Exploring Cyprinid Herpesvirus 3 disease modelling: estimating transmission parameters and compartment-model outcomes

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Motivations

Carp are an environmental concern in the rivers and waterways of South East Australia. Cyprinid Herpes Virus 3 (CyHV-3) has been developed to function as a biocontrol agent to reduce the carp population. Prior research has been conducted to study the efficacy of this biocontrol agent through epidemiological modelling, however, such research made best guess assumptions regarding the transmission of the virus (Durr et al., 2019). Recent research has provided us the opportunity to calculate more accurate transmission parameters and explore the difference in direct and indirect contact transmission (Tolo et al., 2022).

Figure 1. Carp in water. Photo: Pixabay

Parameter Estimation: Model Fit

I imagined the trials conducted in Tolo et al. (2022) as an epidemic model with only susceptible (S), exposed (E) and infectious (I) compartments (Keeling & Rohani, 2008). I fitted the data from the Tolo et al. (2022) trials to this epidemiological model using R to obtain an estimate of transmission parameters.

Figure 2. Experiment Compartment Model

Differential equations for the direct contact trials:

$$\frac{dS}{dt} = -\alpha I + -\beta SI\frac{1}{N}$$
$$\frac{dE}{dt} = \alpha I + \beta SI\frac{1}{N}$$
$$\frac{dI}{dt} = 0$$

β reflects direct transmission (estimates plotted in Figure 3) and α reflects indirect transmission. Population is constant in the Tolo et al. (2022) experiments, with $N = 16$ carp. The differential equations for the indirect contact trials were as above with β set to zero.

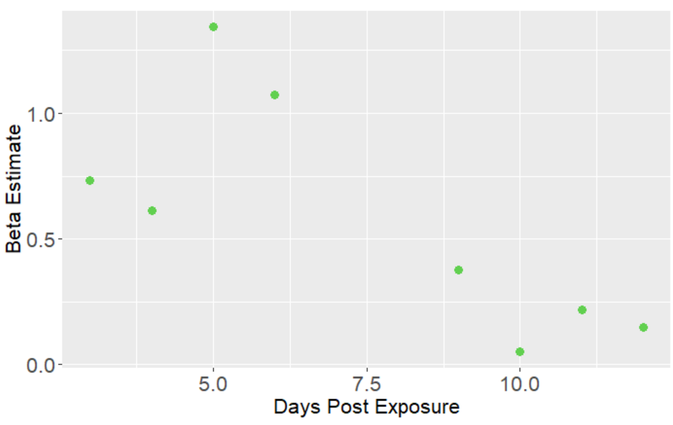

Figure 3. Beta estimates against days post exposure

Acknowledgments

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Parameter Estimation: GLM

I also used a Generalised Linear Model (GLM) to estimate direct contact transmission from the Tolo et al. (2022) experiment data, as recommended by Velthius et al. (2007). I fitted a binomial GLM with complementary log-log link function to the data, where the response variable was the proportion of susceptible carp who became infected during each of the trials. This set-up was described by Velthius (2002), who also detailed the relationship between the proportion of infected cases and the β transmission term:

$$1 - e^{-\beta \Delta t \frac{I}{N}} = p$$

I considered days post exposure, viral load and vector disease score as GLM parameters. I compared Akaike information criterion (AIC) and Bayesian information criterion (BIC) to ascertain which model to extract β estimates from. The model only using vector disease score as a predictor was ranked best.

Model Simulation

I simulated a short-term compartment model with susceptible (S), exposed (E), infected (I) and recovered (R) compartments to review the outcomes associated with the newly estimated transmission parameters. The infectious category was further split into prodromal (I_1) and clinical periods (I_2). I also split the exposed category into four subcategories (E_1, E_2, E_3, E_4) to improve model dynamics. When simulating indirect viral transmission, I added a third infectious category (I_3) to allow for indirect viral transmission that may still occur after recovery from the virus.

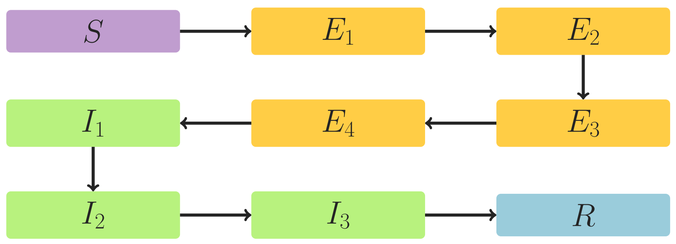

Figure 4. Simulation Compartment Model

Differential equations for simulation model:

$$\frac{dS}{dt} = -\alpha_1 I_1 - \alpha_2 I_2 - \frac{\beta_1 S I_1}{N} - \frac{\beta_2 S I_2}{N} \quad (1)$$
$$\frac{dE_1}{dt} = \alpha_1 I_1 + \alpha_2 I_2 + \frac{\beta_1 S I_1}{N} + \frac{\beta_2 S I_2}{N} - 4E_1\sigma \quad (2)$$
$$\frac{dE_i}{dt} = 4E_{i-1}\sigma - 4E_i\sigma, i = 2, 3, 4 \quad (3)$$
$$\frac{dI_1}{dt} = 4E_4\sigma - I_1\gamma_1 \quad (4)$$
$$\frac{dI_2}{dt} = I_1\gamma_1 - I_2\gamma_2 \quad (5)$$
$$\frac{dR}{dt} = I_2\gamma_2(1 - \mu) \quad (6)$$

When only considering indirect transmission, I modified equations (1), (2) and (6), and added equation (7):

$$\frac{dS}{dt} = -\alpha_1 I_1 - \alpha_2 I_2 - \alpha_3 I_3 \quad (1)$$
$$\frac{dE_1}{dt} = \alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3 - 4E_1\sigma \quad (2)$$
$$\vdots$$
$$\frac{dI_3}{dt} = I_2\gamma_2 - I_3\theta \quad (7)$$
$$\frac{dR}{dt} = I_3\theta(1 - \mu) \quad (6)$$

$1/\sigma$, $1/\gamma_1$ and $1/\gamma_2$ reflect the average length of latency, prodromal and clinical periods accordingly. I set these to values measured in Tolo et al. (2022). The disease mortality rate μ was set to 0.7, the midpoint of values tested in Durr et al. (2019). I approximated the population size N as a constant during the simulation. $1/\theta$ represents how long indirect transmission can occur after virus recovery, arbitrarily set to 5 days.

Model Simulation

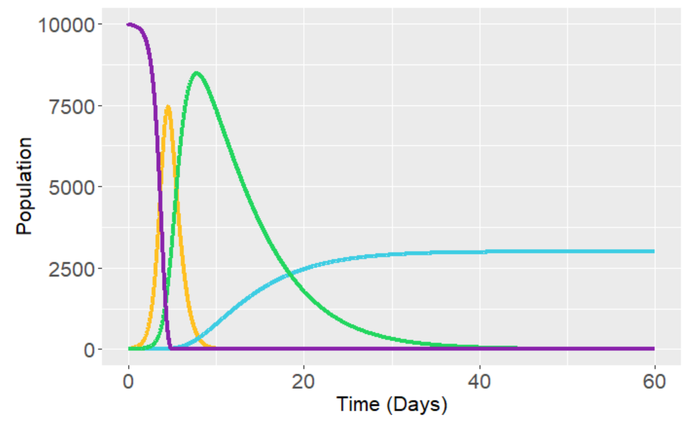

Figure 5. Virus demographics over time (direct and indirect contact)

The graphs in Figure 5 and Figure 6 plot the change in susceptible (purple), exposed (yellow), infected (green) and recovered (blue) populations over time. We see the whole susceptible population becoming infected in just under five days when direct contact is occurring (Figure 5). It takes comparatively longer (around 30 days) when there is only indirect viral transmission occurring (Figure 6).

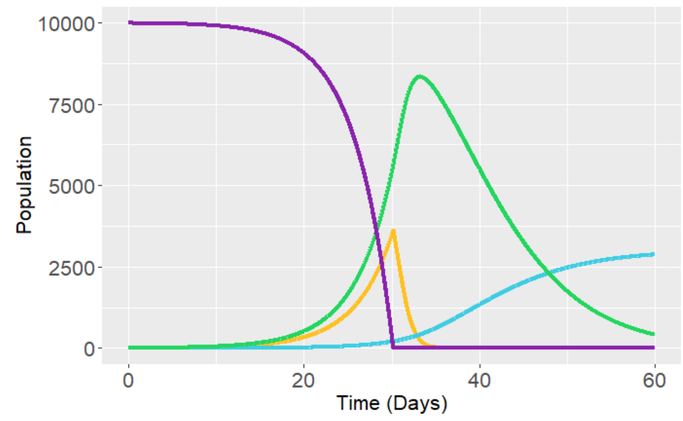

Figure 6. Virus demographics over time (indirect contact only)

Further Research

- New transmission parameter estimates should be applied to a more developed and realistic epidemiological model
- Lifetime of the virus in contaminated water should be tested to gain better insights on indirect contact virus transmission
- Scaling issues and re-infection rates should be investigated to better capture model dynamics

References

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