Longer infections only occur when virus production is high, indicating that multipartite viruses need high production rates to compensate for the challenge of delivering all three genome segments to the same cell. This highlights their increased fragility and dependence on optimal conditions for persistence.

Conclusions

Increasing the number of required viral genome segments (from one to three) generally makes it harder for an infection to be initiated.

Multipartite viruses are less robust and need specific conditions to persist, making them more fragile than monopartite viruses.

Infection rate and viral production must be optimally balanced; high production alone cannot sustain infection if infection rate is too low.

Future directions

- Analyze real-world viral systems (e.g., plant multipartite viruses) and fit model parameters to biological data for validation and application.
- Understand what other underlying factors influence the prominence of multipartite viruses to persist despite its inefficiency.